THE PUBLIC HEALTH IMPACT OF OBESITY

Tommy Leonardus Sebastianus Visscher

Promotores:

Prof. Dr. Ir. D. Kromhout
Hoogleraar Volksgezondheidsonderzoek
Wageningen Universiteit

Prof. Dr. Ir. J.C. Seidell
Hoogleraar Voeding van de Mens
met bijzondere aandacht voor de epidemiologische aspecten
Vrije Universiteit Amsterdam

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Katholieke Universiteit Nijmegen

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PROEFSCHRIFT

ter verkrijging van de graad van doctor
op gezag van de rector magnificus
van Wageningen Universiteit,
Prof. Dr. Ir. L. Speelman,
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op maandag 8 oktober 2001 des ochtends om elf uur in de Aula

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With references - With summary in Dutch

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One life
But we're not the same
We get to carry each other
Carry each other
One

(U2)

Stellingen

behorende bij het proefschrift
The public health impact of obesity

1 Personen met obesitas (ernstig overgewicht) maken meer ongezonde levensjaren door dan personen met een referentiegewicht.
(dit proefschrift)

2 Om veranderingen in energiebalans en lichaamssamenstelling waar te nemen, verdient de buikomvang de voorkeur boven de body mass index.
(dit proefschrift)

3 De studie geneeskunde leidt even goed op tot het bedrijven van wetenschappelijk onderzoek als de studie biomedische gezondheidswetenschappen tot het bedrijven van de geneeskunde.

4 Gebruik van *p*-waarden bij hypothesetoetsing in medisch-wetenschappelijk onderzoek dient naar de achtergrond te verdwijnen.
(naar: GS Sonke and MM Rovers. Dwalingen in de methodologie XXIX. *P*. Ned Tijdschr Geneesk 2001; 145: 74-7)

5 Gezien het belang van de methodeparagraaf van een wetenschappelijk artikel zou deze moeten worden weergegeven in een minstens zo groot lettertype als de overige paragrafen van het artikel.

6 Excessive admiration of authority is one of the most unfortunate preoccupations of intellectual youth.
(naar: S Ramón y Cajal (1852-1934). Advice for a young investigator)

7 Omdat bij Ultimate Frisbee topsport mogelijk is in afwezigheid van een scheidsrechter, verdient het bij uitstek de Olympische status.

8 Als je eenmaal achter de geraniums zit, lig je er snel onder.
(Deelnemer Zutphenonderzoek / naar: F Bijnen. Physical activity and cardiovascular disease risk among elderly men. Proefschrift Wageningen Universiteit)

Tommy LS Visscher
Wageningen, 8 oktober 2001

Abstract

The prevalence of obesity (severe overweight) has been increasing in western societies during the last decades. Epidemiological studies to the public health impact of obesity are therefore warranted. This thesis aimed at describing the long-term and recent time trends of obesity in the Netherlands, and to explore the relations between obesity, mortality, morbidity, and disability.

The prevalence of obesity, body mass index (BMI) ≥30.0 kg/m^2, increased steadily in Dutch adults between 1974 and 1997. Between 1993 and 1997, the prevalence of obesity was estimated at 9% among men and at 10% among men aged 20-59 years, based on data from the Dutch MORGEN project. Levels of waist circumference increased more over time and showed greater seasonal variation than BMI.

Obesity measured by BMI was related to increased all-cause mortality in men who never smoked, although relative risks seemed to decrease somewhat with ageing in European men from the Seven Countries Study. Levels of waist circumference identified more men over 55 years of age who never smoked with increased risk of mortality than levels of BMI in the Rotterdam Study.

Obesity was related to hospitalisation for coronary heart disease and to medication for chronic conditions in Finnish men and women from the Social Insurance Institution's Mobile Clinic study. In the Mini-Finland Health Survey, obesity was associated with the presence of osteoarthritis, low back pain, shoulder joint impairment and neck pain. In addition, obesity was associated with work disability during a 15 years follow-up and to the presence of difficulties in daily life activities. Relative risks of obesity for morbidity and disability were highest in the youngest Finnish adults studied, and exceeded the relative risk for mortality.

Prevention of weight gain (<0.5 kg/year) during a period of ten years, could prevent 26,000 new cases of knee osteoarthritis and 19,000 new cases of work disability in the Dutch working aged population.

Although obesity was related to increased mortality, obese Finns had more unhealthy life years than Finns with normal weight. During a maximal follow-up period of 15 years until age 65 years, obese men had 0.5, 0.4 and 1.7 extra years of work disability, coronary heart disease and morbidity leading to chronic medication, respectively. Obese women suffered respectively 0.5, 0.4 and 1.3 extra years from these conditions.

This thesis provides new evidence based on large epidemiological studies that weight gain prevention programs should get high priority on both the scientific and the political agenda.

Contents

Chapter 1

General introduction

The prevalence of obesity (severe overweight) has been increasing dramatically in western societies during the last decades of the 20th century and in non-western societies recently. Currently, about 20% of adult men and 25% of adult women in the United States is obese,[1] and nearly 10% of the Dutch men and women is obese.[2,3] Worldwide, over 250 million people are obese.[4] In affluent societies, obesity is most common among persons with a relatively low educational level.[5] Overweight and obesity are commonly defined using the body mass index (BMI), also known as the Quetelet Index. BMI is calculated as weight divided by height squared (kg/m^2). According to World Health Organization guidelines, normal weight is defined as BMI 18.5-24.9 kg/m^2, overweight as BMI 25.0-29.9 kg/m^2 and obesity as BMI ≥30.0 kg/m^2 for both sexes.[6] Abdominal fatness can be measured by waist circumference. Action levels for abdominal overweight and obesity differ between men and women.[7] Prevalence estimates of abdominal obesity are scarce.

The public health relevance of obesity became apparent in the 1950's when actuarial studies showed a relation between obesity and increased mortality.[8] This association is now widely accepted, and may be at least partly explained by hypertension and an unfavourable lipid profile, which are in the causal chain between obesity and mortality.[9] Relative risks of mortality for obesity decrease with ageing.[10,11] These decreasing relative risks were established using different birth cohorts. Possibly, different birth years affected both body weight development and mortality risks. A cohort effect may influence relative risks of different age groups. BMI levels change with ageing, because of changes in body composition. BMI is therefore probably not a good indicator of increased risk of mortality in the elderly.[12,13]

Much evidence exists that obesity contributes to morbidity.[14] Obesity is an important risk factor for type 2 diabetes mellitus and cardiovascular diseases, but also for musculoskeletal disorders such as osteoarthritis.[15] Especially fat mass in the abdominal region is an important risk factor for the onset of type 2 diabetes mellitus, as free fatty acids from excess abdominal fat tissues are entering the liver through the vena porta.[16] Free fatty acids in the liver have a restraining effect on insulin clearance, stimulate synthesis of triglycerides and VLDL-lipoproteins, and metabolic products of free fatty acids activate hepatic glyconeogenesis.[17] The combination of obesity, hypertension, hyperlipidaemia, and hyperinsulinaemia is well known as cluster of risk factors for cardiovascular diseases. This cluster is known as the Syndrome X, the metabolic syndrome, or the Deadly Quartet. The relation between obesity and musculoskeletal disorders is explained by mechanical pressure of excess weight on the joints.[18]

The total health care costs directly attributable to obesity are estimated at about 6% in the United States,[19] and at 1%-5% in Europe.[20] The direct health care costs of overweight and obesity in the Netherlands have been estimated at around 4% in a study dating from 1991.[21] Cost estimations might be over-estimations, because the relation between obesity and mortality has not been taken into account.[22] The study using European figures calculated only a limited number of health consequences and may therefore be regarded as conservative. It is possible that obese subjects with for instance coronary heart disease die earlier than normal weight subjects with coronary heart disease. Policy makers and others who are interested in the costs of obesity-related health consequences would need estimations of the number of unhealthy life years in obese, overweight, and normal weight subjects.

The consequences of obesity that lead to indirect health care costs are also of great interest in the public health context. Relatively few epidemiological studies report a relation between obesity and work disability.[23,24] Approximately 10% of the productivity loss due to sick-leave and work disability was attributable to obesity-related diseases, according to a study in obese Swedish women.[24] It remains unknown how many years obese subjects are longer disabled than normal weight subjects. Another form of disability related to obesity, is impaired quality of life for instance due to difficulties in everyday activities.[25] The role of musculoskeletal disorders, which are also important contributors to disability, in the relation between obesity and disability has not been systematically evaluated.

This thesis aimed at studying the impact of obesity on public health by assessing the increase of the prevalence obesity over time in the Netherlands, and elucidating the role of obesity in mortality, morbidity, and disability.

In the literature review in **chapter 2**, the state of the art on the increase in obesity prevalence and its role in mortality, morbidity and disability is described.

In **chapter 3**, the long-term and the recent increase in the prevalence of obesity in the Netherlands is reported. The long-term increase in the prevalence of obesity is assessed between 1976 and 1997 among men and women aged 37-43 years. In addition, the recent increase in the prevalence of obesity between 1993 and 1997 among men and women aged 20-59 years is reported. This recent increase is studied across categories of age, educational level, and smoking. In addition, increases in levels of BMI and waist circumference over consecutive seasons are compared.

In **chapter 4**, overweight and obesity are described in relation to increased mortality among men aged 40-59 and men aged 50-69 years from the European centres of the Seven Countries Study. Smoking has been taken into account by presenting analyses separately for never- ex, and current smokers. In addition, it was studied whether waist circumference and waist-hip ratio were better predictors of mortality than the BMI in men and women aged 55 years and older in the Rotterdam Study.

In **chapter 5**, obesity is reported in relation to morbidity and disability. Endpoints of disability were work disability and having difficulties in performing everyday activities. Data were derived from the Mini-Finland Health Survey on Finnish men and women aged 30-65 years to assess the role of osteoarthritis in the relation between obesity and disability. The relation between obesity and osteoarthritis has been assessed. In addition, it has been assessed whether obesity was related to disability among both subjects with and without osteoarthritis. Moreover, the role of low-back pain, shoulder joint impairment, and chronic neck pain in the relation between obesity and disability was studied. The potential value of weight gain prevention on the avoidable incidence of osteoarthritis and work disability in the Dutch adult population has been calculated by mathematical modelling. Relative risks of obesity were studied for work disability, hospitalisation due to coronary heart disease and medication use for chronic diseases in comparison with the relation between obesity and all-cause mortality. Relative risks were calculated across different age groups. For this purpose data were used from another Finnish population based cohort study: the Social Insurance Institution's Mobile Clinic Study on men and women aged 20-92 years. In the last part of **chapter 5** results of analyses on the number of unhealthy years in normal weight and obese subjects are described. Unhealthy life years are defined as years during which subjects had work disability, coronary heart disease, or morbidity leading to long-term medication.

In **chapter 6**, the evidence based on this thesis is summarised and discussed in the context of the literature. Evidence on the role of obesity in mortality, morbidity, and disability is combined to conclude whether or not number of unhealthy life years will increase with an increasing prevalence of obesity. Finally, suggestions for innovative weight gain prevention programs are shortly described that should be implemented to stop the obesity epidemic. Recommendations are made regarding further research on the consequences of obesity and the implementation of new weight gain prevention programs.

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Chapter 2.1

THE PUBLIC HEALTH IMPACT OF OBESITY

Abstract The increase in obesity worldwide will have an important impact on the global incidence of cardiovascular disease, type 2 diabetes mellitus, cancer, osteoarthritis, work disability, and sleep apnoea. Obesity has a more pronounced impact on morbidity than on mortality. Disability due to obesity-related cardiovascular diseases will increase particularly in industrialised countries, as patients survive cardiovascular diseases in these countries more often than in nonindustrialised countries. Disability due to obesity-related type 2 diabetes will increase particularly in industrialising countries, as insulin supply is usually insufficient in these countries. As a result, in these countries, an increase in disabling nephropathy, arteriosclerosis, neuropathy, and retinopathy is expected. Increases in the prevalence of obesity will potentially lead to an increase in the number of years that subjects suffer from obesity-related morbidity and disability. A 1% increase in the prevalence of obesity in such countries as India and China leads to 20 million additional cases of obesity. Prevention programs will stem the obesity epidemic more efficiently than weight loss programs. Only a few prevention programs, however, have been developed or implemented, and the success rates reported to date have been low. Obesity prevention programs should be high on the scientific and political agenda in both industrialised and industrialising countries.

Tommy LS Visscher and Jacob C Seidell. *Annu Rev Public Health* 2001; 22: 355-75.

Introduction

Awareness of the association of obesity with health problems is longstanding. A classical example of the emergence of an obesity-disease link was the 1921 observation by Joslin that a large proportion of diabetes patients was overweight.[1,2] Another classical observation was the notation, by Hinsworth, of a decrease in the prevalence of diabetes in countries with food shortages in World War I.[1,3] The Metropolitan Life Insurance Company's development of "desirable weight" tables with respect to greatest expected longevity is a major marker for concern about health effects of obesity.[4]

During the past few decades, the prevalence of obesity has grown to epidemic proportions, and this condition is now known to be a major contributor to the global burden of disease.[5] Currently, more than 50% of the US population is overweight and approximately 20% is extremely overweight, or obese.[6] Obesity prevalence is still increasing rapidly, not only in industrialised countries but also in nonindustrialised countries, particularly in those undergoing economic transition.[7] World-wide, around 250 million people are obese, and the World Health Organization (WHO) has estimated that in 2025, 300 million people will be obese.[8] Attitudes toward obesity differ across populations and, with economic changes, may change within populations over time. In industrialised countries, obesity is most common among those with low socio-economic status. The opposite is true in nonindustrialised countries, where obesity is most often seen among individuals with high income and may be considered a status symbol. This effect may change as nonindustrialised countries become more affluent and obesity is seen increasingly in those with low socio-economic status.[9]

The two most important risk factors for mortality in the industrialised countries are cardiovascular diseases (CVD) and cancer. CVD is a major cause of mortality, but also of disability.[10] Costs for survivors of heart disease are enormous because of blood pressure-lowering drugs, antithrombotics and diuretics. Stroke survivors often suffer from such disabilities as mood disorders and impaired neuro-musculoskeletal functions. In many areas of the United States and Europe, there is quick access to a hospital at the time a heart attack or stroke occurs. Fatalities associated with such events are therefore lower and CVD-related disability consequently higher in industrialised than in non-industrialised countries. Thus, although disability due to obesity-related CVD will increase in both industrialised and industrialising countries, the increase will be largest in industrialised countries.

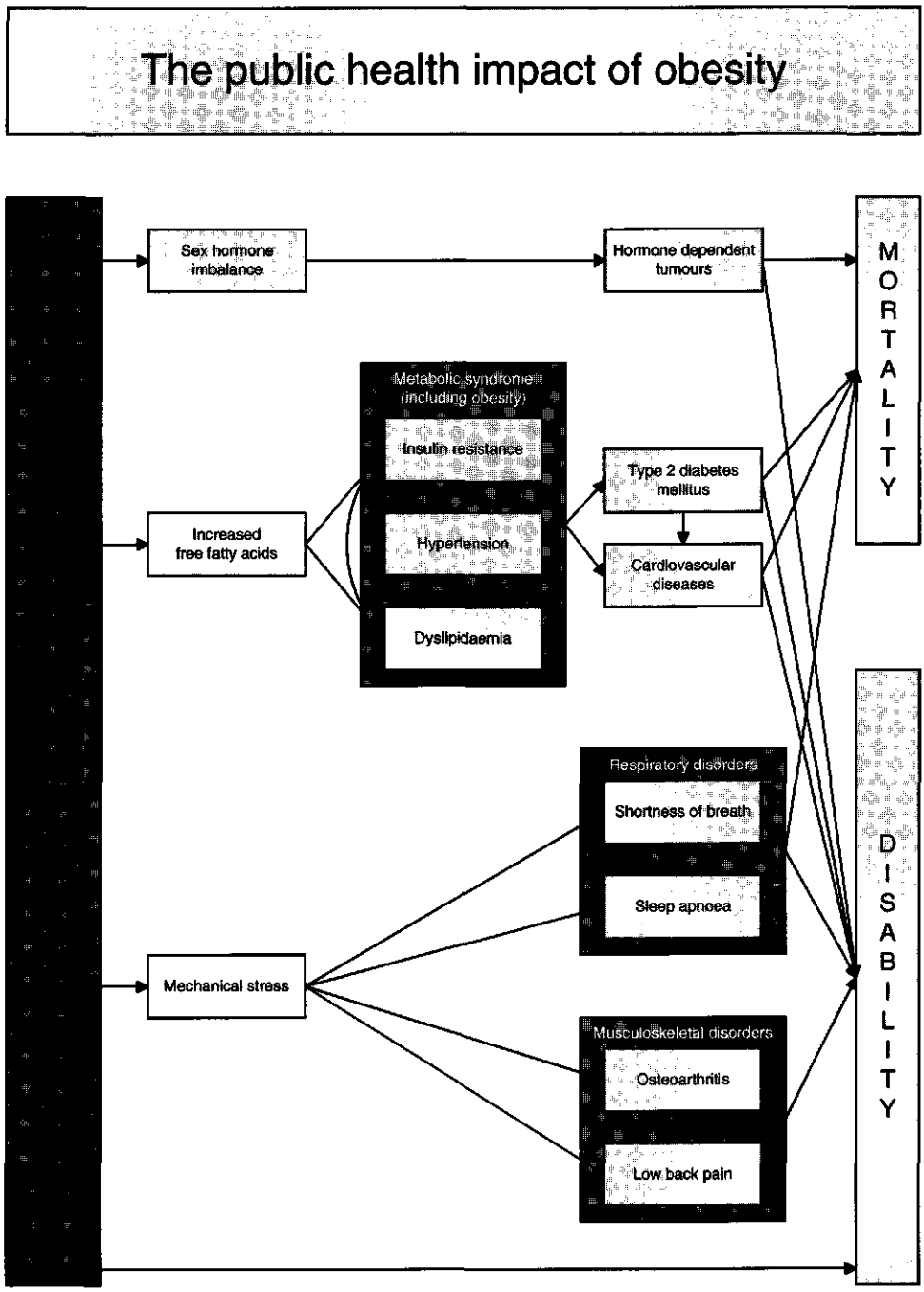

Figure 2.1.1 The public health impact of obesity

Diabetes is by far the most expensive public health consequence of obesity.[11] In industrialised countries, severe forms of type 2 diabetes are controlled relatively well by insulin therapy. The industrialising countries, however, in which a huge obesity-linked diabetes epidemic is expected, will not be able to afford sufficient insulin therapy. Under such circumstances, uncontrolled glucose levels would lead to millions of patients developing nephropathy, arteriosclerosis, neuropathy, retinopathy, and related disability. The increase in disability due to obesity-induced diabetes will, therefore, be larger in industrialising than industrialised countries.

The direct costs of obesity are now estimated to be around 7% of total health care costs in the United States[12] and around 1-5% in Europe.[13] Narbro calculated that approximately 10% of the total costs of loss of productivity due to sick leave and work disability might be attributable to obesity-related diseases.[14] Because of the increasing prevalence and costly consequences, obesity is now being recognised not only as a risk factor in the clinical setting but also as an important threat to public health. The public health impact of obesity should be measured by its combined effect on disability and mortality (figure 2.1.1). Obesity can act through its relation with other morbidities and appears to have a direct effect on disability (figure 2.1.1).[15,16] The current focus is also on outcomes such as quality of life and physical, social, and mental functioning. These obesity-related outcomes increase in importance as population longevity increases.[17]

This review outlines obesity as a public health problem. We first discuss definitions and trends of obesity and describe the role of obesity as a risk factor for all-cause mortality and the development of cancer. We then describe the role of obesity as a risk factor for CVD and type 2 diabetes mellitus. In addition, we address current evidence on obesity as a risk factor for such musculoskeletal disorders as osteoarthritis, work disability, and respiratory disorders. Finally, we discuss the use of body weight measurements in the elderly, who represent an increasingly important population with regard to the impact of obesity on the public health.

Definitions

Obesity

The WHO definitions of overweight and obesity are based not only on the risks of increased mortality but also on increased morbidity risks (table 2.1.1).[5] A body mass index (BMI) below 18.5 kg/m^2 is defined as underweight; a BMI between 18.5 and 24.9 is normal weight. Overweight individuals, those with a BMI between 25.0 and

29.9 kg/m^2, are at increased risk of morbidity and should avoid further weight gain. Weight loss in overweight people is recommended when other risk factors for disease are present. Severely overweight or obese people, those with BMIs of 30.0 kg/m^2 or higher, are at highly increased risk of disease irrespective of the presence of other risk factors and weight loss is recommended for all. Cross-culturally, the implication of a certain BMI level with respect to body fatness and fat distribution might vary across populations. Asian populations, for instance, have a higher absolute risk for the onset of type 2 diabetes mellitus than do Caucasian populations with the same level of BMI.[18] The International Diabetes Institute and the International Obesity Task Force of the WHO argue that lower BMI cut points should be used for Asian populations than for Caucasian populations.[19]

Body fat distribution

The ratio of waist circumference divided by the hip circumference (WHR) is a measure of fat distribution on the body. This ratio may be misinterpreted as specific for abdominal fat (the numerator of the ratio), although it is also influenced by the amount of fat in the gluteal region (denominator). Abdominal fat can be estimated

Table 2.1.1 Definitions of waist circumference and body mass index categories[a]

	Waist circumference	
	Men	Women
Above action level 1	≥94 cm (~37 inch)	≥80 cm (~32inch)
Above action level 2	≥102 cm (~40 inch)	≥88 cm (~35 inch)

	Body mass index (kg/m^2)
	Men and women
Underweight	<18.5
Normal weight	18.5-24.9
Moderate overweight	25.0-29.9
Overweight	≥25.0[a]
In this thesis:	25.0-29.9[b]
Pre-obese	25.0-29.9
Obesity	≥30.0
Obese class I	30.0-34.9
Obese class II	35.0-39.9
Obese class III	≥40.0

a Body mass index categories are defined according to the WHO-guidelines.[5] Waist circumference categories are suggested by Lean et al.[22]

b Alternative definition for overweight, often used in the literature.

with greater precision by the waist circumference alone.[20] The waist circumference is measured midway between the lower rib margin and the iliac crest, with the person in a standing position. Although the waist circumference is associated with stature, the correlation is sufficiently low to ignore adjustment for body height in persons aged 20-59 years.[21]

Lean *et al.* suggested that action levels based on waist circumference replace BMI and WHR as measures of obesity (table 2.1.1).[22] These action levels seemed appropriate for identifying those with cardiovascular risk factors, type 2 diabetes mellitus, or shortness of breath when walking upstairs.[23,24] This issue, however, is still under debate. For example, Molarius and Seidell have noted that criteria underlying these waist circumference action levels were based on arbitrary levels of the WHR and that the evaluations with respect to risk were based on cross-sectional data.[25]

Population attributable fraction

In measuring the impact of obesity on mortality, morbidity, or disability it is useful to calculate the fraction of an outcome in the population that is attributable to obesity (the population attributable fraction), using the proportion of obesity and the relative risk:

$$AF_p = \frac{p(RR-1)}{p(RR-1)+1} \qquad \text{(formula 2.1.1)}$$

with AF_p being the population attributable fraction, p the proportion of subjects in the BMI category, and RR the corresponding relative risk. To evaluate the different impact of obesity on mortality and morbidity, one can easily compare relative risks, as the proportion of obesity will be equal for each attributable fraction calculation. In this review, the relative risks of categories of BMI for all-cause mortality, coronary heart disease, stroke, and type 2 diabetes mellitus are illustrated using US data from the Health Professionals Follow-Up Study[26-29] and the Nurses' Health Study.[30-33] Both studies describe age-adjusted relative risks for these outcomes.

Prevalence and trends

Currently, more than 30% of the US population is overweight (BMI 25.0-29.9 kg/m^2) and around 20% is obese (BMI ≥30.0 kg/m^2).[6] The US National Health and Nutrition Examination Surveys showed a marked increase in obesity between the first survey cycle in 1960-1961 and the third cycle in 1988-1994 in the United States.[6] More recent data on obesity prevalence and trends in the United States are from

the Centres for Disease Control and Prevention telephone survey data. Among respondents aged 18 years and older, obesity prevalence increased by around 50 percent between 1991 and 1998, with higher prevalence rates occurring in eastern states (figure 2.1.2).[34] The absolute prevalence rates reported by Mokdad *et al.* are probably underestimations because they are based on self-reported height and weight. Obese people tend to underreport their weight more than do people with acceptable weight.[35]

Data from the Third National Health and Nutrition Examination Survey (NHANES III) are based on direct measurements of height and weight. These data indicate that for persons aged 20-74 years, the prevalence of overweight (BMI 25.0-29.9 kg/m^2) was 39.4% in men and 24.7% in women. In the same survey, 19.9% of the men and 24.9% of the women were obese (BMI ≥30.0 kg/m^2). In women, the prevalence of those who were overweight or obese was even higher in non-white populations. Among the non-Hispanic black and Mexican-American respondents in NHANES III, 20% of the men and approximately 35% of the women were obese.[6]

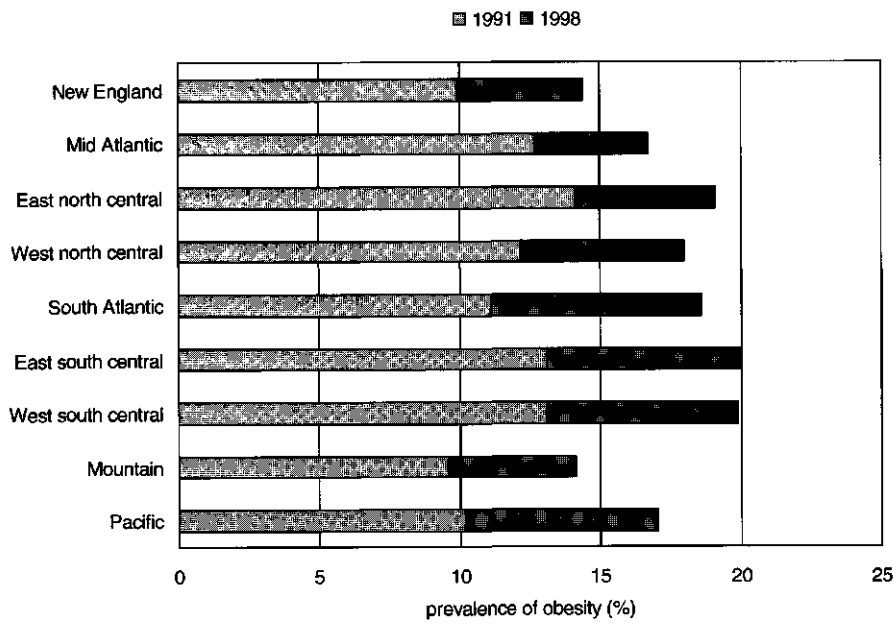

Figure 2.1.2 The increase in obesity in the United States
Data from Mokdad *et al.*, based on self-reported body weight and height.[34]

Cross-national differences

It is less common to be overweight (BMI 25.0-29.9 kg/m^2) in most European countries than it is in the United States, but the prevalence of overweight adults in Germany, Finland, and Britain is substantially more than 50%. Obesity (BMI ≥30.0 kg/m^2) also is generally less common in Europe than in the United States, around 10-20% of adult men and 15-25% of women.[36] In western European study centres participating in the WHO-MONICA study, the prevalence of obesity ranged from 10% to 24% among men and from 9% to 25% among women aged 35-64 years in 1989-1996. Obesity was more common in eastern Europe, especially among women. In Polish and Russian study centres, the prevalence of obesity was around 40%.[37] The increase in obesity between the initial MONICA survey in 1979-1989 and the final survey in 1989-1996 was less marked for the European than the US study centre in Stanford, California.[37] The increase in the US study centre was nearly as large as the 50% increase reported for the overall US population between 1991 and 1998.[34]

Martorell *et al.* reported obesity rates for women aged 15-49 years from countries in various levels of development. In the poorest countries, there was a strong relation between the gross national product and the prevalence of obesity. Prevalence was estimated at 0.1% in South Asia, 2.5% in sub-Saharan Africa, 9.6% in Latin America and the Caribbean, 15.4% in Kazakhstan, Turkey, and Uzbekistan, 17.2% in the Middle East and north Africa, and 20.7% in the United States.[38]

Within-country differences

Data from NHANES and from the Centers for Disease Control and Prevention Behavioral Risk Factor Surveillance System showed equivalent increases in obesity across different race/ethnic groups and educational categories in the United States.[6,34] Molarius *et al.* described most of the increase in obesity in the European MONICA study populations as being among those with the lowest socio-economic status. Thus, the inequality in obesity prevalence widened between categories of socio-economic status.[37] In nonindustrialised countries, obesity often is a marker of relatively high socio-economic status. Seidell and Rissanen described the increase in obesity as most notable in those countries undergoing rapid economic transition and more notable in urban areas than in rural areas.[9] Martorell *et al.* described obesity as mostly concentrated among urban and higher-educated women in very poor countries, such as in sub-Saharan Africa. In more developed countries, such as Latin American countries and Kazakhstan, Turkey, and Uzbekistan, obesity rates were more equal across categories of urbanisation and education.[38] Popkin *et al.* reported a difference in the association between socio-economic status and obesity

in rural and urban areas in China in 1993. In urban areas, obesity was most common among those with low socio-economic status, whereas in rural areas, obesity was most common in those with relatively high socio-economic status.[39]

Obesity and mortality

Although obesity has been considered a risk factor for mortality for several decades, not all studies confirmed the relation between obesity and mortality. Sjöström's review indicated that studies showing no positive association between BMI and mortality had short follow-up or small sample size, or did not account for smoking habits.[40] Manson *et al.* argued that adjustment for hypertension and unfavourable lipid levels could lead to underestimation of the effect of obesity on mortality. These authors pointed out that high BMI is related to the increased blood pressures and unfavourable lipid levels that predispose to increased mortality. When analysing the impact of obesity on increased mortality, one should therefore not adjust for these intermediates of the BMI-mortality relation in the statistical models.[41] Manson *et al.* also argued that the first five years of mortality should be eliminated from such analyses to account for possible weight loss, as a consequence of subclinical disease among individuals who died early in the follow-up period.[41] Furthermore, as smokers are known to be leaner and to have higher risks of obesity, and the risk of death for obesity may differ between smoking categories, the effect of obesity on mortality must be calculated across different smoking categories.[42]

Recent studies reaffirmed high BMI levels as risk factors for all-cause mortality.[40,41] Mortality risk increased for BMI above 27 kg/m^2 in both the Nurses' Health Study[30] and the US Health Professionals Follow-Up Study (tables 2.1.2 and 2.1.3).[26] In these studies, the relative risks associated with high BMI are lower for all-cause mortality than for disease incidence, i.e., for type 2 diabetes mellitus, myocardial infarction, and ischaemic stroke (figures 2.1.3 and 2.1.4).[26-33]

Stevens *et al.* showed that relative risks of mortality associated with high BMI were lower at older ages. This finding was based on analyses of BMI-mortality relation in approximately 62,000 men and 262,000 women who had never smoked and who were followed from 1960 through 1972.[43] Calle *et al.* concluded that the relation between high BMI and increased mortality was more pronounced in white than in black people and was stronger among those who never smoked than among smokers. Their analysis was based on follow-up of more than 1 million US men and women aged 30 years and over (mean age: 57 years) from 1982 through 1996.[44]

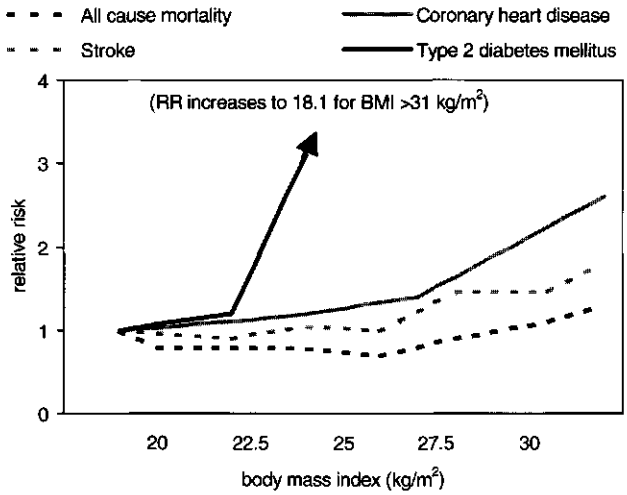

Figure 2.1.3 Age-adjusted relative risks by categories of body mass index for different endpoints among US women from the Nurses' Health Study[26-29]

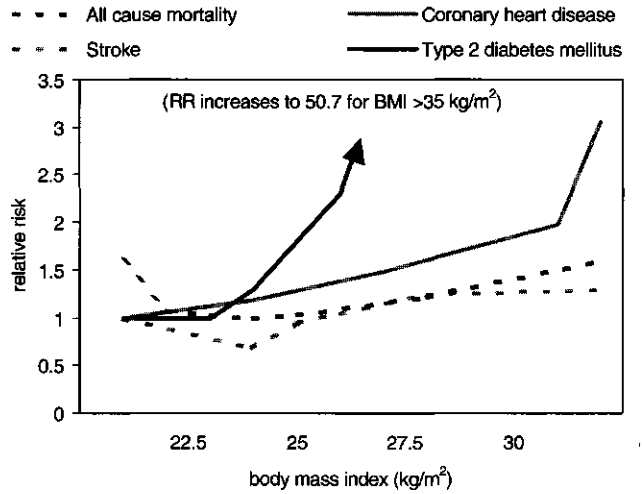

Figure 2.1.4 Age-adjusted relative risks by categories of body mass index for different endpoints among US men from the Health Professionals Study[30-33]

Table 2.1.2 Characteristics of the Nurses' Health Study on US women as presented in figure 2.1.3

Outcome	Baseline	Follow-up	Subjects at baseline	Cases
All-cause mortality[30]	1976	1976-1984	115,195	4,726
Coronary heart disease[31]	1976	1976-1992	155,886	306
Nonfatal myocardial infarction				
Stroke[32]	1976	1976-1992	116,759	403
Ischaemic stroke				
Type 2 diabetes mellitus[33]	1986	1986-1994	43,581	705
Self-reported				

Table 2.1.3 Characteristics of the Health Professionals Follow-up Study on US men[a]

Outcome	Baseline	Follow-up	Subjects at baseline	Cases
All-cause mortality[26]	1986	1986-1996	39,756	1,972
Coronary heart disease[27 b]	1986	1987-1996[c]	29,122	420 (53 fatal)
Stroke[28]	1986	1987-1992[c]	28,643	118
Ischaemic/haemorrhagic				
Type 2 diabetes mellitus[29]	1986	1986-1991	27,983	302
Self-reported				

a see figure 2.1.4
b Fatal myocardial infarction, nonfatal myocardial infarction, coronary artery bypass graft, percutaneous transluminal coronary angioplasty
c Participants contributed follow-up time from 1987.

Obesity and cancer

The relation between obesity and several types of cancer has been relatively neglected in most recent monographs on obesity. The comprehensive review of diet and cancer by the American Institute for Cancer Research and World Cancer Research Fund (WCRF), however, includes extensive coverage of this topic.[45] The incidence of some cancers is related to body size or to BMI. According to the WCRF review, evidence relating BMI and cancer is strongest for endometrial cancer (table 2.1.4). A BMI exceeding 30.0 kg/m^2 is associated with a one and a half to three times higher risk of developing endometrial cancer than a BMI between 20 and 25 kg/m^2.[45] The WCRF review classified the relation between high BMI and breast and kidney cancer as "probable," with an approximately 1.8-fold higher risk for those with a BMI exceeding 27 kg/m^2 compared with those having a BMI below 17 kg/m^2.

Table 2.1.4 Relations between obesity and several forms of cancer[a]

Tumoursite	Evidence
Endometrium	Convincing
Breast (postmenopausal)	Probable
Kidney	
Gallbladder (particularly in women)	Possible
Colon (less consistent for women)	
Thyroid	Insufficient
Pancreas	None
Prostate	

a Data were adapted from the World Cancer Research Fund and the American Institute for Cancer Research.[45]

There is evidence for a relation between high BMI and colon cancer, less consistent for women than for men.[45] Gallbladder cancer is also possibly associated with high BMI, particularly among women.[45] The importance of obesity-induced gallstones, which are themselves a risk factor for gallbladder cancer, in the association of obesity and gallbladder cancer is uncertain.[45-47] Based on a small number of case-control studies, little evidence exists for a relation between obesity and cancer of the thyroid.[45] There is also a relation between cancer and low BMI, although it is probably confounded by smoking and cancer-induced weight loss. Smokers tend to be leaner than non-smokers and are at increased risk of cancer.[45]

Breast cancer risks are often considered separately pre- and postmenopausally. In the Nurses' Health Study follow-up from 1986-1994, a relation was found between large waist circumference and postmenopausal breast cancer incidence except for current and past postmenopausal hormone users.[48] Obesity apparently has a small protective effect for premenopausal breast cancer. Some studies reported a positive relation between obesity and premenopausal breast cancer. Such findings, however, might be explained by weight gain shortly after diagnosis, especially among women receiving chemotherapy.[49] Tall women have a greater risk of breast cancer than short women, because of the larger number of potential cancer target cells.[50]

The American Cancer Society's follow-up study assessed the association of obesity with cancer mortality among 750,000 subjects aged over 30 years followed from 1960 to 1972.[51] Obese men had a 1.33 obese women a 1.55 times higher mortality rate from cancer than their normal-weight peers. In this study, overweight was defined with the relative weight index, calculated as the individual's body weight divided by

the average weight of all respondents in that sex-age group and multiplied by 100. Obesity was defined as a relative weight index over 140, normal weight was defined an index of 90-109 or within 10% of group average. Among men, the relative risk of obesity was highest for mortality due to cancer in the colon and the prostate.

Among women, the relative risk was highest for cancer of the endometrium (5 times higher risk in obese than in normal-weight women), followed by cancer of the gallbladder (3.5 times higher risk), cervix (two times higher risk), ovary (1.6 times higher risk), and breast (1.5 times higher risk).[51] Based on five-year follow-up figures of 42,000 women from Iowa aged 55-69 years, cancer mortality was twofold among those with a waist-hip ratio in the fifth quintile compared to those in the lowest quintile. Neoplasms accounted for 50% of deaths in that study.[52] In a 33-year follow-up of 3,000 men aged 39-59 years in California, cancer mortality was highest in those with a high waist-to-calf obesity index. Cancer mortality accounted for 31% of all deaths in this cohort.[53]

A possible mechanism for the relation between high body weight and cancer, discussed in the WCRF, relates to the metabolic abnormalities (metabolic syndrome) that result from high BMI levels.[45] This physiological milieu promotes cell growth in general and especially that of tumour cells-because of their differential capacity to use glucose and because of their up-regulation of receptors for the insulin-like growth factor. Increased levels of bioavailable endogenous estrogen in abdominally obese women may lead to an increased risk of breast cancer.[54,55] Stoll argues, in a review of this topic, that weight reduction combined with a program of physical exercise might reduce both estrogen and insulin concentrations and thereby inhibit the development of postmenopausal breast cancer.[56]

Obesity might also influence cancer detection. Obese women are more reluctant than normal-weight women to participate in cervical and breast cancer screening programs. Late identification of tumours decreases the chance of therapeutic success.[57] Also, the presence of abundance of fat complicates mammographic screening.[58] Furthermore, underlying lifestyle factors related to obesity may play a direct role. Physical activity may promote the access of toxins through the gastroenterologic system, which has a relatively protective effect. Exposure time of toxins in the gastrointestinal tract is shorter in physically active individuals. Dietary practices among obese individuals might predispose to cancer risk. The WCRF panel estimated that 30-40% of all cancers are attributable to inappropriate diet, lack of physical activity, and high body weight.[45]

Obesity and cardiovascular diseases

Kannel has stated that no risk factor has as strong an impact on the cardiovascular risk profile as obesity.[59] Obesity was identified as a risk factor for CVD not long after it was identified as a mortality risk factor. Abdominal adiposity in particular is associated with CVD risk.[60-62] Obesity is a risk factor for increased blood pressure and unfavourable lipid profile (decreased high-density lipoprotein (HDL) cholesterol level and increased low-density lipoprotein cholesterol and triglyceride levels) and, as discussed in the next section, for CVD resulting from diabetes.[63] Weight loss has been shown to improve blood pressure and lipid levels, at least for the short term.[64,65] Increased blood pressure or unfavourable lipid levels are related to CVD.[66,67] Obesity, however, is also directly related to CVD independent from blood pressure and lipid levels.[68] That is, when adjustments are made for blood pressure and cholesterol levels, the relation between obesity and CVD is attenuated, but relative risks remain high and significant.[60,69] Manson *et al.* and Shaper *et al.* argue that it may be inappropriate to adjust for blood pressure and cholesterol levels when the question is to what extent obesity adversely affects cardiovascular risk profiles, as these variables are in the causal chain between obesity and CVD.[41,69] The relation of low body weight and weight loss with CVD and the confounding effects of smoking are other explanations for observations of lower relative risks or absent relations between high body weight and CVD.[41,70]

Figure 2.1.3 shows that the age-adjusted relative risk for incident coronary heart disease (CHD) among men and women was higher than the relative risk of high BMI for mortality. US women from the Nurses' Health Study with BMI above 30.0 kg/m^2 had a threefold risk of developing nonfatal myocardial infarction compared to women with a BMI below 21 kg/m^2 (figure 2.1.3).[31] Among men in the Health Professionals Study, those with a BMI between 29 and 33 kg/m^2 had a twofold risk and those with BMI higher than 33 kg/m^2 had a threefold risk of developing CHD compared to men with a BMI below 23 kg/m^2 (figure 2.1.4).[27] Among these men and women, high BMI was also related to the onset of stroke.[28,32] The Nurses' Health Study reported that high BMI levels were especially related to the onset of ischaemic stroke. Haemorrhagic strokes, which occurred less often than ischaemic strokes, seemed to be less common in those with high BMIs compared with those whose BMIs were low.[32] Refer to tables 2.1.2 and 2.1.3 for characteristics of the Nurses' Health Study and Health Professionals Follow-Up Study.

Framingham data, based on 26 years of follow-up of approximately 5,200 men and women aged 28-62 years, showed that high relative weights were predictive of

myocardial infarction, sudden death, congestive heart failure, and atherothrombic strokes. Myocardial infarction in women over 50 years old and stroke in men over 50 years old were not excessive in the upper categories of relative weight.[68] It was estimated from the Framingham Study that if everyone could be kept at optimal weight, there would be 25% less CHD and 35% fewer strokes or episodes of heart failure. A 20% weight reduction in the obese should confer a 40% reduced risk of a coronary event.[68] The British Regional Heart Study of 7,700 men aged 40-59 years, followed for a mean period of 14.8 years, showed that high BMI levels were related to incident coronary heart events and, although to a lesser extent, to stroke.[69]

Obesity and type 2 diabetes mellitus

Besides being the major risk factor for CVD, obesity, in particular abdominal obesity, is the most important risk factor in the onset of type 2 diabetes. In the Nurses' Health Study[33] and the Health Professionals Follow-Up Study,[29] it was found that compared with the lowest BMI category, risks for developing type 2 diabetes mellitus were increased more than tenfold among women with BMIs higher than 29 kg/m^2 and among men with BMIs larger than 31 kg/m^2 (figures 2.1.3 and 2.1.4). In addition, being moderately overweight was closely related to the onset of type 2 diabetes mellitus. Weight loss of more than 4% during the first five years of follow-up showed a 1.5 times reduced risk of developing type 2 diabetes among British men aged 40-59 years, followed for a mean period of 16.8 years, compared with men with stable weight. Weight loss reduced the risk of type 2 diabetes by a factor of around 2.5 compared with those who gained weight more than 10%.[71]

The WHO has calculated that about 64% of type 2 diabetes in US men and 74% in US women could be avoided if there was no BMI above 25 kg/m^2.[5,29,72] The WHO also predicted that the number of diabetics would double from 143 million in 1997 to about 300 million in 2025.[7,8] In Asian countries, the prevalence of type 2 diabetes mellitus will increase more rapidly over time than the increase in obesity.[7] King *et al.* calculated that in 2025, India and China, together with the United States, would be the countries with the largest numbers of diabetics.[73]

Concentrations of free fatty acids are excessive in individuals with abdominal obesity and amplify insulin resistance.[74] In his Banting Lecture in 1988, Reaven suggested a direct relation between plasma insulin concentration and blood pressure.[75] Thus, he raised the possibility that insulin- stimulated glucose uptake and hyperinsulinaemia are involved in the aetiology and clinical course of three

major related diseases: type 2 diabetes, hypertension, and coronary artery disease.[75] Björntorp subsequently described abdominal obesity as an integral part of this disease cluster.[74] Ferrannini *et al.* recognised hyperinsulinaemia as the key feature in this clustering of diseases, from their study of 2,930 Mexican-Americans and non-Hispanic whites from San Antonio, Texas.[76] From an analysis of 515 European men aged 38 years old, Cigolini *et al.* argued that obesity and abdominal fat distribution were even more correlated than was hyperinsulinaemia to unfavourable risk profiles for CVD (increased total cholesterol, decreased HDL cholesterol, decreased HDL cholesterol, and high blood pressure levels).[77]

The clustering within individuals of major cardiovascular risk factors, such as abnormal glucose metabolism, an unfavourable lipid profile, hypertension, and abdominal obesity were later described as Syndrome X, the Deadly Quartet, and the metabolic syndrome.[74,76]

Obesity and musculoskeletal disorders

Obesity is one of the most important preventable risk factors of osteoarthritis in knee and hip joints, and osteoarthritis, in turn, is an important risk factor for disability.[78] Osteoarthritis is more common among women than among men. The relation between being overweight and having osteoarthritis is explained, at least in part, by the high joint pressure in overweight individuals. There might also be a metabolic explanation, because obesity also seems to be related to incident osteoarthritis in the hands.[78] A case-control study by Oliveria *et al.* found odds ratios of incident osteoarthritis between 1990 and 1993 of 3.0 and 10.5, respectively, for women aged 20-80 years in the highest tertiles of BMI compared to the lowest.

Associations between obesity and herniated lumbar intervertebral disc, low back pain, and chronic neck pain have been suggested. The strength of these associations, however, is generally weaker than those for osteoarthritis. In addition, the associations have been derived from cross-sectional studies.[79-81] Longitudinal studies are needed to confirm these associations.

Obesity and work disability

In most European countries, in cases of work disability and sick leave, pensions are, at least partly, reimbursed. Therefore, data on the relation between obesity and work disability come mainly from European studies. In Finland, disability pensions were granted 2.0 and 1.5 times more often to obese men and women, respectively,

compared with those with low BMIs.[10] This study was based on a National Survey sample of 31,000 Finns who were followed from 1966-1972 until 1982 (figure 2.1.5). Of 1,300 obese Swedish women aged 30-59 years, 12% were recorded to have disability pensions compared with 5% of the general population, and the obese women reported 1.5-1.9 times more sick leave during a one-year period compared with the normal Swedish population.[14]

Obesity is also related to mobility limitations, which affect quality of life particularly with ageing. Limitations in daily activities requiring mobility occurred twice as often among US women with a mean age of 65 years who were in the highest BMI tertile compared to those in the lowest tertile, i.e. approximately 5% during the 4-year follow-up.[82] Self-reported onset of difficulties in walking and climbing a flight of stairs occurred 2.3 times more often in the obese among a population with mainly African Americans and Mexican Americans aged 51-61 years, with an overall incidence rate of 6% during a two year follow-up.[83] The role of musculoskeletal disorders in the causal chain between being overweight and having a disability should be further assessed.

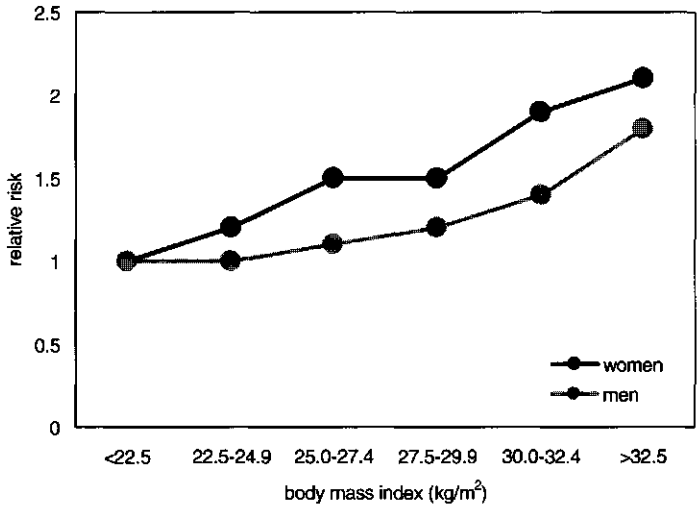

Figure 2.1.5 Relative risk of work disability per category of body mass index in a Finnish population
Relative risks were adjusted for age, geographical region, smoking habits, and occupation.
Data were derived from Rissanen *et al.*[10]

Obesity and respiratory disorders

During the past decade, the role of excess fat became known as an obesity-related public health problem because of its link with shortness of breath and sleep apnoea. Based on a sample of Dutch adults aged 20-59 years, the odds ratios for shortness of breath when walking upstairs in those with a BMI of 30 kg/m^2 or higher compared with those with BMIs below 25 kg/m^2 was 3.5 in men and 3.3 in women.[24] Furthermore, obese patients are more likely to suffer from obstructive sleep apnoea syndrome and concurrent psychosocial morbidity. Based on their random sample of 602 employed US men and women aged 30-60 years, Young *et al.* estimated that sleep-disordered breathing was around four times more common when BMI was 5 kg/m^2 higher.[84] The role of bearing weight or body fat on different parts of the body on the lung function is indicated by comparing odds ratios for sleep-disordered breathing for smaller versus larger girths at different parts of the body. Comparing odds of girths of neck, waist, and hip, Young *et al.* found that odds ratio for sleep-disordered breathing was lowest for a large hip girth and highest for a large neck girth.[84] Hypoventilation during sleep leads to nocturnal hypoxia during sleep and extreme sleepiness during the day. It could well be that sleep apnoea promotes weight gain and prevents weight loss because of visceral fat-related hormone disturbances.[85] Obesity-induced sleep apnoea is an important risk factor for psychosocial morbidity and seems associated with some of the components of the metabolic syndrome.[86] Young *et al.* estimated that the sleep apnoea syndrome was present in 2% of women and 4% of men.[84]

Obesity among the elderly

The elderly represent a particularly important age category with respect to the public health. This age group is increasing in magnitude in industrialised societies and in nonindustrialised societies because of the increased life expectancy associated with improved standards of living. BMI levels increase with ageing until age 60-70 years, after which BMI decreases.[87]

Changes in body composition with ageing imply a change in the relation between BMI and fatness and the relation between BMI and mortality may change concurrently.[88] It is unclear whether the BMI is the most appropriate measurement of body weight for the elderly, because muscle mass usually decreases with aging.[89] Molarius *et al.* found promising results for the use of the waist circumference alone in a cross-sectional study on a population aged 55 years and older from Rotterdam, the Netherlands. High levels of waist circumference indicated a worsened

cardiovascular risk profile in this population.[90] Which measurements of obesity are most appropriate and informative in the elderly population needs clarification.

Relative risks of mortality for obesity are reported to be lower in elderly populations than in younger populations.[43,44] Absolute incidence rates of morbidity and disability, however, are higher among the elderly than in younger populations. Small relative increases in morbidity and disability due to obesity will thus have a higher impact in elderly than in younger populations. In addition, living without disability is highly important for functioning and quality of life in ageing.[17]

Discussion

Obesity is related to all-cause mortality and cancer and, even more strongly, to the onset of type 2 diabetes, CVD musculoskeletal disorders, work disability, and sleep apnoea. Many of the preceding comparisons of relative risks for mortality, coronary heart disease, stroke, and diabetes were adjusted for age only, and combined never-smokers and smokers. Such comparisons, although not appropriate for more specific purposes, suffice to provide a general impression of the impact of obesity across a spectrum of conditions.

As noted previously, the direct and indirect costs of obesity are estimated at 7% of the total health care costs in the United States[12] and at around 1%-5% in Europe.[13] These estimates are based on prevalence rates and relative risks. Because of its closer relation to morbidity and disability than mortality, obesity will increase the number of unhealthy life years enormously. Oster *et al.* calculated that weight loss of about 10% of initial body weight would reduce the number of life years with hypertension by 1.2-2.9 years, and type 2 diabetes mellitus by 0.5-1.7 years. Life expectancy would be increased by two to seven months.[91] Again, these estimates are based on calculations using relative risks for the specific outcomes. Empirical data on the number of years obese persons suffer more than normal weight persons from morbidity and disability have yet to be published. Nevertheless, it is clear that the public health impact of obesity is enormous and will increase rapidly with each percentage point increase in the prevalence of obesity. Public health programs should include in their targets goals for reducing the obesity epidemic. Countries such as China and India are of particular importance in the obesity epidemic. In these countries, every percentage point increase in obesity prevalence involves 20 million more obese people.

The increasing obesity epidemic points to the urgent need for strategies to develop multifaceted global and national plans for adequate prevention and management of obesity.[9] A reduction in obesity is among the National Health Promotion and Disease Prevention Objectives in the USA. In Europe, England has set goals for reducing obesity. Such targets, however, are lacking in most European countries.

Based on a study of persons aged 20-72 years, who were followed for six years, Russell *et al.* concluded that prevention of weight gain would be more successful than treatment of people who are already obese.[92] The International Task Force on Obesity, a work group of the WHO, points to several possibilities for implementing prevention programs.[93] Unfortunately, however, the few weight gain prevention programs reported to date have not been very successful.[94-97] Swinburn *et al.* describe the societal elements that influence food intake and physical activity as the "obesogenic" environment.[98] Intervention programs should take these factors into account.[96] New programs should change the prevalence of obesity during the long run by minimal changes in the energy balance.

Conclusion

The impact of obesity on morbidity and disability is higher than its impact on mortality. Therefore, each increase in obesity prevalence will increase obesity-related disability, not only in industrialised countries but also, on a very large scale, in industrialising countries. Weight gain prevention programs should be high on the scientific and political agendas.

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Chapter 3.1

LONG-TERM AND RECENT TIME TRENDS IN THE PREVALENCE OF OBESITY AMONG DUTCH MEN AND WOMEN

Abstract In this chapter the long-term and recent time trends in the prevalence of obesity by age and educational level are described. For this purpose data were used from repeated cross-sectional population based monitoring studies: the Consultation Bureau Heart Project was carried out between 1976-1980, the Monitoring Project on Cardiovascular Diseases between 1987-1991, and the Monitoring project on risk factors for chronic diseases (MORGEN) project between 1993-1997. Between 1976 and 1997, 29,141 men and women aged 37 to 43 years have been measured. Between 1993 and 1997, data were also available from 21,926 men and women aged 20 to 59 years. Body mass index was calculated as weight divided by height squared (kg/m^2). Between 1976 and 1997 the prevalence of obesity increased from 4.9 to 8.5% among men and from 6.2 to 9.3% among women aged 37-43 years. Between 1993 and 1997, the prevalence of obesity among men aged 20-59 years was 8.5% and increased with 0.54 percentage points per year ($p<0.01$). The prevalence of obesity among women was 9.6% and increased with 0.35 percentage points per year ($p=0.07$). The increase in the prevalence of obesity in the period 1993-1997 was strongest in men with a relatively low educational level and in women with a high educational level. It is concluded that there has been a steady increase in the prevalence of obesity in the last quarter of the 20th century. In addition, a recent increase in the prevalence of obesity has been seen. To stop the increase in the prevalence of obesity, effective strategies for the management and prevention of obesity need to be developed.

Tommy LS Visscher, Daan Kromhout, and Jacob C Seidell. Submitted for publication.

Introduction

Obesity is an important contributor to several chronic diseases and disabilities.[1,2] Obesity-related costs have been estimated at about seven percent of the total health care expenditure in the US and at one to five percent in Europe.[3,4] Such calculations are usually based on fractions of chronic diseases such as type 2 diabetes mellitus and cardiovascular diseases and disabilities that are attributable to obesity.[5] These 'population attributable fractions' estimations depend on relative risks of obesity for different diseases and disabilities and also on the prevalence of obesity.[2] Therefore, it is important to study time trends in the prevalence of obesity.

Time trend data on obesity prevalence rates are also needed to identify specific categories in which the prevalence is exceptionally high or to recognise categories in which strong increases in the prevalence of obesity are observed. Weight gain prevention programs could aim at these high-risk categories.[1,6,7] In western societies obesity is most common among those with relatively low education.[8] In order to study increases in the level of body mass index (BMI) across educational levels, Molarius *et al.* analysed data from 42,000 men and women measured in the period 1979-1989, and from 35,000 men and women measured in the period 1989-1996. Data were used from 26 centres participating in the WHO-MONICA project. They reported that the difference in BMI levels between high and low educational categories generally increased, because BMI levels increased more in low than in high educational categories.[9]

In the Netherlands the long-term time trend of overweight and obesity between 1976 and 1997 was assessed among men and women aged 37-43 years in repeated cross-sectional population based samples. Recent time trends in the prevalence of obesity in the period 1993-1997 were assessed in sex, age- and educational categories, among subjects aged 20-59 years.

Methods

Study populations

Long-term trend

We studied long-term time trends in the prevalence of overweight and obesity using original data from three monitoring projects on risk factors for chronic diseases from the National Institute of Public Health and the Environment, Bilthoven, the Netherlands. To allow comparisons of prevalence rates between

different periods, original data were used from subjects aged 37-43 years who participated in one of the three monitoring studies. The Consultation Bureau Heart Project was carried out in the period 1976-1980.[10] The Monitoring Project on Cardiovascular Diseases was carried out in 1987-1991.[11] The subsequent Monitoring project on risk factors for chronic diseases (MORGEN) project was carried out in 1993-1997. All three monitoring projects were carried out in the same three municipal health centres in the towns of Amsterdam, Doetinchem, and Maastricht. Data on the Consultation Bureau Heart Project and the Monitoring Project on Cardiovascular Diseases have been reported earlier by Blokstra and Kromhout[10] and Seidell *et al.*[11] Data on the period 1981-1986, also described by Blokstra and Kromhout,[10] were not used for the present study, because data were only available from men aged younger than 37 years. Response rates in different towns and years of the Consultation Bureau Heart Project varied between 70 and 80%. Response rate of the Monitoring Project on Cardiovascular Diseases was 50% in men and 57% in women. Response rate of MORGEN project varied between 40 and 51% between 1993 and 1997. Data on 13,779 men and 15,362 women were used for the long-term time trend analyses.

Recent trends

We studied recent time trends in the prevalence of overweight and obesity using data of the MORGEN project on men and women aged 20-59 years who visited the municipal health centres between 1993 and 1997. We excluded 142 women who were pregnant. Data on educational level was missing in 164 subjects and 55 subjects had missing data regarding smoking status. Data on body weight and height were available from 9,981 men and 11,945 women.

Measurements

Body weight and height were measured with participants wearing light indoor clothing without shoes, with emptied pockets, by trained staff.[12] Body weight was measured to the nearest 100 g on calibrated scales. To adjust for the weight of clothing, 1 kg was subtracted from body weight. BMI was calculated as weight divided by height squared in kg/m^2. Overweight was considered as BMI 25.0-29.9 kg/m^2, and obesity as BMI $\geq$30.0 kg/m^2. For the period 1993-1997 level of education was measured as the highest level reached and categorised in five groups: primary school, junior (vocational) education, secondary (vocational) education, vocational colleges, university. Subjects were classified as never, ex-, or current smokers.

STATISTICAL ANALYSIS

Mean values and prevalence rates regarding the age-range 20 to 59 years were standardised to the five-years age-distribution in the Netherlands in the year 1995.[13] Linear trends per year and *p*-values for trend were calculated by generalised linear models (procedure GLM, SAS version 6.12), with and without adjustment for five-years age-categories, educational level, and town.

Results

Long-term trend

During the period 1976-1997, mean BMI and the prevalence of overweight were higher among men than among women aged 37-43 years. The prevalence of obesity was slightly higher among women (table 3.1.1). Between 1976 and 1997, mean BMI and the prevalence of obesity increased steadily from 4.9 to 8.5% in men and from 6.2 to 9.3% in women aged 37-43 years. The overweight prevalence did not increase clearly between 1976 and 1997. Body height increased about 3-4 cm and weight by about 5 kg in men and over 3 kg in women. High quintiles of the BMI distribution increased more strongly than the lower during the long term between 1976 and 1997 among men and women aged 37 to 43 years (figure 3.1.1).

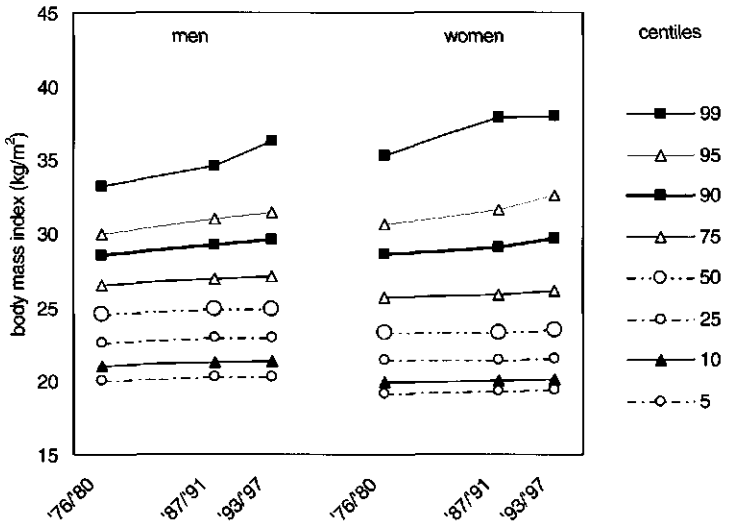

Figure 3.1.1 Long-term time trend of the body mass index distribution in the Netherlands among men and women aged 37-43 years
Data from the Consultation Bureau Heart Project 1976-1980,[10] the Monitoring Project on Cardiovascular Diseases 1987-1991,[11] and the MORGEN project 1993-1997.

Table 3.1.1 Mean values of height, weight, and body mass index and prevalence of overweight and obesity among Dutch men and women aged 37-43 years

		1976-1980[a]	1987-1991[b]	1993-1997[c]
Number of subjects	Men	8,086	3,588	2,105
	Women	8,922	3,922	2,518
Mean body height (m)	Men	1.75	1.78	1.79
	Women	1.63	1.65	1.66
Mean body weight (kg)	Men	76.1	79.7	81.0
	Women	63.8	65.6	67.1
Mean body mass index (kg/m^2)	Men	24.7	25.2	25.2
	Women	23.9	24.1	24.4
Overweight (%);	Men	38.3	41.5	40.2
BMI 25.0-29.9 kg/m^2	Women	24.6	23.9	25.0
Obesity (%);	Men	4.9	7.4	8.5
BMI ≥30.0 kg/m^2	Women	6.2	7.6	9.3

a Original data of the Consultation Bureau Heart Project[10]
b Original data of the Monitoring Project on Cardiovascular Diseases[11]
c Original data of the Monitoring project on risk factors for chronic diseases (MORGEN-) project

Recent trend

During the period 1993-1997, mean height, weight, and BMI and the prevalence of overweight were higher among men than among women aged 20-59 years. Obesity was more common among women than among men (table 3.1.2). The increase in the prevalence of obesity was strongest in men between 1993 and 1997. The prevalence of overweight decreased among men and increased among women between aged 20-59 years, although these trends were not statistically significant. Increases in BMI levels and the prevalence of obesity were strongest if adjustment for educational level was made.

Table 3.1.2 Changes in mean height, weight, and body mass index (BMI) and prevalence of overweight and obesity among Dutch men and women aged 20-59 years in the period 1993-1997

	Mean/prevalence [a]						
	1993-1997	Crude	(95% CI)	Adjusted [b]	(95% CI)	Adjusted [c]	(95% CI)
Mean body height (m)							
Men	179.2	0.25	(0.15-0.35)	0.24	(0.14-0.33)	0.17	(0.08-0.27)
Women	166.1	0.19	(0.11-0.28)	0.14	(0.06-0.22)	0.05	(-0.03-0.14)
Mean body weight (kg)							
Men	80.4	0.27	(0.10-0.44)	0.28	(0.11-0.45)	0.31	(0.14-0.48)
Women	67.1	0.20	(0.05-0.35)	0.23	(0.09-0.38)	0.32	(0.17-0.46)
Mean body mass index (kg/m^2)							
Men	25.1	0.02	(-0.03-0.07)	0.02	(-0.02-0.07)	0.05	(0.00-0.10)
Women	24.4	0.02	(-0.04-0.07)	0.04	(-0.01-0.09)	0.10	(0.05-0.15)
Overweight (%); BMI 25-29.9 kg/m^2							
Men	37.8	-0.47	(-1.16-0.22)	-0.43	-1.10-0.24()	-0.28	(-0.95-0.40)
Women	25.9	-0.13	(-0.70-0.43)	0.07	(-0.49-0.62)	0.34	(-0.22)
Obesity (%); BMI ≥30 kg/m^2							
Men	8.5	0.34	(-0.07-0.76)	0.38	(-0.04-0.79)	0.54	(0.13-0.96)
Women	9.6	-0.02	(-0.41-0.37)	0.06	(-0.33-0.45)	0.35	(-0.03-0.73)

a Standardised for the five-years age distribution in the Netherlands
b Adjusted for five-years age distribution and town
c Adjusted for five-years age distribution, town, and education
95% CI denotes 95% confidence interval

Table 3.1.3 Prevalence of obesity (body mass index ≥30 kg/m²) in 1993-1997 and increase in the prevalence of obesity during this period in percentage points per year according to age-category

Age (years)	Number	Prevalence 1993-1997 (%)	Increase per year[a] (%-points per year)	(95%-confidence interval)
Men				
20-29	1,581	4.4	0.35	(-0.40-1.09)
30-39	2,374	6.7	0.48	(-0.23-1.19)
40-49	3,083	10.5	-0.38	(-1.14-0.38)
50-59	2,943	14.7	1.67	(0.75-2.59)
Women				
20-29	2,191	5.4	0.33	(-0.35-1.02)
30-39	2,826	7.4	0.70	(0.04-1.36)
40-49	3,695	11.1	0.09	(-0.60-0.79)
50-59	3,233	17.0	0.50	(-0.40-1.39)

a adjusted for educational category and town

The prevalence of obesity increased with age (table 3.1.3). A slight increase in the prevalence of obesity between 1993 and 1997 was seen in most age-categories. The increase in the prevalence of obesity was particularly strong in men aged 50-59 years and relatively strong in women aged 30-39 years.

The prevalence of obesity was more than three times higher among men with a low educational level compared to men with a high educational level (table 3.1.4). Among women, the prevalence of obesity was more than five times higher among those with low education than among women with high education. A significant increase in the prevalence of obesity was observed in men with a relatively low educational level and in women with a high educational level.

Obesity was more prevalent among never smokers than among current smokers (table 3.1.5). The increase in the prevalence of obesity was observed in all smoking-categories and was largest among never smokers.

Table 3.1.4 Prevalence of obesity (body mass index ≥30 kg/m^2) in 1993-1997 and increase in the prevalence of obesity during this period in percentage points per year according to educational category

Educational level	Number	Prevalence [a] 1993-1997 (%)	Increase per year [b] (%-points per year)	(95%-confidence interval)
Men				
Primary school	1,089	15.4	1.70	(0.08-3.32)
Junior (vocational) school	2,249	11.4	1.29	(0.29-2.30)
Secondary (vocational) school	986	9.9	1.04	(-0.42-2.49)
Vocational colleges	2,939	7.1	0.33	(-0.34-1.01)
University	2,655	4.7	-0.48	(-1.08-0.12)
Women				
Primary school	1,446	17.8	-0.36	(-1.79-1.08)
Junior (vocational) school	2,758	13.7	0.23	(-0.72-1.17)
Secondary (vocational) school	1,998	10.1	0.08	(-0.90-1.06)
Vocational colleges	3,103	7.1	0.82	(0.21-1.43)
University	2,539	3.4	0.66	(0.15-1.16)

a standardised to the five-years age-distribution in the Netherlands
b adjusted for five-years age-distribution and town

Discussion

The prevalence of obesity increased during the last quarter of the previous century in the Netherlands. Between 1976 and 1997, the prevalence of obesity increased from 4.9 to 8.5% among men and from 6.2 to 9.3% among women aged 37-43 years. During the recent years 1993-1997, the prevalence of obesity continued to increase in the Netherlands. Between 1993 and 1997, the prevalence of obesity was 8.5% and increased with 0.54 percentage points per year among men aged 20-59 years. The prevalence of obesity among women aged 20-59 years was 9.6% and increased with 0.35 percentage points per year during the period 1993-1997. An increase in the prevalence of obesity was found in nearly all age-categories, and was exceptionally strong in men aged 50-59 years. The increase in the prevalence of obesity was largest in men with a relatively low educational level and in women with a high educational level. An increase in the prevalence of obesity was noted within all smoking categories and was largest among never smokers.

Table 3.1.5 Prevalence of obesity (body mass index ≥30 kg/m²) in 1993-1997 and increase in the prevalence of obesity during this period in percentage points per year according to smoking status

	Number	Prevalence [a] 1993-1997 (%)	Increase per year [b] (%-points per year)	(95%-confidence interval)
Men				
Current smokers	3,662	7.7	0.50	(-0.15-1.14)
Ex-smokers	3,221	9.9	0.45	(-0.36-1.26)
Never smokers	3,065	8.3	0.74	(0.04-1.44)
Women				
Current smokers	4,388	8.4	0.24	(-0.36-0.84)
Ex-smokers	3,113	9.0	0.37	(-0.39-1.13)
Never smokers	4,422	11.1	0.48	(-0.16-1.13)

a standardised to the five-years age-distribution in the Netherlands
b adjusted for five-years age-distribution, educational category and town

Relatively few countries have monitoring systems that allow comparisons of long-term time trends based on measured body weight and height obtained from representative study populations.[12,14,15] These studies also show strong increases in the prevalence of obesity. During the last quarter of the previous century, the prevalence of obesity in the Netherlands has been lower than in the United States, England, and Germany (table 3.1.6).[10,11] Data from the National Health and Nutrition Examination Survey (NHANES) I and NHANES III[14] showed a strong increase in the prevalence of obesity in the United States between 1971 and 1994. In the United Kingdom an even more rapid increase in the prevalence of obesity between 1980 and 1997 has been reported, although the prevalence of obesity seems still lower in the United Kingdom than in the United States.[12] German data were available from the German National Health Interview and Examination Survey. The prevalence of obesity was higher in 1998 than in 1990-1992 in men and women aged 25-69 years.[15] The WHO-MONICA project reported time trend data taken from surveys in towns or regions across Europe, in men and women aged 35-64 years who were measured in the periods 1979-1989 and 1989-1996.[9] An increase was seen in the prevalence of obesity in most centres[16]. Although the WHO-MONICA study does not yield national prevalences and time trends, it can be tentatively concluded that prevalences of obesity vary widely, especially in women, with the highest prevalences in women from eastern and central Europe and the Mediterranean region. The recent prevalence of obesity in the Netherlands seems comparable to that in Scandinavian countries and France.[9,17]

Table 3.1.6 Prevalence of obesity (body mass index ≥30 kg/m^2) in the United States, England, Germany, and the Netherlands

Study population	Country	Period	Age (years)	Prevalence (%) Men	Women
NHANES I[14a]	The United States	1971-1974	20-74	11.8	16.2
NHANES III[14b]	The United States	1988-1994	20-74	20.0	24.9
Health Survey for England[12]	England	1980	16-64	6	8
Health Survey for England[12]	England	1998	16-64	17	22
German National Health Interview and Examination Survey[15]	Germany, East	1990-1992	25-69	20.6	25.8
	Germany, East	1998	25-69	21.8	24.2
German National Health Interview and Examination Survey[15]	Germany, West	1990-1992	25-69	17.4	19.6
	Germany, West	1998	25-69	19.4	20.9
CB Heart Project[b]	The Netherlands	1976-1980	37-43	4.9	6.2
MORGEN[c]	The Netherlands	1993-1997	37-43	8.5	9.3
MORGEN[c]	The Netherlands	1993-1997	20-59	8.5	9.6

a National Health and Nutrition Examination Survey
b Present Consultation bureau heart project
c Present Monitoring project on risk factors for chronic diseases project

In the present study, the centiles above the median level of the BMI distribution increased clearly between 1976 and 1997, while the increase in the lower centiles was less pronounced. Consequently, the increase in the prevalence of obesity (BMI ≥30.0 kg/m^2) was stronger than the increase in overweight (BMI 25.0-29.9 kg/m^2). The observation that the skewness of the BMI-distribution shifted to the left has been reported earlier by Thomsen *et al.*, who studied the increase of BMI levels among children, aged 7 to 13 years from Copenhagen, Denmark.[18] Because the lower centiles of the BMI distribution also increased, although slightly, Thomsen *et al.* concluded that some environmental changes are influencing the entire population, but others mainly a subgroup in the population that is especially susceptible for obesity. We deduce from the steeper increase of high centiles that subjects who already gained weight, for instance those who are overweight, are at high risk to gain even more weight. Therefore, prevention of weight gain is important in all people but especially in those already overweight.

The prevalence of obesity increased in nearly all age-categories between 20 and 59 years, although not statistically significant in most age-categories, and was exceptionally high in men aged 50-59 years. We expect that the prevalence of obesity will increase probably more strongly in the coming decades, because an increase in BMI levels among Dutch boys and girls aged 0-21 years has been reported during the last two decades that was stronger than that in the adults in the present study.[19] Particular attention is warranted for the increase in BMI levels at already young age. Many obese children are likely to become obese adults.[20] Moreover, duration of obesity is among the determinants of health consequences of obesity.[21]

Between 1993 and 1997, the increase in obesity was strongest among men with a relatively low educational level and among women with a high educational level. The prevalence of obesity decreased among men with a high educational level and among women with a low educational level, although not statistically significant. An increase in the prevalence of obesity among those with a high educational level has also been reported by Mokdad *et al.* based on self-reported data from the US. They reported that men and women with relatively high educational level showed a larger increase in the prevalence of obesity between 1991 and 1998 than those with a lower educational level, although the prevalence of obesity remained inversely associated with educational level.[16] Studies that are less recent than Mokdad's study concluded that the increase in the prevalence of obesity has been generally strongest in individuals with low educational level or low socio-economic status. Concurrently, the difference in the prevalence of obesity increased between subjects with low and high socio-economic status.[9,22] Also in the Netherlands, the prevalence of obesity is still highest among lowly educated men and women. If the increase in the prevalence of obesity among highly educated individuals is confirmed in other studies, these subjects will also become a target for intervention programs.

Across smoking categories, the prevalence of obesity increased most strongly among never smokers. We presented data for all smoking categories separately, as changing smoking behaviour could affect BMI levels since smoking cessation is associated with weight gain.[23] Among smokers, body weight depends on the amount of cigarettes smoked and the time since quitting smoking.[23] It could be questioned how much of quitting smoking is contributing to the increase in the prevalence of overweight and obesity. Williamson *et al.* reported from the first National Health and Nutrition Examination Survey (NHANES I) that quitting smoking was associated with more than 13 kg increase in about 10% of persons who quitted smoking and were followed between 1971 and 1984. The average person who quits smoking, however,

will gain 2-4 kilograms. At the end of their study the mean body weight of persons who quitted smoking had increased to average body weight as persons who never smoked.[24] Flegal *et al.* quantified the part of the noted increase in the prevalence of overweight that could be due to quitting smoking. In their study weight increased also largely in a part of the persons who quitted smoking during the last ten years, but this group was small and contributed only slightly to the increase in the prevalence of overweight. About a quarter (2.3 of the 9.6 percentage points) in men and about a sixth (1.3 of the 9.6 percentage points) increase in the prevalence of overweight was due to quitting smoking.[25] Boyle *et al.* concluded earlier that the increase in obesity in Australia could not be explained by decreasing rates of cigarette smokers, since they found similar increases in obesity among never smokers, ex-smokers and current smokers.[26]

Among the advantages of our monitoring projects are the anthropometric data collection by trained staff and the time-span that was covered. Self-reports on body weight would have lead to underestimation, especially among those who are obese.[27,28] As data were collected throughout the year, seasonal variation in body weight could not affect the prevalence estimations.[29] Among the disadvantages is that the three towns in which measurements were performed may not be nationally representative. Another disadvantage of the present study is the decreasing response rate over time. Highly educated men and women were over-represented in the MORGEN project 1993-1997. The higher educational level of the examined population in most recent years, may explain why increases in the prevalence of obesity became stronger after adjustment for educational level. The somehow selective participation did not seem to affect the adjusted time-trend estimations, as the Central Bureau for Statistics, with a much higher response rate, but based on self-reported body weight and height, estimated a similar time trend in the prevalence of obesity between 1993 and 1997 as the present study.[30]

CONCLUSION

The increase in the prevalence of obesity reported in western societies is also seen in recent years in the Netherlands. The strongest increase in the prevalence of obesity was noticed in men with a relatively low educational level and in women with a high educational level. The increasing prevalence of obesity is a threat for the public health as it is related to several chronic morbidity and disability.[2] In order to stop this burden of disease and disability, implementation of new weight gain prevention programs is urgently needed.

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Chapter 3.2

SEASONAL VARIATION IN WAIST CIRCUMFERENCE IS LARGER THAN THAT IN BODY MASS INDEX

Abstract In this chapter, the time trend and seasonal variation in body mass index and waist circumference are compared. Data were derived from a continuous monitoring health survey (spring 1993-autumn 1997) that was carried out in three towns in the Netherlands. A total of 9,571 men and 11,382 women aged 20 to 59 years participated. The time trend in abdominal obesity, measured by levels of waist circumference, was stronger than the time trend in general obesity, measured by levels of body mass index. Moreover, the seasonal variation in waist circumference was larger than the seasonal variation in body mass index. It is concluded that surveys on waist circumference are only comparable if season is taken into account. Furthermore, the waist circumference may be more sensitive than the body mass index to detect changes in the energy balance and body composition.

Tommy LS Visscher and Jacob C Seidell. Submitted for publication.

Introduction

Increases in the prevalence of obesity are widely reported.[1] Weight gain is the result of a positive energy balance. Disruptions of energy balance are often reported to occur during holidays or the festive season. Yanovski *et al.* reported that subjects gained weight during the December holiday between Thanksgiving and New Year's Eve.[2] We hypothesise that waist circumference is more sensitive to seasonal variation in energy balance than is body mass index.

Methods

Study population

Between spring 1993 and autumn 1997, the population based Monitoring Project on Risk Factors for Chronic Diseases was carried out to study levels of risk factors for chronic diseases in the Dutch population.

A total of 9,571 men and 11,382 women aged 20-59 years from the towns of Amsterdam, Doetinchem and Maastricht, the Netherlands were measured. Participation rate was 45%.

Measurements

Body weight and height were measured with participants wearing light indoor clothing without shoes and with empty pockets, by trained staff at a visit to the municipal health centre. Body weight was measured to the nearest 100 g on calibrated scales. To adjust for the weight of clothing, one kilogram was subtracted from the measured weight. Body mass index was calculated as weight divided by height squared (kg/m^2). Waist circumference was measured at the level midway between the lower rib margin and the iliac crest, with participants in standing position and breathing out gently. We defined general obesity as body mass index ≥ 30 kg/m^2 according to the World Health Organization guidelines.[1] Abdominal obesity was defined as waist circumference ≥ 102 cm for men and ≥ 88 cm for women according to the action levels as suggested by Lean *et al.*[3] Winter was defined as December-January-February. Subsequently, spring was defined as March-April-May, summer as June-July-August, and autumn as September-October-November.

Table 3.2.1 Body mass index and waist circumference[a] (95%-confidence interval) per season between March 1993 and November 1997.

	Spring	Summer	Autumn	Winter	*p*-value[b]
Men, n=9,571					
Body mass index, kg/m^2	25.4 (25.3-25.6)	25.2 (25.0-25.3)	25.3 (25.2-25.4)	25.4 (25.3-25.6)	0.02
Waist circumference, cm	91.8 (91.4-92.2)	90.9 (90.5-91.3)	91.5 (91.1-91.9)	91.9 (91.4-92.3)	<0.01
Prevalence of obesity (%) [BMI ≥30 kg/m^2]	10.8 (9.6-11.9)	9.8 (8.6-11.0)	9.6 (8.5-10.8)	10.7 (9.4-12.1)	0.32
Prevalence of abdominal obesity (%) [waist circumference ≥102 cm]	18.5 (17.0-20.0)	16.1 (14.6-17.6)	17.6 (16.1-19.1)	19.3 (17.5-21.0)	<0.01
Women, n=11,382					
Body mass index, kg/m^2	24.7 (24.6-24.8)	24.6 (24.4-24.7)	24.8 (24.6-24.9)	24.8 (24.6-25.0)	0.03
Waist circumference, cm	80.8 (80.4-81.2)	80.4 (80.0-80.8)	81.0 (80.6-81.4)	81.3 (80.8-81.7)	<0.01
Prevalence of obesity (%) [BMI ≥30 kg/m^2]	10.6 (9.5-11.6)	10.8 (9.7-11.9)	11.2 (10.1-12.3)	11.9 (10.6-13.1)	0.20
Prevalence of Abdominal obesity (%) [waist circumference ≥88 cm]	23.0 (21.5-24.4)	22.2 (20.7-23.7)	24.9 (23.4-26.3)	25.5 (23.8-27.2)	<0.01

Figures are mean values unless otherwise specified

a Adjustments were made for monthly changes between spring 1993 and autumn 1997, five-years age-categories and level of education.

b *P*-value for difference between summer and winter

Statistical analysis

Mean values and prevalence rates were calculated per season, adjusting for five-years age-categories, level of education and for the general monthly changes between 1993 and 1997. In addition, the prevalence of general and abdominal obesity was calculated across consecutive seasons, adjusting for five-years age-categories and level of education (proc GLM, SAS-version 6.12).

Results

Both mean body mass index and mean waist circumference were higher in winter than in summer for both men and women, and the seasonal difference in waist circumference was considerably larger than the seasonal difference in body mass index (table 3.2.1). Also, prevalence of general and abdominal obesity was higher in winter than in summer among men and women, and the seasonal difference was largest for abdominal obesity. Between 1993 and 1997, obesity prevalence increased

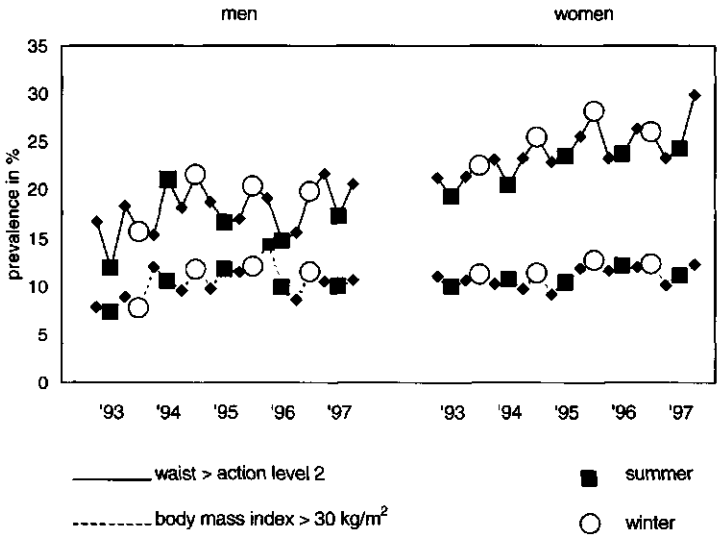

Figure 3.2.1 Prevalence of obesity (body mass index ≥30 kg/m²) and abdominal obesity (waist circumference ≥action level 2[a]) over seasons[b]
a Action level 2 is defined as 102 cm among men and 88 cm among women
b Adjusted for age-category and educational level

with 0.57 percentage points per year (p<0.00) among men and with 0.34 percentage points per year (p=0.10) among women. Prevalence of abdominal obesity increased with 0.70 percentage points per year (p=0.01) among men and with 1.33 percentage points per year (p<0.01) among women. Moreover, increases during the winter seasons and decreases during summer seasons were most clearly seen for abdominal obesity, especially among women (figure 3.2.1).

Discussion

We suggest that the time trend changes in energy balance and the seasonal variation in energy balance be best reflected by changes in waist circumference. Both changes in food intake and in physical activity influence waist circumference. There is no evidence that changes in food intake have a different impact on waist circumference and body mass index. Changes in physical activity, however, may lead to changes in body composition (increase in muscle mass, decrease in fat mass), and thus to a decreasing waist circumference, but stable body weight, and thus stable body mass index.[4]

Measuring waist circumference has been recommended earlier as a useful tool for health promotion since the measurement of waist circumference is informative, easy, cheap, and reliable.[5] Han *et al.* showed that a large waist circumference was clearly predictive of unfavourable levels of cardiovascular disease risk factors based on the same study population as used for the present study.[6]

Conclusion

The strong seasonal variation in waist circumference should be taken into account in the case of planning epidemiological surveys or time trend analyses. In addition, the more pronounced seasonal changes in waist circumference compared to body mass index changes suggest that waist circumference is a more sensitive indicator of variations in lifestyle and body composition. Therefore, in reaction to Little's and Byrne's editorial,[7] we suggest that it is now time to implement measuring of waist circumference in the routine screening of changes in lifestyle and body composition.

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Chapter 4.1

Underweight and overweight in relation to mortality among men aged 40-59 and 50-69 years. The Seven Countries Study

Abstract This study investigated the relation between body mass index (BMI) and the all-cause mortality rate among 7,985 European men. Starting around 1960, when all men were aged 40-59 years, mortality was followed for 15 years (1960-1975); starting around 1970, the survivors were followed for an additional 15 years (1970-1985). For the first and second follow-up periods, a BMI of 18.5-24.9 kg/m^2 around 1960 and 1970, respectively, was considered the reference category. The authors found that the hazard ratio (HR) of mortality for a BMI of <18.5 kg/m^2 was 2.1 (95% confidence interval (CI): 1.5-2.8) for the first follow-up period and 1.7 (95% CI: 1.3-2.2) for the second. A BMI 25.0-29.9 kg/m^2 was not related to increased mortality. Among never smokers, the HRs for a BMI ≥30.0 kg/m^2 was 1.8 (95% CI: 1.2-2.8) for the 1960-1975 follow-up period and 1.4 (95% CI: 1.0-1.9) for the 1970-1985 follow-up period. A BMI of ≥30.0 kg/m^2 was not related to increased mortality among current smokers. When mortality was followed for more than 15 years, the HR for a BMI <18.5 kg/m^2 declined and the HR for a BMI of >30.0 kg/m^2 did not change. Underweight among those in all smoking categories and severe overweight in never smokers remained predictors of increased mortality when middle-aged men became older.

Tommy LS Visscher, Jacob C Seidell, Allesandro Menotti, Henry Blackburn, Aulikki Nissinen, Edith JM Feskens, and Daan Kromhout for the Seven Countries Study Research Group. *Am J Epidemiol* 2000; 151: 660-6.

Introduction

The effect of both high and low body mass index (BMI) on the mortality rate has been assessed in several large prospective cohort studies.[1-6] The U- or J-shaped relation between BMI and the all-cause mortality rate among adult men is well established,[7,8] although its interpretation is still under debate.

Average BMI increases until age 65 years and then declines.[9-11] Changes in BMI are explained by the decrease in stature and by changes in body composition that occur with ageing.[12] Most studies also report a decline in the risk ratio of all-cause mortality for overweight with ageing and conclude that overweight is less important as a risk factor for mortality in the elderly than in younger populations.[1,2,9,13-16]

Lower risk ratios have been explained by selective survival and a higher mortality rate among older people. Declines in risk ratios, however, may also be explained by confounding due to a cohort effect. When compared with cohorts of younger people, cohorts of older people may have different levels of potential confounders of the BMI-mortality relation because of a different historic risk profile. These cohorts are from different generations. They grew up during different time periods, which may affect both body weight and mortality.

To avoid confounding by a cohort effect, the present study investigated the BMI-mortality relation in one cohort of men born in similar years and started the second follow-up period ten years after the first. The men were aged 40-59 years around 1960. Categories of BMI were defined according to the World Health Organization guidelines[10] to enable us to determine whether these categories were still useful when the men were ten years older. Furthermore, different lengths of follow-up were assessed for their effects on the BMI-mortality relation among the elderly.

Methods

Study population

Around 1960, that is, between 1958 and 1964, 12,761 men aged 40-59 years were enrolled in the Seven Countries Study.[7,17,18] The study sample consisted of men from Finland (east and west), the former Yugoslavia (Croatia (Slavonia and Dalmatia) and Serbia (Velika Krsna, Zrenjanin, and Belgrade)), Italy (Crevalcore, Montegiorgio and Rome), Greece (Corfu and Crete), the Netherlands (Zutphen), Japan (Ushibuka and Tanushimaru), and the United States. Most of the men lived in rural areas. In the town of Zutphen, four of every nine men were invited to

participate in the study. In Serbia, workers from a large co-operative in Zrenjanin and professors from the University of Belgrade were invited. In Rome and the United States, railroad workers were recruited. Overall, the participation rate was higher than 90 percent. Studies on the BMI-mortality relation in the Seven Countries Study have already been published.[7,19-22] To our knowledge, however, our study is the first to present results based on analyses of the same cohort, defining categories of BMI at the beginning of follow-up, presenting results separately for men in different smoking categories, not adjusting for intermediate factors, and starting the follow-up periods at different ages.

For the present study, we used data from the 13 European centres of the Seven Countries Study. The US railroad cohort was excluded because BMI was not measured around 1970 at this centre. At the two Japanese centres, the relation between BMI and mortality differed from the relation found at the other centres, although it was not statistically significant, probably because of small numbers. We excluded Japan to improve the homogeneity and representativeness of the present study for European countries. The reason that we included centres from Japan, the United States, and Europe at the beginning of the Seven Countries Study was to assess different levels of diet-related risk factors throughout the world and their effects on cardiovascular diseases.[17] To be able to compare BMI-mortality associations between regions of Europe, we pooled centres into four regions on the basis of their cultural similarities: 1) Northern Europe (east and west Finland and Zutphen), 2) inland Southern Europe (Rome, Crevalcore, Slavonia, and Belgrade), 3) Mediterranean Southern Europe (Crete, Corfu, Montegiorgio, and Dalmatia), and 4) Serbia (Velika Krsna and Zrenjanin).[18] Men for whom data on BMI, age, and smoking were available around 1960 and 1970 were included in the analyses. The analyses were restricted to subjects with full data to improve the comparability of different analyses applied to the same cohort. Of the 12,761 men who were enrolled in the Seven Countries Study, 9,180 were European and 7,985 had complete data.

Measurements

Body weight and height were measured around 1960 and again for the same men around 1970 while they were wearing light underwear without shoes. BMI was calculated as body weight to the nearest 0.1 kg divided by height in meters squared (kg/m^2). Four categories of BMI were defined by using the World Health Organization guidelines,[10] which consider less than 18.5 kg/m^2 as underweight, 18.5-24.9 kg/m^2 as normal weight, 25.0-29.9 kg/m^2 as grade I overweight, and 30.0-39.9 kg/m^2 as grade II overweight (also called obesity or severe overweight). Six men

whose BMI was more than 40 kg/m^2 (grade III overweight) were added to the grade II overweight category. Age was rounded to the nearest birthday. Information about cigarette smoking was obtained from a standardised questionnaire around 1960 and again around 1970.[17] Subjects were classified as never, ex-, or current smokers.

Mortality follow-up

Vital status was checked by visiting the local register offices periodically. Two main periods of follow-up were defined. One 15-year follow-up period began around 1960 and ended around 1975. For the survivors, a second 15-year follow-up period started around 1970 and ended around 1985. In addition, the influence of follow-up length on the BMI-mortality relation was assessed by following the men for 15-, 20-, and 25-year periods, all starting around 1960 when the men were aged 40-59 years. During 25 years of follow-up, 3,777 men died. One man from a total of 7,985 was lost to follow-up. Six men were censored between 1960 and 1965, two between 1965 and 1970, six between 1970 and 1975, and 13 between 1975 and 1985.

Statistical analysis

A hazard ratios (HR) was calculated for each category of BMI at the beginning of follow-up by using Cox's proportional hazards model (proc PHREG, SAS-version 6.12). For the analyses based on follow-up starting around 1960 and 1970, a BMI of 18.5-24.9 kg/m^2 around 1960 and 1970, respectively, was the reference category.

The baseline categories of BMI around 1960 and 1970 did not comprise exactly the same men; for 28 percent, their BMI category changed between 1960 and 1970. To assess whether these changes affected the results, we also calculated HRs for 15 years of mortality from 1970 onward for those men who were in the same BMI category in both 1960 and 1970 and for those who changed categories between 1960 and 1970. For this analysis only, men whose BMI was 18.5-24.9 kg/m^2 around both 1960 and 1970 were considered the reference group.

HRs were adjusted for age at baseline as a continuous variable and for centres by using dummy variables. Because cardiovascular diseases and their risk factors are acknowledged to be intermediates in the causal chain linking overweight to increased mortality,[23-25] adjustments were not made for blood pressure and cholesterol levels. HRs were calculated for different categories of smoking separately, because smoking has been shown to confound or modify the relation between body weight and mortality.[23,26]

The effect of early mortality, which may be attributable to lower weight because of clinical or subclinical disease, was studied by carrying out analyses excluding and not excluding the men who died or were censored within five years after baseline.[23] The results presented are based on analyses in which early mortality was excluded.

Results

For all men combined, the mean BMI was 24.2 kg/m^2 around 1960 and 25.3 kg/m^2 for the survivors around 1970. As shown in tables 4.1.1 and 4.1.2, a BMI less than 18.5 kg/m^2 was rare around both 1960 and 1970 and was most prevalent among current smokers. A BMI 25.0-29.9 kg/m^2 and a BMI ≥30.0 kg/m^2 were more prevalent among never and ex-smokers than among current smokers. A total of 405 men died between 1960 and 1965, 648 men died between 1965 and 1970, 699 men died between 1970 and 1975, and 2,025 men died between 1975 and 1985.

Table 4.1.1 Prevalence of body mass index categories around 1960[a] and follow-up characteristics of European men in the Seven Countries Study, by category of body mass index, 1960-1975[b]

Smoking category and characteristics	Body mass index (kg/m^2)			
	<18.5	18.5-24.9	25.0-29.9	≥30.0
Never smokers				
Subjects at baseline (%)	15 (0.8)	984 (52.6)	708 (37.9)	163 (8.7)
Total person-years	205	14,275	10,216	2,318
Number of deaths	4	102	87	29
Deaths per 1,000 person-years	19.6	7.1	8.5	12.5
Ex-smokers				
Subjects at baseline (%)	8 (0.7)	573 (49.7)	467 (40.5)	105 (9.1)
Total person-years	104	8,072	6,698	1,473
Number of deaths	2	96	68	23
Deaths per 1,000 person-years	29.3	11.9	10.2	15.6
Current smokers				
Subjects at baseline (%)	111 (2.4)	3,037 (66.7)	1,203 (26.4)	199 (4.4)
Total person-years	1,405	42,562	17,000	2,789
Number of deaths	42	636	214	44
Deaths per 1,000 person-years	29.9	14.9	12.6	15.8

a Age around 1960, 40-59 years
b Mortality during the first five years of follow-up was excluded

Table 4.1.2 Prevalence of body mass index categories around 1970[a] and follow-up characteristics of European men in the Seven Countries Study, by category of body mass index, 1970-1985[b]

Smoking category and characteristics	Body mass index (kg/m²) and number (%)			
	<18.5	18.5-24.9	25.0-29.9	≥30.0
Never smokers				
Subjects at baseline	11 (0.7)	614 (39.2)	723 (46.2)	217 (13.9)
total person-years	133	8,491	10,111	2,928
Number of deaths	6	156	167	67
Deaths per 1,000 person-years	45.1	18.4	16.5	22.9
Ex-smokers				
Subjects at baseline	15 (1.0)	587 (37.5)	759 (48.4)	206 (13.1)
total person-years	168	7,826	10,191	2,710
Number of deaths	10	196	245	79
Deaths per 1,000 person-years	59.6	25.0	24.0	29.2
Current smokers				
Subjects at baseline	85 (2.8)	1,733 (56.2)	1,022 (33.1)	246 (8.0)
total person-years	1,005	22,985	13,836	3,283
Number of deaths	46	631	335	87
Deaths per 1,000 person-years	45.8	27.4	24.2	26.5

a Age around 1970, 50-69 years
b Mortality during the first five years of follow-up was excluded

Table 4.1.3 Hazard ratios (95% confidence intervals) of all-cause 15-year mortality[a] among European men in the Seven Countries Study, by category of body mass index[b]

Follow-up period and smoking category	Body mass index (kg/m²)			
	<18.5	18.5-24.9	25.0-29.9	≥30.0
1960-1975				
Never smokers	2.1 (0.8-5.7)	1	1.3 (0.9-1.7)	1.8 (1.2-2.8)
Ex-smokers	2.0 (0.5-8.2)	1	1.0 (0.7-1.3)	1.3 (0.8-2.1)
Current smokers	2.1 (1.5-2.8)	1	0.9 (0.8-1.1)	1.0 (0.7-1.4)
1970-1985				
Never smokers	2.3 (1.0-5.3)	1	1.0 (0.8-1.2)	1.4 (1.0-1.9)
Ex-smokers	2.5 (1.3-4.8)	1	1.1 (0.9-1.4)	1.4 (1.0-1.8)
Current smokers	1.5 (1.1-2.1)	1	1.0 (0.9-1.1)	1.0 (0.8-1.3)

a Mortality during the first five years of follow-up was excluded.
b Adjustments were made for age and study centre

Table 4.1.4 Fifteen-year mortality[a] from 1970 onward, by different categories of body mass index, among European men in the Seven Countries Study[b]

	Body mass index (kg/m^2)		Hazard ratio (95% confidence interval)
Smoking category	1960	1970	
All men[c]	18.5-24.9	18.5-24.9	1
	≥18.5	<18.5	1.8 (1.3-2.5)
	<18.5	<18.5	1.5 (0.9-2.4)
Never smokers	18.5-24.9	18.5-24.9	1
	<30.0	≥30.0	1.4 (1.0-2.1)
	≥30.0	≥30.0	1.5 (1.0-2.2)
Ex-smokers	18.5-24.9	18.5-24.9	1
	<30.0	≥30.0	1.3 (0.9-1.8)
	≥30.0	≥30.0	1.5 (1.0-2.2)
Current smokers	18.5-24.9	18.5-24.9	1
	<30.0	≥30.0	1.0 (0.7-1.3)
	≥30.0	≥30.0	1.2 (0.8-1.7)

a Mortality during first five years of follow-up was excluded.
b Adjustments were made for age and study centre.
c Adjustment was also made for smoking at baseline for the analysis on all men.

The 15-year all-cause mortality rate (actually, 15 year mortality minus the first five years of mortality) was clearly higher among those with a BMI <18.5 kg/m^2 than among those whose BMI was 18.5-24.9 kg/m^2 (table 4.1.3). HRs for BMI <18.5 kg/m^2 were similar across all smoking categories. When the smoking categories were pooled, the HRs for BMI <18.5 kg/m^2 were 2.1 (95 percent confidence interval (CI): 1.5-2.8) for the follow-up period starting around 1960 and 1.7 (95 percent CI: 1.3-2.2) for the follow-up period that began around 1970. Men whose BMI was 25.0-29.9 kg/m^2 and those whose weight was normal had similar 15-year mortality rates. A BMI ≥30.0 kg/m^2 was related to increased 15-year mortality among never smokers and ex-smokers but not among current smokers. The HR for BMI ≥30.0 kg/m^2 among never smokers was slightly higher for the follow-up period starting around 1960 compared with that for the follow-up period that began around 1970.

Table 4.1.5 Hazard ratios (95%-confidence intervals) for all-cause mortality[a] among European men in the Seven Countries Study, by category of body mass index, for different lengths of follow-up starting around 1960[b]

Smoking category and length of follow-up (years)	Body mass index (kg/m^2)			
	<18.5	18.5-24.9	25.0-29.9	≥30.0
Never smokers				
15	2.1 (0.8-5.7)	1	1.3 (0.9-1.7)	1.8 (1.2-2.8)
20	1.8 (0.8-4.1)	1	1.1 (0.9-1.4)	1.9 (1.4-2.6)
25	1.6 (0.8-3.2)	1	1.1 (0.9-1.3)	1.8 (1.4-2.4)
Ex-smokers				
15	2.0 (0.5-8.2)	1	1.0 (0.7-1.3)	1.3 (0.8-2.1)
20	1.0 (0.3-4.2)	1	1.1 (0.8-1.4)	1.5 (1.0-2.2)
25	2.1 (0.8-5.1)	1	1.3 (1.0-1.5)	1.6 (1.2-2.3)
Current smokers				
15	2.1 (1.5-2.8)	1	0.9 (0.8-1.1)	1.0 (0.7-1.4)
20	1.8 (1.4-2.4)	1	0.9 (0.8-1.1)	0.9 (0.7-1.2)
25	1.5 (1.2-1.9)	1	1.0 (0.9-1.1)	1.0 (0.8-1.3)

a Mortality during the first five years of follow-up was excluded.
b Adjustments were made for age and study centre.

If mortality during the first five years after baseline was not excluded, the HRs for underweight were generally larger than when early mortality was excluded. HRs for BMI of 25.0-29.9 kg/m^2 and for BMI ≥30.0 kg/m^2 were similar when early mortality was excluded or included and were also similar in northern Europe, inland southern Europe, Mediterranean southern Europe, and Serbia (data not shown).

As shown in table 4.1.4, the HR for BMI <18.5 kg/m^2 around both 1960 and 1970 was 1.5 (95 percent CI: 0.9-2.4) for the 15-year follow-up period starting around 1970; a BMI of 18.5-25.0 kg/m^2 around both 1960 and 1970 was considered the reference category. The HR was 1.8 (95 percent CI: 1.3-2.5) for men who reduced their BMI to <18.5 kg/m^2 between 1960 and 1970. These HRs were similar to the HR for all men whose BMI was <18.5 kg/m^2 around 1970; again, the category of all men whose BMI was 18.5-29.9 kg/m^2 around 1970 was used as the reference. Also shown in table 4.1.4 are HRs, within smoking categories, for men whose BMI was ≥30.0 kg/m^2 around 1960 and 1970 and HRs for men whose BMI increased to ≥30.0 kg/m^2 between these years. These HRs were similar to those found within the smoking categories for all men whose BMI was ≥30.0 kg/m^2 around 1970; men whose BMI was 18.5-24.9 kg/m^2 around 1970 were considered the reference group.

The HRs of mortality for BMI <18.5 kg/m^2 among never and current smokers declined with the length of follow-up (table 4.1.5). HRs for BMI ≥30.0 kg/m^2 among

never and ex-smokers were not associated with the length of follow-up. Among current smokers, BMI≥ 30.0 kg/m^2 was not related to increased mortality.

Discussion

This study showed that BMI <18.5 kg/m^2 was clearly related to excess all-cause mortality among men aged 40-59 years followed for 15 years. Similar results were found when the survivors were ten years older and were followed for another 15 years. A BMI 25.0-29.9 kg/m^2 was not associated with mortality, but BMI ≥30.0 kg/m^2 was related to excess mortality among never and ex-smokers. The highest HR for BMI ≥30.0 kg/m^2 was found for never smokers aged 40-59 years. A BMI of more than 30.0 kg/m^2 was not related to excess all-cause mortality in current smokers.

For never and current smokers, the association between BMI <18.5 kg/m^2 and all-cause mortality tended to decrease with an increasing follow-up period. Explanations for decreasing HRs with longer follow-up include a higher mortality rate during longer follow-up periods and confounding by the presence of subclinical illness. In this study, we tried to minimise the effects of underlying illness on mortality by excluding the first five years of follow-up, although excluding early mortality will not fully guarantee the absence of confounding by subclinical illness.[27] No information was available regarding intentional versus unintentional weight loss, which made it difficult to interpret the higher mortality rate among those with a low BMI. Increased mortality associated with weight loss is reported previously.[22,28] It has been hypothesised that higher mortality among those with a low BMI is the result of low lean body mass rather than low fat mass.[29]

Among men non-smokers, the finding that the HR of increased mortality for BMI ≥30.0 kg/m^2 was not associated with the length of follow-up supports the hypothesis that a BMI of ≥30.0 kg/m^2 is also related to excess mortality among old men. HRs are expected to decrease with longer follow-up periods as subjects are followed until old age. Thus, mortality rates are higher for a longer follow-up period.

The finding that a BMI of 25.0-29.9 kg/m^2 was not related to mortality concurs with Sjöström's conclusion that it may well be that the BMI range associated with minimal mortality shifts upward with increasing age.[8] Andres *et al.* found that for persons more than 50 years of age, the mortality rate was lower for those whose BMI was 25.0-27.5 kg/m^2 than for those whose BMI was about 22.5 kg/m^2.[13] Rissanen *et al.* observed that minimal mortality among men more than 75 years of age occurred

for those whose BMI was 28-31 kg/m^2.[2,2] It cannot be concluded, however, that a BMI of 25.0-29.9 kg/m^2 is an optimal range for old men. Although Shaper *et al.* found a low mortality rate among men whose BMI was 24-30 kg/m^2 they also found an elevated risk for incident cardiovascular events and diabetes in this BMI range.[6]

BMI ≥30.0 kg/m^2 was not related to increased mortality among current smokers. Lee *et al.* also showed BMI-mortality associations separately for smoking categories. Although they found a U-shaped relation between BMI and mortality among current smokers, the HRs for BMI ≥30.0 kg/m^2 among smokers were clearly lower than among non-smokers.[4] In the present study, absolute risks of all-cause mortality among smokers were higher than among never smokers (tables 4.1.1 and 4.1.2). Smoking is such a dominant risk factor for increased mortality that overweight adds only a small additional risk to the already increased absolute risk among smokers. By using Framingham Heart Study data, Sempos *et al.* assessed the relation between metropolitan relative weight and mortality among subjects aged 28-62 years. They concluded that an interaction not necessarily exists between smoking and body weight.[30] As smoking is often reported as a confounder and in some studies as an effect modifier for the relation between overweight and mortality rate, however, it seems sensible in further research to stratify the associations into categories of smoking.

One strength of the present study was that the same cohort of men was followed during more than one period, and a second mortality follow-up was started ten years after the first. As mentioned previously, the advantage of our study design was that a cohort effect was impossible. BMI categories around 1960 and 1970 did not comprise the exact same men, but a change in BMI categories did not affect the results. As far as we know, the present study is the first to analyse the BMI-mortality relation using this study design. It also included centres from many parts of Europe. Analyses were similar for different regions of Europe. Thus, it is appropriate to generalise our results to ageing European men. Note, however, that the data were collected years ago, when smoking was more common among men than nowadays.

Conclusion

We concluded that BMI <18.5 kg/m^2 was clearly associated with increased mortality. A BMI ≥30.0 kg/m^2 was more prevalent in older men and was associated with increased mortality in ex- and never smokers. Underweight in all smoking categories and severe overweight in ex- and never smokers remain important predictors of increased mortality in middle-aged men when they get older.

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Chapter 4.2

A COMPARISON OF BODY MASS INDEX, WAIST-HIP RATIO AND WAIST CIRCUMFERENCE AS PREDICTORS OF ALL-CAUSE MORTALITY AMONG THE ELDERLY. THE ROTTERDAM STUDY

Abstract The aim of this study was to compare body mass index (BMI), waist-hip ratio, (WHR) and waist circumference as predictors of all-cause mortality among the elderly. Data were available from 6,296 men and women who participated in the Rotterdam Study, a population-based cohort study. Participants were aged 55-102 years at baseline and mean duration of follow-up was 5.4 years. Sex-specific all-cause mortality was compared between quintiles of BMI, WHR, and waist circumference and between predefined categories of BMI, and waist circumference, stratified for smoking category. High quintiles of waist circumference, but not high quintiles of BMI and WHR were related to increased mortality among never smoking men, without reaching statistical significance. Only the highest category of BMI (BMI ≥30.0 kg/m^2) among never smoking men was related to increased mortality, compared to normal BMI (hazard ratio 2.6 (95% confidence interval: 1.3-5.3)). Waist circumference between 94 and 102 cm and waist circumference 102 cm and larger were related to increased mortality compared to normal waist circumference (hazard ratios 1.7 (95% confidence interval: 1.1-2.8) and 1.6 (95% confidence interval 1.0-2.8), respectively). The proportion of mortality attributable to large waist circumference among never smoking men was three-fold the proportion attributable to high BMI. Among never smoking women and ex- and current smokers, categories of large body fatness did not predict increased mortality. It is concluded that, among never smoking elderly men, waist circumference may have more potential for detecting overweight than the BMI.

Tommy LS Visscher, Jacob C Seidell, Anu Molarius, Deirdre van der Kuip, Albert Hofman, and Jacqueline CM Witteman. *Int J Obes* 2001;25: in press.

Introduction

A high body mass index (BMI) in the elderly is found to be related to increased mortality in some but not all studies. The BMI-mortality relation, however, seems to be less pronounced in elderly than in younger populations.[1-11] Explanations for the weaker BMI-mortality relation in the elderly are selective survival and the higher mortality rates among older populations. Another explanation is the different association between BMI and body fatness in older compared to younger populations, as the fat-free mass declines and the body height diminishes with ageing.[12,13]

Therefore, our study examined the usefulness of other measurements of body fatness than BMI to detect overweight in the elderly. The use of the waist circumference has been proposed as an index of intra-abdominal fatness and overall body fatness. At least in middle-aged populations a large waist circumference identified subjects at increased cardiovascular risk and with a high prevalence of other health outcomes.[14,15] BMI, waist-hip ratio (WHR) and the waist circumference are compared as predictors of increased all-cause mortality in the elderly.

Methods

Study population

The Rotterdam Study is a cohort study among 7,893 subjects aged 55 years and over from Ommoord, a suburb of Rotterdam, the Netherlands.[16] All 10,275 eligible participants were invited to participate, of which 78% responded. Baseline examinations took place from March 1990 until July 1993. The Medical Ethical Committee of Erasmus University Medical Centre approved the study and written informed consent was obtained from all participants. The original objective of the Rotterdam Study was to investigate determinants of chronic and disabling cardiovascular, neurogeriatric, locomotor, and ophthalmologic diseases. For the purpose of the present study, data were used from all 6,296 subjects who had full data on all three body fatness measurements and smoking.

Measurements

During a home visit, trained interviewers administered a questionnaire, including questions on smoking behaviour. Subjects were defined as never, ex- or current smokers at baseline. The home visit was followed by two extensive clinical examinations at a research centre in the suburb of Ommoord, which included

anthropometric measurements. Participants residing at homes for the elderly who were not able to visit the research centre because of a disability were examined at their home. Height and weight were measured with the participants standing without shoes and heavy outer garments. BMI was calculated as weight divided by height squared (kg/m^2). Waist circumference was measured at the level midway between the lower rib margin and the iliac crest with participants in standing position without heavy outer garments and with emptied pockets, breathing out gently. Hip circumference was recorded as the maximum circumference over the buttocks. WHR was consequently calculated as the ratio of waist circumference over the hip circumference.

Sex-specific quintile cut-off points were defined for BMI, WHR, and waist circumference for each smoking category (table 4.2.2). Predefined categories for BMI were defined according to the World Health Organization guidelines.[17] A BMI under 18.5 kg/m^2 was considered underweight; BMI 18.5-24.9 kg/m^2 as normal weight; BMI 25.0-29.9 kg/m^2 as grade I overweight; and BMI 30.0-39.9 kg/m^2 as grade II overweight, which is also referred to as obesity or severe overweight. Ranges include the left endpoint, not the right. One male and 22 female subjects, who had BMI over 40 kg/m^2 were added to the grade II overweight class. For the predefined categories of large waist circumference the sex-specific action levels suggested by Lean *et al.* were used.[18] Regarding men, we defined waist circumference under 79 cm as small, and waist circumference between 79 and 94 cm as normal. Waist circumference between 94 and 102 cm is above action level 1; waist circumference above 102 cm is above action level 2. Regarding women, we defined waist circumference less than 68 cm as small, and waist circumference between 68 and 80 cm as normal. Waist circumference between 80 and 88 cm is above action level 1, and waist circumference above 88 cm is above action level 2. Predefined categories of WHR were not assessed in relation to all-cause mortality. Only dichotomous classifications have been proposed regarding WHR and, while different cut-off points have been suggested for WHR, no consensus has been reached.[19]

Mortality follow-up

Information on vital status was acquired at regular intervals from the municipal authorities of Rotterdam. In addition, general practitioners in the study district of Ommoord provided computerised reports on the deaths of participants on a regular basis. General practitioners outside the study region were contacted yearly to obtain information on vital status. The end of follow-up was set at 1 January 1998. The mean duration of follow-up was 5.4 years.

STATISTICAL ANALYSIS

Sex-specific hazard ratios of all-cause mortality were calculated for BMI, WHR and waist circumference as continuous variables to study linear trends between the body fatness measurements and mortality using Cox's proportional hazards model (proc PHREG, SAS-version 6.12). To calculate whether there was a U-shaped relation between the body fatness measurements and mortality, a quadratic term was included in the model. Hazard ratios were also calculated for quintiles of BMI, WHR, and waist circumference. In addition, hazard ratios were calculated per predefined category of BMI and waist circumference. The second quintile and second predefined category of body fatness measurements were taken as the reference because the mortality rate was expected to be elevated at the lower end of the body fatness measurements, as at least observed for low BMI.[1-3,10] The population attributable fractions (AF_p) of mortality were calculated according to

$$AF_p = \frac{p(RR-1)}{p(RR-1)+1} \qquad \text{(formula 4.2.1)}$$

with p being the proportion of men in the body fatness category, and RR the corresponding hazard ratio.

Adjustments were made for age as a continuous variable, but not for levels of cholesterol and blood pressure. Cholesterol and blood pressure are possible intermediates in the causal chain between body weight and mortality.[20] Smoking is known to confound or modify the overweight-mortality relation.[2,3,20] Therefore, analyses were performed for never, ex- and current smokers separately.

Results

Average BMI was higher among women than among men. Mean WHR and waist circumference were higher among men than among women (table 4.2.1). BMI was not linearly related to increased mortality among never smoking men (p=0.93) and never smoking women (p=0.26) when assessed as continuous variable. WHR was linearly related to increased mortality in never smoking men (p=0.04), but not in never smoking women (p=0.98). Also waist circumference was linearly related to increased mortality in never smoking men (p=0.03), but not in never smoking women (p=0.64). In current and ex-smokers BMI, WHR and waist circumference were not linearly related to increased mortality.

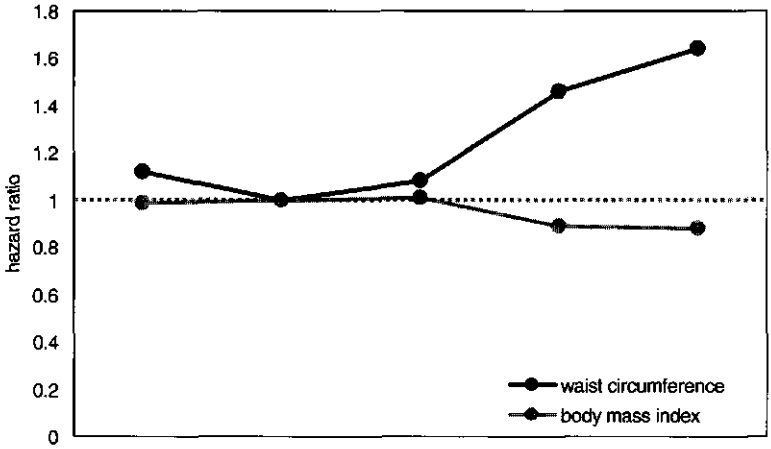
Table 4.2.1 Baseline characteristics (1990-1993) and follow-up data (until 1 January 1998) on participants of the Rotterdam Study

		Smoking category		
	Men	Current smokers	Ex-smokers	Never smokers
Number of subjects		631	1,547	424
Total person-years		3,332	8,167	2,210
Number of deaths		127	262	90
Age (years)		66.9 (7.9)[a]	68.1 (7.6)	69.9 (10.0)
Body mass index (kg/m^2)		24.9 (3.2)	26.0 (2.8)	25.5 (3.0)
Waist hip ratio		0.96 (0.07)	0.96 (0.07)	0.95 (0.07)
Waist circumference (cm)		92.9 (10.0)	95.1 (9.2)	93.4 (9.2)
	Women			
Number of subjects		678	1,026	1,990
Total person-years		3,804	5,764	10,959
Number of deaths		83	112	282
Age (years)		65.5 (7.4)[a]	68.1 (8.3)	71.5 (9.5)
Body mass index (kg/m^2)		25.9 (4.3)	27.0 (4.1)	26.9 (3.9)
Waist hip ratio		0.86 (0.09)	0.87 (0.09)	0.87 (0.09)
Waist circumference (cm)		85.8 (11.9)	88.0 (11.5)	88.3 (11.2)

a Mean (standard deviation)

A U-curved relation between BMI as continuous variable and mortality was observed in never smoking men (p for the quadratic BMI term is 0.00) and never smoking women (p=0.04). *P*-value for the quadratic WHR term was 0.06 for never smoking men and 0.55 for never smoking women. No U-curve was observed for the relation between waist circumference and mortality among never smoking men (p=0.10) and women (p=0.69). In the other smoking categories, statistical significance for a quadratic term was found for BMI and waist circumference in ex-smoking women, and for WHR in current smoking women.

High quintiles of BMI and WHR were not related to increased all-cause mortality among never smoking men (table 4.2.2). High quintiles of waist circumference, however, were related to increased mortality compared to the second quintile, although not statistically significantly (figure 4.2.1). Among never smoking women, and ex- and current smokers quintiles of BMI, WHR and waist circumference were not related to increased mortality (tables 4.2.2 and 4.2.3).



95% ci	0.5-2.6	ref	0.5-2.3	0.7-3.1	0.8-3.4
95% ci	0.5-1.9	ref	0.5-1.9	0.5-1.8	0.5-1.8

Figure 4.2.1 Age-adjusted hazard ratios of all-cause mortality among men who never smoked for quintiles of body mass index and waist circumference; Rotterdam Study
Ref. denotes reference category, 95% ci denotes 95% confidence interval around the hazard ratio

BMI ≥30.0 kg/m^2, but not BMI 25.0-29.9 kg/m^2 was related to increased mortality compared to BMI 18.5- 24.9 kg/m^2 among never smoking men (table 4.2.4). Both categories of waist circumference between 94 and 102 cm and waist circumference above 102 cm were related to increased mortality among never smoking men. Waist circumference larger than 94 cm (49%) was much more common than BMI above 30.0 kg/m^2 (7%) among never smoking men.

The proportion of mortality attributable to BMI above 30.0 kg/m^2 was 10.1% among never smoking men. The proportion of mortality attributable to a waist circumference larger then 94 cm was 27.6% among the never smoking men. Among never smoking women, and among ex- and current smokers predefined categories of BMI and waist circumference were not related to all-cause mortality (data not shown).

Table 4.2.2 Age-adjusted hazard ratios and 95% confidence intervals of all-cause-mortality for quintiles of body mass index, waist-hip ratio and waist circumference among men aged 55 years and older; Rotterdam Study (1990-1998)

	Quintiles				
Measurement (quintile cut-off points)	I	Reference	III	IV	V
Never smokers					
Body mass index (23.1 - 24.6 - 26.2 - 27.9 kg/m^2)	1.0 (0.5-1.9)	1	1.0 (0.5-1.9)	0.9 (0.5-1.8)	0.9 (0.4-1.8)
Waist hip ratio (0.89 - 0.93 - 0.96 - 1.00)	1.0 (0.5-2.2)	1	1.4 (0.7-2.8)	0.9 (0.4-1.8)	1.4 (0.7-2.6)
Waist circumference (86 - 90 - 95 - 101 cm)	1.1 (0.5-2.6)	1	1.1 (0.5-2.3)	1.5 (0.7-3.1)	1.6 (0.8-3.4)
Ex-smokers					
Body mass index (23.7 - 25.3 - 26.6 - 28.3 kg/m^2)	1.1 (0.8-1.6)	1	0.7 (0.5-1.1)	0.9 (0.6-1.4)	0.8 (0.6-1.2)
Waist hip ratio (0.90 - 0.94 - 0.97 - 1.01)	1.1 (0.7-1.7)	1	1.2 (0.8-1.8)	1.0 (0.7-1.5)	1.1 (0.7-1.6)
Waist circumference (88 - 93 - 97 - 102 cm)	0.9 (0.6-1.3)	1	0.7 (0.5-1.1)	0.8 (0.6-1.2)	0.8 (0.6-1.2)
Current smokers					
Body mass index (23.1 - 24.6 - 26.2 - 27.9 kg/m^2)	1.3 (0.8-2.1)	1	0.8 (0.4-1.3)	0.9 (0.5-1.6)	0.6 (0.3-1.1)
Waist hip ratio (0.89 - 0.93 - 0.96 - 1.00)	1.1 (0.6-2.0)	1	0.9 (0.5-1.7)	1.0 (0.6-1.7)	0.9 (0.5-1.6)
Waist circumference (86 - 90 - 95 - 101 cm)	1.2 (0.7-2.0)	1	1.0 (0.6-1.8)	1.0 (0.6-1.8)	0.8 (0.5-1.5)

Table 4.2.3 Age-adjusted hazard ratios and 95% confidence intervals of all-cause-mortality for quintiles of body mass index, waist-hip ratio and waist circumference among women aged 55 years and older; Rotterdam Study (1990-1998)

	Quintiles				
Measurement (quintile cut-off points)	I	Reference	III	IV	V
Never smokers					
Body mass index (23.6 - 25.5 - 27.5 - 30.0 kg/m^2)	1.0 (0.7-1.5)	1	0.8 (0.5-1.2)	0.8 (0.6-1.2)	0.8 (0.5-1.1)
Waist hip ratio (0.80 - 0.84 - 0.88 - 0.94)	0.9 (0.6-1.4)	1	1.1 (0.8-1.7)	1.0 (0.7-1.5)	1.0 (0.7-1.4)
Waist circumference (79 - 85 - 91 - 97 cm)	0.8 (0.5-1.3)	1	0.9 (0.6-1.3)	1.0 (0.7-1.4)	0.8 (0.6-1.1)
Ex-smokers					
Body mass index (23.6 - 25.6 - 27.5 - 30.3 kg/m^2)	1.3 (0.7-2.3)	1	1.2 (0.6-2.2)	1.3 (0.7-2.3)	1.0 (0.5-1.9)
Waist hip ratio (0.79 - 0.84 - 0.88 - 0.93)	1.2 (0.6-2.4)	1	1.3 (0.7-2.3)	1.1 (0.6-2.1)	0.9 (0.5-1.6)
Waist circumference (78 - 85 - 90 - 97 cm)	1.5 (0.8-2.8)	1	1.1 (0.6-2.0)	0.9 (0.5-1.7)	1.2 (0.7-2.2)
Current smokers					
Body mass index (23.6 - 25.5 - 27.5 - 30.0 kg/m^2)	1.7 (0.8-3.7)	1	1.4 (0.6-3.0)	1.0 (0.5-2.4)	0.9 (0.4-2.1)
Waist hip ratio (0.80 - 0.84 - 0.88 - 0.94)	0.6 (0.3-1.6)	1	1.1 (0.5-2.3)	1.0 (0.5-2.1)	1.4 (0.7-2.7)
Waist circumference (79 - 85 - 91 - 97 cm)	0.7 (0.3-1.6)	1	0.5 (0.2-1.1)	0.9 (0.4-1.7)	0.9 (0.4-1.7)

Table 4.2.4 Population attributable fractions of all-cause mortality among men aged 55 years and older who never smoked never smoking elderly men for predefined categories of body mass index and waist circumference; Rotterdam Study (1990-98)

Body mass index (kg/m^2)	<18.5	18.5-24.9	25.0-29.9	≥30.0
Hazard ratio (95 % CI)[a]	4.5 (1.4-14.5)	Reference	0.8 (0.5-1.2)	2.6 (1.3-5.3)
Number of subjects	5	187	203	29
Population attributable fraction	3.4	Reference	N.C.	10.1
Waist circumference (cm)	**<79**	**79- 93.9**	**94-101.9**	**≥102**
Hazard ratio (95 % CI)[a]	1.0 (0.2-4.2)	Reference	1.7 (1.1-2.8)	1.6 (1.0-2.8)
Number of subjects	20	198	127	79
Population attributable fraction	N.C.	Reference	17.4	10.2

a Hazard ratios were adjusted for age
NC denotes not calculated because hazard ratio was equal to or smaller than one.
CI denotes confidence interval

Discussion

High quintiles of waist circumference, but not of BMI and WHR, predicted an increased risk of all-cause mortality among men who had never smoked. Analyses on predefined categories showed that waist circumference predicted increased mortality risk at a much lower level than BMI among these never smoking men. The fraction of mortality attributable to a large waist circumference (≥94 cm) was almost three times higher than the fraction attributable to a high BMI (≥30.0 kg/m^2) in never smoking men. Among never smoking women and ex- and current smokers, high levels of body fatness did not predict increased mortality. The use of waist circumference seems a promising alternative to BMI to detect overweight among elderly never smoking men.

BMI is not an optimal predictor of body fatness in the elderly, because body height diminishes and fat-free mass decreases with ageing.[12,13] We confirmed earlier findings that BMI ≥30.0 kg/m^2, but not BMI 25.0-29.9 kg/m^2, is related to increased mortality among never smoking elderly men.[1-3,10] Allison *et al.* calculated that for men aged 70 years and over minimal mortality occurred at a BMI between 27 and 30 kg/m^2, and for women at a level between 30 and 35 kg/m^2.[10]

We found only one other study that assessed the relation between waist circumference and all-cause mortality among the elderly. Larsson *et al.* found that in men aged 54 years and older mean BMI and waist circumference were similar in

those who died and those who survived a 4.5 years period of follow-up.[21] Seidell *et al.* showed that the sagittal waist diameter (waist depth), which is an alternative measurement for abdominal fatness, predicted subsequent mortality among men younger than 55 years, but not among men who were older than 55 years.[22] These two studies, however, did not take smoking into account, and thereby probably underestimated the role of abdominal fatness on mortality rates.

The relation between large waist circumference and increased mortality was found in never smoking men only, who constituted 16.3% of the men. It is not surprising that large levels of waist circumference did not predict mortality in ex- and current smokers. It was found earlier that relative risks of mortality for high BMI were lower among smokers than among never smokers.[2,3] Being overweight does not add a detectable risk to the high absolute risk of mortality older smokers already have, and controlling body weight to prevent early mortality seems thus most relevant in never smokers. The proportion of never smokers among the elderly in society will increase in the future to more than 16.3% as the participants of the Rotterdam Study grew up in a time period in which smoking was much more common than it is today. There is no reason to believe, however, that the relation between large waist circumference and increased mortality will be different among never smoking men from populations in which smoking is less common.

An explanation for the different relation between large waist circumference and all-cause mortality among men and women may be a relatively late onset of abdominal obesity among women compared to men. Among women, a redistribution of fat is seen after the menopause from the locations around the hips and buttocks to the abdominal region.[23] Also, levels of bioavailable endogenous estrogens are relatively increased in postmenopausal women with abdominal obesity.[24] Increased levels of estrogens in obese women may lead to a slightly increased risk of breast cancer, but may favourably affect risk of coronary heart disease. Possibly, the balance of these effects leads to a relatively reduced all-cause mortality rate among obese women who are older than menopausal age.[25,26] A large waist circumference predicted future coronary heart disease among women from the Nurses Health Study aged 60-65 years, but less strongly than among women aged 40-59 years.[27] Furthermore spinal shrinkage at older age[28] leading to a larger waist circumference even when amount of fat remains constant, could lead to different relations between waist circumference and body fat between men and women.

Quintiles of WHR were less clearly related to increased mortality than quintiles of waist circumference. In Japanese-American men aged 71-93 years, Kalmijn *et al.* found a positive association between quintiles of WHR and all-cause mortality, whereas quintiles of BMI were negatively related to all-cause mortality.[29] Larsson *et al.* found that in men aged 54 years mean WHR was higher in those who died than in those who survived a 4.5 years period of follow-up.[21] A large WHR, however, may not only reflect a large waist circumference, but also a small muscle area in the thigh measured, as shown by computed tomography.[30] In elderly populations lean body mass is known to decline with age.[11] The waist circumference is easier to interpret than the ratio between waist circumference and hip circumference (WHR), especially in the elderly.[31]

The participation rate of the Rotterdam Study was high, 78%, and included subjects with poor mobility as they were visited at home. Unfortunately we did not have complete data on life-threatening disease status at baseline and did not ask for weight change before baseline. Excluding subjects with a life-threatening disease would have made it possible to adjust for pre-mortal weight loss caused by pre-mortal morbidity. A more commonly used method to take into account an effect of pre-mortal weight loss on the relation between overweight and mortality, is to disregard mortality within the first few years of follow-up.[20] Obviously, our period of follow-up was too short to do so. Allison *et al.*, however, concluded from a large meta-analysis that this may have only a minuscule impact on the relative risks, especially for the categories of large body weight.[32]

Action levels used for waist circumference are based on studies by Lean *et al.*.[18] In their studies, which focused on middle-aged men and women, waist circumferences above the action levels were related to respiratory symptoms, increased levels of cardiovascular risk factors, increased prevalence of diabetes, low back pain and difficulties of physical functioning.[15] Measuring waist circumference is easy and can be done by individuals themselves. The reliability of self-measured waist circumference is high, at least in the middle-aged.[33] The action levels of 94 and 102 cm for men and 80 and 88 cm for women are currently widely recommended but it should be noted that they are still under debate.[19] To define age-specific action levels and to learn more about waist circumference as potential measurement of fatness among women, further studies are needed that assess waist circumference in relation to morbidity and disability. Morbidity and disability are highly important outcomes with regard to successful ageing.[34]

CONCLUSION

It was thought that being overweight is related to increased mortality risk among the elderly in a small number of individuals with extreme overweight. We conclude that measuring waist circumference in never smoking men detected more individuals that were at increased risk of mortality than did measuring BMI. The present study suggests that measuring waist circumference may have more potential for detecting overweight among elderly men than measuring BMI.

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Chapter 5.1

OVERWEIGHT, OSTEOARTHRITIS, AND THE RISK OF DISABILITY

Abstract Overweight and osteoarthritis are related to disability. Evidence for a relation between overweight and osteoarthritis is often based on non-representative studies. The relation between overweight and disability in the presence and absence of osteoarthritis has not been systematically evaluated. In a Finnish representative cohort study (Mini-Finland Health Survey), 5,625 men and women, aged 30 to 65 years, have been examined at baseline 1978/1980, and were followed until the end of 1995. Participation rate was higher than 90%. Categories of overweight were defined according to the World Health Organization guidelines. Osteoarthritis in knee and hip joints, chronic low back pain, shoulder joint impairment and neck pain were diagnosed at baseline in a clinical setting. Difficulties in everyday activities were assessed at baseline; work disability was evaluated during the follow-up. Overweight was associated with osteoarthritis and the other musculoskeletal disorders. Overweight was associated with difficulties in everyday activities at baseline and with risk of work disability during follow-up, among subjects both with and without osteoarthritis. Odds ratio of difficulties in everyday activities for subjects with both obesity and osteoarthritis was 7.9 (95% confidence interval: 4.4-13.9) compared to subjects with normal weight and no osteoarthritis. Relative risk of future work disability for subjects with both obesity and osteoarthritis was 2.4 (95% confidence interval: 1.3-4.3). It is concluded that control of body weight has great potential in reducing musculoskeletal disorders and disability in a healthy population. Moreover, control of body weight should get high priority in the treatment of osteoarthritis.

Tommy LS Visscher, Markku Heliövaara, Aila Rissanen, Jacob C Seidell, Paul Knekt, Matti Mäkelä, Antti Reunanen, and Arpo Aromaa. Submitted for publication.

Introduction

Overweight is an alleged risk factor for osteoarthritis in the knee and hip joints[1-4] and may have a role in other musculoskeletal disorders.[5-8] The evidence, however, is often based on non-representative studies. Both overweight and musculoskeletal disorders are strong determinants of disability.[1,8-12] The relation between overweight and the onset of disability in the presence and absence of osteoarthritis has not been systematically evaluated.

The present study elucidates the relations between overweight and clinically defined osteoarthritis, low back pain, shoulder joint impairment and neck pain in a general population. Moreover, the relation between overweight and the development of disability is assessed separately among subjects with and without osteoarthritis.

The Mini-Finland Health Survey is used for this purpose because of its unique combination of population based data on measured body weight, clinically diagnosed osteoarthritis, low back pain, shoulder joint impairment and chronic neck pain, comprehensive data on difficulties in everyday activities, and longitudinal data on work disability.[13]

Methods

Study population

The Mini-Finland Health Survey was carried out in 1978-1980 by the Mobile Clinic of the Social Insurance Institution in 40 areas of Finland.[13] A random sample was drawn from the population register and comprised 8,000 persons (3,637 men and 4,363 women) aged 30 years and over from 69 municipalities. A total of 7,219 persons, 90 percent of the sample, participated. The sample was highly representative for Finnish adults aged 30 years and over.[14] For the present study, the 2,714 men and 2,911 women who were aged 64 years or less were selected. Data on work disability is only relevant for this age-category, as 65 years is the age of retirement in Finland. For the longitudinal analyses on work disability, only those participants were included who were fit enough to work at baseline.

Measurements

Body mass index (BMI) was calculated as weight in kg divided by height in meters squared (kg/m^2). Four categories of BMI were defined according to the World Health Organization guidelines.[15] A BMI under 18.5 kg/m^2 was considered as

underweight, a BMI between 18.5 and 24.9 kg/m^2 as normal weight, a BMI between 25.0 and 29.930 kg/m^2 as grade-I overweight or moderate overweight, and a BMI between 30.0 and 39.9 kg/m^2 as grade-II overweight, also called severe overweight or obesity. Because of small numbers of subjects with BMI of 40.0 kg/m^2 or higher (grade-III overweight) these subjects were classified as grade-II overweight. Ranges include the lower limit, not the upper.

To screen all participants for musculoskeletal disorders, a specific structured interview for the musculoskeletal system was performed. Together with the invitation to attend the first health examination, the subjects received a questionnaire eliciting information about previous diseases, hospitalisations, operations, and medications. They were also asked to bring along all documents relevant for assessment of health status, such as drug prescriptions and medical records. In addition, specially trained nurses who were unaware of the interview results carried out a standardised joint function test. Subjects with disease history, symptoms, or findings suggestive of musculoskeletal diseases were invited to participate in a second diagnostic, clinical phase, on average three and a half months after the screening examination.[13] That the screening was sensitive was confirmed by inviting a randomly selected validation sample of 740 participants to the second phase, regardless of their screening status, for a validation study.[16] Of the 3,775 subjects who met at least one of the screening criteria, 3,434 (91.0%) participated in the second examination. Physical examinations were carried out by specially trained physicians who applied uniform diagnostic criteria, according to a standardised written protocol. A full medical history was taken comprising the development of the musculoskeletal symptoms, previous medical examinations, and any previous diagnosis. Immediately after the examination, the physicians made a final diagnosis based on medical history, symptoms, and clinical findings.

Osteoarthritis was diagnosed if there was either a convincing disease history or definite findings in the physical status of one or both knee or hip joints.[4,13] Physicians took detailed medical histories including the development of joint symptoms and previous examinations and diagnoses. The physicians also investigated all documents (X-rays, health records and doctor's certificates) that the subjects had been asked to bring along. Tenderness and mobility of the knee and hip were tested according to standard protocols regardless of the screening results.[4]

Low back pain was diagnosed if the subject had a convincing symptom history of chronic low back pain as well as symptoms during the preceding month and one or

more major pathologic findings upon physical examination. These included fingertip-floor distance of 25 cm or more at flexion, upper body rotation restricted to 25° or less, objective signs of back pain in motion, scoliosis of 20° or more, clearly straightened lumbar lordosis at inspection, Lasegue's test positive at 60° or less, or other severe abnormality. If the subject had both a convincing symptom and disease history, then the physician diagnosed low back syndrome even in the case of only a minor pathologic finding in any physical test.[5]

Shoulder joint impairment was defined as limited mobility in or pain from the joint. Active shoulder elevation was observed while standing or sitting, and was considered limited when less than 160°. Active shoulder rotation (combined internal and external rotation) was visually evaluated with the shoulder at 90° (passive) abduction. It was considered limited if the range of combined internal and external rotation was less than 120°. Any pain during passive or active movement, or any tenderness, was recorded.[7]

Chronic neck pain was diagnosed if there was a convincing history of severe, long-standing neck pain that had manifested symptoms during the previous month, a documented history of a previously diagnosed neck syndrome with convincing observable signs on physical examination, or mild or moderate neck pain with observable physical signs at the time of the examination. Current neck pain of short (<3 months) duration was not considered a neck syndrome.[8] For the purpose of the present study the existence of a low back pain syndrome, a shoulder joint impairment, or chronic neck pain was labelled as 'other musculoskeletal disorder'.

Information on difficulties in everyday activities was elicited from the basic health questionnaire and the health interview. Participants were assessed for their ability to perform physical functions without difficulty, with minor difficulties, with major difficulties or not at all. Subjects were defined as experiencing a difficulty in everyday activities if they had at least a minor difficulty in one or more of the following: carrying a 5kg bag, shopping, going to bed without help, cutting toenails, domestic cleaning, dressing, moving without restrictions, travelling by public transport, climbing one flight of stairs, walking 500 meters without a rest.

Information on work disability was obtained for all participants by a linkage with the nation-wide register of pensions granted to individuals by the Finnish Social Insurance Institution. Participants were followed from the start of the study in 1978/1980, until the end of 1995.

STATISTICAL ANALYSIS

Age-adjusted odds ratios of the presence of osteoarthritis and other musculoskeletal disorders at baseline per category of BMI were calculated using logistic regression (proc LOGISTIC, SAS-version 6.12).

Odds ratios of difficulties in everyday activities were calculated per category of BMI adjusted for age and the presence of osteoarthritis. In addition, odds ratios were calculated separately among those with and without osteoarthritis. Those with BMI between 18.5 and 25.0 kg/m^2 and no osteoarthritis were then taken as the reference category. Relative risks of future work disability, adjusted for age and the presence of osteoarthritis, were calculated per category of BMI using Cox's Proportional Hazards model (proc PHREG, SAS-version 6.12). In addition, relative risks were calculated separately among those with and without osteoarthritis. Those with BMI between 18.5 and 24.9 kg/m^2 and no osteoarthritis were then the reference. Furthermore, odds ratios of difficulties in everyday activities and relative risks of work disability were adjusted for the presence of the other musculoskeletal disorders. When calculations were performed for those with and without musculoskeletal disorders separately, those with BMI between 18.5 and 24.9 kg/m^2 and no other musculoskeletal disorder were taken as the reference category. The fraction of work disability that was attributable to overweight (BMI ≥25.0 kg/m^2) and osteoarthritis was calculated by the use of formulas 5.1.1 and 5.1.2.

$$AF_p = \frac{\sum p_c(RR_c - 1)}{1 + \sum p_c(RR_c - 1)} \qquad \text{(formula 5.1.1)}$$

with AF being the attributable fraction, c the category of subjects, p the proportion of men in the category, and RR the corresponding relative risk.

$$AF_f = \frac{p_c(RR_c - 1)}{\sum p_c(RR_c - 1)} * \frac{\sum p_c(RR_c - 1)}{1 + \sum p_c(RR_c - 1)} \qquad \text{(formula 5.1.2)}$$

with AF_f being the fraction of the attributable fraction due to a specific (combination of) risk factors, c the category of subjects, p the proportion of men in the category, and RR the corresponding relative risk.

Results

About half of the men and women were overweight (BMI ≥25.0 kg/m^2), and 11%-16% of them were obese (≥30.0 kg/m^2) (table 5.1.1). About three percent of the men and nearly ten percent of the women had osteoarthritis in the knee joint. About two percent of men and three percent of women had osteoarthritis in the hip joint. Osteoarthritis in hips and especially in knees was strongly associated with overweight. The odds ratio of knee osteoarthritis for obesity was 2.7 (95% confidence interval: 1.5-5.1) among men and 4.3 (95% confidence interval: 3.0-6.2) among women (table 5.1.2). Low back pain, shoulder joint impairment, and chronic neck pain were more common among men with BMI between 25.0 and 29.9 kg/m^2, but the prevalence was not increased in men with BMI ≥30.0 kg/m^2. These musculoskeletal disorders were more common in women with BMI between 25.0 and 29.9 kg/m^2, and in women with BMI ≥30.0 kg/m^2 (table 5.1.2).

Table 5.1.1 Subjects (%) per category of body mass index among subjects aged 30 to 65 years; Mini-Finland Health Survey

		Body mass index (kg/m^2)			
Sex	Number	<18.5	18.5 - 24.9	25.0 - 29.9	≥30.0
Men	2,727	0.5	43.3	44.9	11.3
Women	2,946	1.2	50.0	32.5	16.4

Table 5.1.2 Age-adjusted odds ratios (95% confidence intervals) of chronic musculoskeletal disorders at baseline; Mini-Finland Health Survey

		Body mass index (kg/m^2)		
Men, n = 2,727	Total no. of cases (%)	18.5 - 24.9	25.0 - 29.9	≥30.0
Hip osteoarthritis	59 (2.2)	1	1.0 (0.5-1.8)	2.0 (1.0-4.1)
Knee osteoarthritis	89 (3.3)	1	1.6 (0.9-2.7)	2.7 (1.5-5.1)
Low back pain	471 (17.3)	1	1.3 (1.0-1.6)	1.1 (0.8-1.6)
Chronic neck pain	252 (9.2)	1	1.4 (1.0-1.8)	1.1 (0.7-1.7)
Shoulder joint impairment	108 (4.0)	1	1.5 (1.0-2.3)	1.0 (0.5-1.9)
Women, n = 2,946				
Hip osteoarthritis	92 (3.1)	1	1.8 (1.0-3.0)	1.9 (1.1-3.5)
Knee osteoarthritis	282 (9.6)	1	2.1 (1.5-3.0)	4.3 (3.0-6.2)
Low back pain	478 (16.2)	1	1.4 (1.1-1.7)	1.3 (1.0-1.7)
Chronic neck pain	412 (14.0)	1	1.4 (1.1-1.8)	1.5 (1.1-2.0)
Shoulder joint impairment	163 (5.5)	1	1.3 (0.9-1.9)	1.2 (0.8-1.9)

Body mass index below 18.5 kg/m^2 is not presented because of low numbers

Difficulties in everyday activities at baseline

A total of 2,257 men and women experienced at least one minor difficulty in one of the everyday activities listed in table 5.1.3. Difficulties in everyday activities were 1.4 to 3.2 times more common among obese subjects than among normal weight subjects (table 5.1.3). Also, osteoarthritis and the other musculoskeletal disorders were associated with difficulties in everyday activities at baseline in each BMI-category (figure 5.1.1). Overweight remained associated with difficulties in everyday activities when adjustments were made for the presence of osteoarthritis and for the presence of the other musculoskeletal disorders (table 5.1.4). Among subjects without osteoarthritis, the odds ratio of difficulties in everyday activities for obesity was 1.4 (95% confidence interval: 1.2-1.7) referred to normal weight. Among subjects with osteoarthritis, the odds ratio of difficulties in everyday activities for obesity was 1.9 (7.9 divided by 4.1) referred to normal weight. Among those with both obesity and osteoarthritis difficulties in everyday activities were 7.9 times (95% confidence interval: 4.4-13.9) more common than among those with normal weight and no osteoarthritis. Also, overweight was associated with difficulties in everyday activities among subjects both with and without other musculoskeletal disorders.

Table 5.1.3 Age- and sex adjusted odds ratios (95% confidence intervals) of difficulties in everyday activities at baseline; Mini-Finland Health Survey[a]

		body mass index (kg/m^2)		
Everyday activity	Number of subjects with difficulty	18.5 - 24.9	25.0 - 29.9	≥30.0
Getting in and out of bed	363	1	1.1 (0.9-1.5)	1.5 (1.1-2.0)
Cutting toenails	345	1	1.1 (0.9-1.5)	3.2 (2.3-4.2)
Carrying a shop bag or some other object of 5 kilos or so at least 100 meters	608	1	0.9 (0.7-1.1)	1.4 (1.1-1.7)
Heavy cleaning work (e.g. carrying and beating, cleaning windows)	1,935	1	1.2 (1.0-1.3)	1.7 (1.4-2.0)
Dressing and undressing	467	1	1.2 (0.9-1.5)	2.0 (1.6-2.7)
Shopping, going to a bank, office or similar establishment	536	1	1.0 (0.8-1.2)	1.6 (1.2-2.0)
Travelling by train, bus or tram	525	1	1.0 (0.8-1.3)	1.7 (1.3-2.1)
Moving	707	1	1.2 (1.0-1.5)	1.9 (1.5-2.4)
Climbing one flight of stairs without a rest	640	1	1.2 (1.0-1.5)	2.3 (1.8-2.9)
Walking a distance of about half a kilometre without a rest	740	1	1.2 (1.0-1.4)	2.2 (1.8-2.8)
A minor difficulty in at least one of above mentioned everyday activities	2,257	1	1.1 (1.0-1.3)	1.6 (1.3-1.9)

a Difficulties in everyday activities defined as 'minor difficulty' in at least one of the activities listed
Body mass index below 18.5 kg/m^2 is not presented because of low numbers

WORK DISABILITY DURING FOLLOW-UP

At total of 1,339 men and women were not fit enough to work at baseline. During the follow-up period, 490 work disability pensions were granted, and they were clearly related to overweight (figure 5.1.2). Osteoarthritis and the other musculoskeletal disorders were related to work disability in each BMI-category. Work disability remained associated with overweight after adjustment for the presence of osteoarthritis and after adjustment for the presence of other musculoskeletal disorders (table 5.1.5). Among subjects without osteoarthritis, the relative risk of developing work disability for obesity was 1.8 (95% confidence interval: 1.4-2.4) referred to normal weight. Among subjects with osteoarthritis, the relative risk of developing work disability for obesity was 1.3 (2.4 divided by 1.8) referred to normal weight. Among those with both obesity and osteoarthritis, work disability developed 2.4 times (95% confidence interval: 1.3-4.3) more often than among those with normal weight and no osteoarthritis. Also, overweight was associated with the onset of work disability among subjects both with and without other musculoskeletal disorders.

Using the relative risk of work disability from figure 5.1.2A and the proportions of men and women per category, it can be calculated that 16.1% of the work disability pensions was attributable to overweight (BMI $\geq$25.0 kg/m^2) and osteoarthritis, of which 82.6% to overweight alone, 4.0% to osteoarthritis alone and 13.4% to having both overweight and osteoarthritis.

Table 5.1.4 Odds ratios (95% confidence interval) of difficulties in everyday activities at baseline; Mini-Finland Health Survey

	Body mass index (kg/m^2)		
Adjustment made for age, gender, and	18.5 - 24.9	25.0 - 29.90	$\geq$ 30.0
Baseline presence of osteoarthritis in knee or hip	1	1.1 (1.0-1.3)	1.4 (1.2-1.7)
Baseline presence of other musculoskeletal disorders[a]	1	1.1 (0.9-1.2)	1.6 (1.3-1.9)

a Other musculoskeletal disorders are low back pain, shoulder joint impairment or chronic neck pain
Body mass index below 18.5 kg/m^2 is not presented because of low numbers

Table 5.1.5 Relative risks (95% confidence interval) of future work disability; Mini-Finland Health Survey

	Body mass index (kg/m^2)		
Adjustment made for age, gender, and	18.5 - 24.9	25.0 - 29.90	$\geq$ 30.0
baseline presence of osteoarthritis in knee or hip	1	1.2 (1.0-1.5)	1.8 (1.4-2.3)
baseline presence of other musculoskeletal disorders[a]	1	1.2 (1.0-1.4)	1.8 (1.4-2.3)

a Other musculoskeletal disorders are low back pain, shoulder joint impairment or chronic neck pain
Body mass index below 18.5 kg/m^2 is not presented because of low numbers
Subjects who were not fit enough to work at baseline were exluded

Discussion

The present study shows a strong association between overweight and osteoarthritis of the knee and hip, and somewhat weaker associations between overweight and chronic low back pain, shoulder joint impairment and neck pain. Moreover, overweight was associated with difficulties in everyday activities at baseline and with increased risk of work disability during follow-up among both subjects with and without osteoarthritis and both with and without the other musculoskeletal disorders. The effects of overweight and osteoarthritis were multiplicative, resulting in an almost eight-fold risk of difficulties in everyday activities and a nearly 2.5-fold risk of work disability among subjects with both obesity and osteoarthritis. The relative risk of disability was higher for osteoarthritis than for overweight, but overweight was much more common than osteoarthritis. Therefore, more disability was attributable to overweight than to osteoarthritis.

The suggestion that overweight is associated with osteoarthritis is not new,[1-4,17-23] but evidence for a relation that is based on clinical data from a general population is scarce. In our population based study the presence of osteoarthritis was measured using the same objective protocol for every individual, regardless of their BMI level, which excludes reporting bias. We cannot, however, exclude the possibility that subjects became overweight as a result of suffering from osteoarthritis, but the available studies with longitudinal data strongly suggest that overweight predicts the onset of osteoarthritis during a follow-up.[20-23] The relation between overweight and osteoarthritis can be explained by the high pressure in overweight individuals on the weight bearing joints, such as knee and hip. The stronger association of overweight with osteoarthritis in the knee than in the hip is compatible with this explanation. Also, a metabolic explanation is possible, as suggested by the association between overweight and incident osteoarthritis in the hand.[18,20]

The findings concerning overweight and chronic low back pain, shoulder joint impairment and neck pain have been inconsistent in previous studies, of which many are beset with methodological problems.[5-8,24] The association between overweight and these musculoskeletal disorders in the present study was not straightforward. Among men, a BMI between 25.0 and 29.9 kg/m^2 was, but a BMI $\geq$ 30.0 kg/m^2 was not associated with these musculoskeletal disorders. Among women a BMI $\geq$30.0 kg/m^2 was not more associated with these musculoskeletal disorders than a BMI between 25.0 and 29.9 kg/m^2. It is possible that subjects with a BMI $\geq$ 30.0 kg/m^2 tend to avoid physically demanding tasks in general life and at work, and are therefore relatively protected from an onset of low back pain, shoulder joint

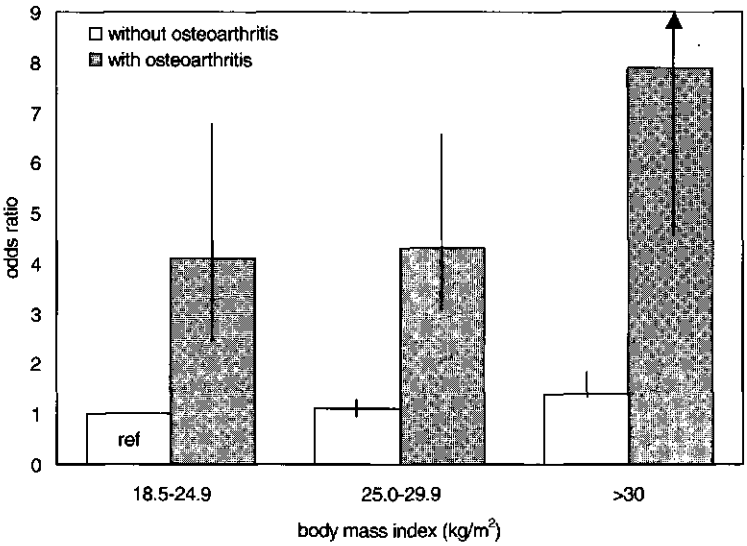

Figure 5.1.1a Age- and sex adjusted odds ratios with 95% confidence interval of difficulties in everyday activities at baseline, among subjects with and without osteoarthritis
Ref denotes reference category
Body mass index <18.5 kg/m² is not presented because of low numbers.

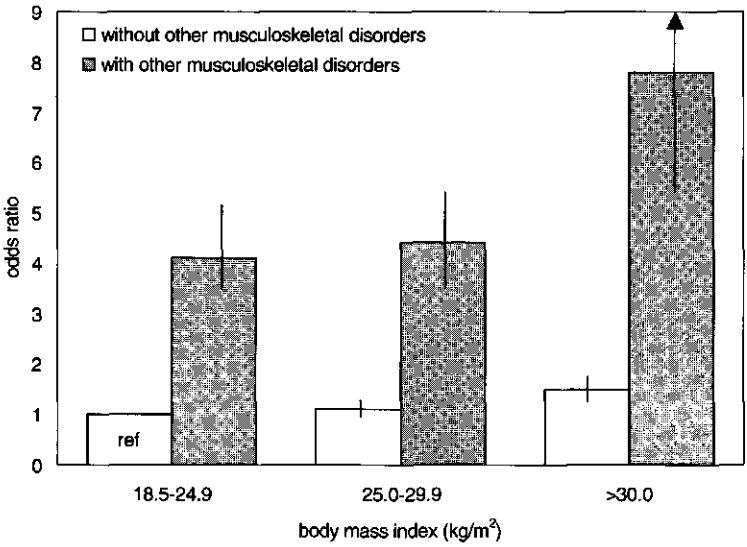

Figure 5.1.1b Age- and sex adjusted odds ratios with 95% confidence interval of difficulties in everyday activities at baseline, among subjects with and without other musculoskeletal disorders
Ref denotes reference category
Body mass index <18.5 kg/m² is not presented because of low numbers.

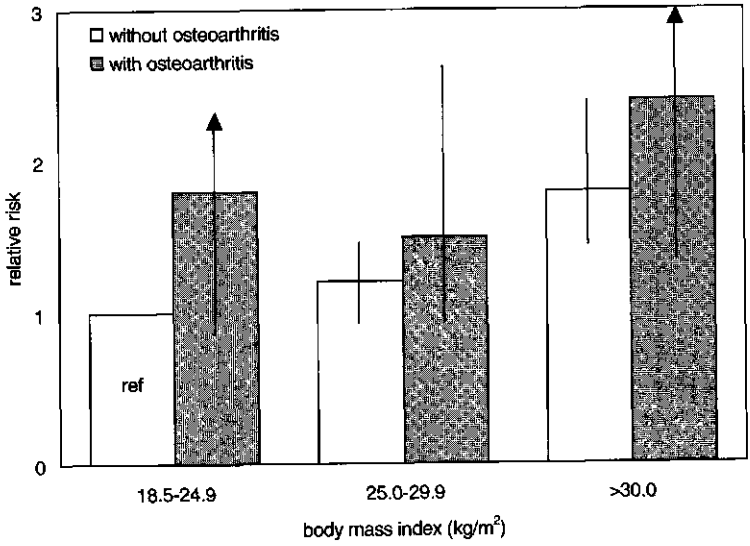

Figure 5.1.2a Age- and sex adjusted relative risks with 95% confidence interval of future work disability, among subjects with and without osteoarthritis
Ref denotes reference category
Body mass index <18.5 kg/m^2 is not presented because of low numbers.

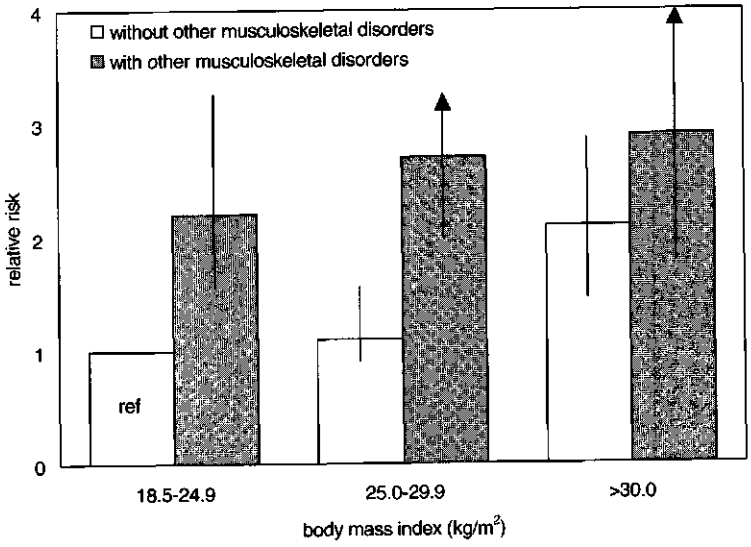

Figure 5.1.2b Age- and sex adjusted relative risks with 95% confidence interval of future work disability, among subjects with and without other musculoskeletal disorders
Ref denotes reference category
Body mass index <18.5 kg/m^2 is not presented because of low numbers.

impairment and chronic neck pain. The potentially causal relation between overweight and low back pain might be explained by high intradiscal pressure and increased stress in other spinal structures in overweight individuals.[5,6] Higher odds ratios of low back pain for high waist circumference than for high BMI, found by Han *et al.*, suggest that an altered gait in subjects with a large waist may have a causal role in the onset of low back pain.[25] Longitudinal studies should further assess the association between overweight and these musculoskeletal disorders.

The present study clearly shows the strong role of overweight in the onset of disability. First, overweight is associated with the presence of osteoarthritis, which is an important cause of disability. Second, overweight determines disability during follow-up in a healthy population without osteoarthritis or other musculoskeletal disorders. Third, even among patients with osteoarthritis or other musculoskeletal disorders, in which the risk of disability is already increased, overweight is an important extra risk factor for developing disability during follow-up.

Given the about 8-fold increased risk of difficulties in everyday activities and the nearly two-and-a-half-fold risk of future risk of work disability in obese osteoarthritis patients, a new paradigm of the treatment of osteoarthritis is warranted in which the control of body weight gets high priority. Lack of controlling body weight is a crucial risk factor for a vicious circle of gaining weight, developing osteoarthritis, developing disability, becoming less physically active and thereby gaining weight. The finding that relative risks of developing work disability were lower than the very high odds ratios of difficulties in everyday activities, could be explained by the exclusion of subjects with musculoskeletal disorders from the longitudinal analyses already work disabled. Also, subjects with musculoskeletal disorders experiencing difficulties in everyday activities could have had less physically demanding jobs, and could thus be protected from work disability.

Participation rate in the Mini-Finland Health survey was high (>90%), the set up was representative for the Finnish population, the screening phase was effective,[16] and all definitions of disease status were based on objective and clinical definitions by professionals. We assumed that all given prevalence data are very close to the prevalence in the Finnish population aged 30 to 65 years. Linking our population data to the incident work disability data of the Social Insurance Institution's nation-wide register was easily done by using the Finnish personal identity code. There is no indication suggesting that our results cannot be generalised to other western societies.

Conclusion

Overweight determines chronic musculoskeletal morbidity, especially the prevalence of osteoarthritis. Overweight also independently predicts the development of disability. Control of body weight has great potential in reducing musculoskeletal disorders and disability in a healthy population. Moreover, control of body weight should get high priority in the treatment of osteoarthritis.

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Chapter 5.2

THE POTENTIAL EFFECT OF WEIGHT GAIN PREVENTION ON THE INCIDENCE OF OSTEOARTHRITIS AND WORK DISABILITY

Abstract Obesity is related to osteoarthritis and work disability. For the purpose of this study, the mathematical Chronic Diseases Model was used to study the potential effect of prevention of small weight gain on the incidence of knee osteoarthritis and work disability in the Dutch working aged population. Input data for the model were required on baseline distribution of body mass index (BMI) categories, general and BMI-specific occurrence of osteoarthritis and work disability, and on all-cause mortality rates. A weight gain prevention program was simulated in which nobody changed between BMI categories during a follow-up of ten years. BMI categories were defined as BMI <22.5, BMI 22.5-24.9, BMI 25.0-27.4, BMI 27.5-29.9, BMI 30.0-32.4, and BMI ≥32.5 kg/m^2. If weight gain prevention was carried out during a period of ten years, the increase in the prevalence of obesity with 3.5 percentage points, which would have occurred without prevention, was prevented. Consequently, there were 8,000 (5%) fewer new cases of osteoarthritis in men and 18,000 (6%) in women, if weight gain was prevented. In addition, 6,000 (2%) cases of work disability in men and 13,000 (3%) in women could be prevented by weight gain prevention during a follow-up of ten years. Although results should be interpreted with caution, it can be concluded that prevention of small amounts of weight gain, are potentially effective in preventing large number of osteoarthritis and work disability. The present results are supportive to put effort in taking action in the field of weight gain prevention.

Tommy LS Visscher, Rudolf T Hoogenveen, and Jacob C Seidell. Submitted for publication.

Introduction

The prevalence of obesity has increased steadily during the last few decades of the 20th century in western societies.[1] Increasing obesity prevalence rates have consequences for public health, because obesity is related to excess mortality and to excess morbidity and disability in particular.[2] The role of obesity in cardiovascular diseases and type 2 diabetes mellitus is well accepted.[3] In addition, evidence is accumulating that obesity is related to musculoskeletal disorders such as osteoarthritis.[4-9] Osteoarthritis, in turn, is an important risk factor for work disability. Obesity is also linked to disability independently from osteoarthritis (chapter 5.1). A longitudinal study in a Finnish representative population showed that obesity was related to the onset of work disability due to cardiovascular diseases, musculoskeletal disorders and accidents that occurred most often in obese subjects.[10] Based on a study on obese Swedish women, it has been calculated that approximately 10% of the total cost of loss of productivity due to sick leave and work disability is attributable to morbid obesity.[11]

Weight gain is the result of an imbalance between energy intake and energy expenditure. Small changes in energy balance may lead to relatively large yearly weight chances.[12,13] For instance, a reduction in energy expenditure of 20 kcal/day is estimated to lead to one kg weight increase per year. If large yearly changes in body weight could indeed be prevented, prevention of minor changes in the energy balance may be important for prevention of disease and disability.

The present study assessed the impact of partial prevention of relatively small positive changes in the energy balance on the incidence of knee osteoarthritis and work disability. For this purpose, we used mathematical modelling to assess the effects of a reduction in weight gain at the level of the Dutch working-aged population.

Methods

Study population

The Dutch population aged 20-59 years serves as study population in our mathematical model. Age 60-64 years is the general age of retirement in the Netherlands, as in most other European countries. The five-years age distribution in the Netherlands in 1994 was derived from Statistics Netherlands.[14]

Mathematical simulation model

The Chronic Diseases Model was used to simulate the study population's life course regarding changes in body mass index (BMI). The Chronic Diseases Model is a dynamic multistage life-table based model, which has been constructed at the National Institute of Public Health and the Environment. Yearly time steps are simulated in which subjects change between risk factor categories; BMI categories in the present study. By manipulating these time steps, different changes in BMI level can be evaluated regarding different outcomes of disease and disability. Input data are required regarding the baseline distribution of BMI categories in the study population, on the general occurrence of disease or disability in the study population, and on BMI specific incidence of disease and disability. For the purpose of the present study the occurrence of new osteoarthritis and work disability was evaluated after ten yearly time steps.

Body mass index categories

Distribution of BMI at baseline is derived from the Dutch Monitoring on risk factors for chronic diseases (MORGEN) project 1993-1997 on subjects aged 20-59 years (chapter 3.1). Changes in BMI for those who become older than 60 during follow-up is derived from the Rotterdam Study.[15] BMI is calculated as body weight divided by height squared (kg/m^2). BMI categories were defined as follows: BMI <22.5, 22.5-24.9, 25.0-27.4, 27.5-29.9, 30.0-32.4, and ≥32.5 kg/m^2. Overweight is defined as BMI 25.0-29.9 kg/m^2 and obesity as BMI ≥30.0 kg/m^2 by the World Health Organization.[12]

Osteoarthritis

Input data on the general incidence of knee osteoarthritis, regardless of BMI, is estimated from the Dutch studies EPOZ and CMR-Nijmegen. In EPOZ nine cases of knee osteoarthritis occurred per 1,000 person-years in men and 24 cases of knee osteoarthritis occurred per 1,000 person-years in women. Subjects were aged 46-68 years at baseline 1975-1978. In 1988-1989, a radiograph was taken to define the presence of osteoarthritis. For our population aged 20-45 years, we also used data from EPOZ as input data in the Chronic Diseases Model. As osteoarthritis is more common in older than in younger ages, however, a correction on the EPOZ data had to made to derive incidence rates on subjects aged younger than 45 years and younger. This correction factor was based on the different occurrence in osteoarthritis between young men and women from CMR-Nijmegen. CMR-Nijmegen defined osteoarthritis symptomatically. Although this may lead to different incidence rates compared to radiographically defined cases, we assume that

the difference between old and young age groups may not differ with different case definitions. Data on the longitudinal relation between BMI and osteoarthritis in the knee were scarce, and most studies were not appropriate as input data in the Chronic Diseases Model for the purpose of the present study. One study presented an odds ratio for the third compared to the first tertile of BMI,[5] one presented relative risks for the highest two quintiles of Metropolitan Relative Weight,[6] two studies included symptomatic osteoarthritis in the case definitions,[7,8] and one study was based on recalled weight 35 years before the baseline.[9] Data from the Framingham Study was most appropriate to use as input data for the Chronic Diseases Model, although the age was higher (mean: 70 years, range: 63-92 years) than our study population.[4] It was assumed that relative risks of obesity for OA are similar across age-categories. The relative risk that was presented for men and women combined (1.6 per unit of BMI) was used as input data for the Chronic Diseases Model, under the assumption that the relation between BMI and osteoarthritis is similar in men and women. Although the presented relative risks differed between men and women, confidence intervals were widely overlapping. Relative risk for osteoarthritis was 1.0 (95% confidence interval: 0.5-2.2) in men and 1.8 (95% confidence interval: 1.2-2.6) in women per unit BMI. From the relative risk per unit BMI presented for men and women combined, relative risks were calculated per BMI-category for men and women separately, according to

$$RRi = 1.6\ \mathrm{EXP}((\text{mean BMI}i - \text{mean BMI}_{ref})/5) \qquad \text{(formula 5.2.1)}$$

with RRi indicating relative risk for BMI category i, and BMI_{ref} indicating the reference BMI category.

Work disability

Incidence data on work disability in the Netherlands were derived from the Dutch National Institute of Social Insurances (LisV). Working people are eligible to receive a work disability pension after 52 weeks of sick leave in the Netherlands. For the purpose of the present study, work disability was defined as 80-100% work disabled, which is the most severe category according to the LisV classifications. Relative risks for work disability were derived from a Finnish population-based cohort study that presented relative risks of BMI categories <22.5, 22.5-24.9, 25.0-27.4, 27.5-29.9, 30.0-32.4, and ≥32.5 kg/m^2. This study derived data on work disability from the Finnish Social Insurance Institution. Work disability was defined as 100% work disability in this study. BMI categories were based on

measured body weight and height. Follow-up on work disability was complete because of the use of the unique identity code for all individuals studied.[10] Only one other longitudinal study on the relation between BMI and work disability could be found, but this study comprised mainly severely overweight women.[11]

All-cause mortality

Standard mortality data in the Dutch population is derived from Statistics Netherlands.[14]

Weight gain prevention scenarios

The reference scenario is the situation in which no prevention of weight gain is undertaken during a period of ten years. For this reference scenario, we defined the increase in BMI and the prevalence of obesity according to the increases that are associated with increasing age. Age-related differences in mean BMI and the prevalence of obesity in the cross-sectional MORGEN project 1993-1997 were small enough to assume that prevention of such weight gain is potentially reasonably achieved. Regarding the main scenario on weight gain prevention, we defined yearly time steps such that no individual could change between BMI categories. In addition, we modelled weight gain prevention scenarios in which changes between BMI categories were not possible in individuals with BMI <27.5 kg/m^2 and in individuals with BMI ≥27.5 kg/m^2 separately.

Results

Obesity (BMI ≥30.0 kg/m^2) was present in 8.4% of the 4.5 million men and in 9.6% of the nearly 4.5 million women that comprised the study population aged 20-59 years at baseline (table 5.2.1).

If no prevention would be undertaken, mean BMI would rise with 0.9 kg/m^2 in both men and women. The prevalence of obesity would rise with 3.5 percentage points to 11.9% in men. In women, the prevalence of obesity would rise with 3.5 percentage point to 13.0% during a follow-up of ten years (table 5.2.1). Concurrently, about 175,000 and 320.000, new cases of knee osteoarthritis would occur in men and women, respectively, during the ten years of follow-up (table 5.2.2). Work disability would occur in more than 300,000 men and 450,000 women if weight gain was not prevented.

Table 5.2.1 Mean body mass index (kg/m^2) and the prevalence of obesity (%) in the Netherlands at baseline and ten years after baseline if no weight gain prevention would have been undertaken (according to the reference scenario)

	Age at baseline (years)								
	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	All
	Men and women per age group (%)								
Men (n=4.530.055)	0.14	0.15	0.14	0.13	0.13	0.13	0.10	0.08	
Women (n4.359.900)	0.14	0.15	0.14	0.13	0.13	0.13	0.10	0.08	
	Mean body mass index (kg/m^2)								
Men									
Baseline	23.3	23.9	24.5	25.0	25.5	26.0	26.4	26.7	25.0
Ten years after baseline	24.7	25.1	25.6	26.0	26.4	26.8	27.0	26.9	25.9
Change during follow-up	1.4	1.2	1.1	1.0	0.9	0.8	0.6	0.2	0.9
Women									
Baseline	23.2	23.4	23.7	24.1	24.6	25.2	25.9	26.5	24.4
Ten years after baseline	23.8	24.1	24.6	25.2	25.9	26.5	27.0	26.8	25.3
Change during follow-up	0.6	0.7	0.9	1.1	1.3	1.3	1.1	1.3	0.9
	Prevalence of obesity (%); Body mass index ≥30 kg/m^2								
Men									
Baseline	3.2	4.7	6.2	7.8	9.6	11.6	13.7	15.1	8.4
Ten years after baseline	6.7	8.5	10.2	11.8	13.7	15.6	16.6	15.6	11.9
Change during follow-up	3.5	3.8	4	4	4.1	4.0	2.9	0.5	3.5
Women									
Baseline	5.1	5.8	6.9	8.2	10.1	12.4	15.4	17.8	9.5
Ten years after baseline	7.5	8.5	10.0	12.1	14.8	18.0	20.3	19.2	13.0
Change during follow-up	2.4	2.7	3.1	3.9	4.7	5.6	4.9	1.4	3.5

If weight gain prevention would be undertaken at population level, mean BMI will not change in men and women. The prevalence of obesity will decrease with 0.3 percentage points in men and with 0.2 percentage points in women due to weight gain prevention at population level (table 5.2.2). If weight gain would be prevented, 8,000 (5%) and 18,000 (6%) new cases of osteoarthritis in men and women, respectively, could be prevented during the ten years follow-up (table 5.2.3). In addition, 6,000 (2%) and 13,000 (3%) new cases of work disability could be prevented in men and women, respectively, if weight gain was prevented in all individuals (table 5.2.4).

Table 5.2.2 Mean body mass index (kg/m^2) and the prevalence of obesity (%) in the Netherlands at baseline and after ten years if weight gain prevention had been undertaken at population level

	Age at baseline (years)								
	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	20-59
	Mean body mass index (kg/m^2)								
Men									
Baseline	23.3	23.9	24.5	25.0	25.5	26.0	26.4	26.7	25.0
Ten years after baseline	23.3	23.9	24.5	25.0	25.5	26.0	26.4	26.6	25.0
Change during follow-up	0.0	0.0	0.0	0.0	0.0	0.0	0.0	-0.1	0.0
Women									
Baseline	23.2	23.4	23.7	24.1	24.6	25.2	25.9	26.5	24.4
Ten years after baseline	23.2	23.4	23.7	24.1	24.6	25.2	25.9	26.4	24.4
Change during follow-up	0.0	0.0	0.0	0.0	0.0	0.0	0.0	-0.1	0.0
	Prevalence of obesity (%)								
Men									
Baseline	3.2	4.7	6.2	7.8	9.6	11.6	13.7	15.1	8.4
Ten years after baseline	3.2	4.7	6.2	7.7	9.5	11.4	13.3	14.4	8.1
Change during follow-up	0.0	0.0	0.0	0.1	-0.4	-0.2	-0.4	-0.7	-0.3
Women									
Baseline	5.1	5.8	6.9	8.2	10.1	12.4	15.4	17.8	9.5
Ten years after baseline	5.1	5.8	6.8	8.1	10.0	12.2	15	17.1	9.3
Change during follow-up	0.0	0.0	-0.1	-0.1	-0.1	-0.2	-0.4	-0.7	-0.2

If weight gain would be prevented in men and women with a BMI <27.5 kg/m^2, the number of knee OA cases that could be theoretically prevented was similar as if weight gain would be prevented in men with BMI ≥27.5 kg/m^2 (table 5.2.3). Among men the number of new cases of work disability that could be prevented was 1.5 times higher when weight gain was prevented in men with BMI <27.5 kg/m^2, compared to weight gain prevention in men with BMI ≥27.5 kg/m^2. Among women, the opposite was reported. Nearly three times more new cases of work disability could be prevented if weight gain was prevented in women with BMI ≥27.5 kg/m^2 than if weight gain was prevented in women with BMI <27.5 kg/m^2 (table 5.2.4).

Discussion

Prevention of a small amount of weight gain may prevent an increase in the obesity prevalence with 3.5 percentage points in both men and women from the Dutch population aged 20-59 years that would occur if no prevention would be performed.

Table 5.2.3 Number of new cases of knee osteoarthritis that could be prevented due to weight gain prevention in the Dutch working aged-population during a follow-up of ten years

	Category of subjects in whom weight gain prevention is carried out		
		Body mass index (kg/m^2)	
	All subjects	<27.5	≥27.5
Men			
five years after baseline	2,143	1,136	1,046
ten year after baseline	8,268	4,324	4,291
Women			
five years after baseline	4,776	2,471	2,414
ten year after baseline	18,413	9,367	9,996

Moreover, the prevalence of obesity was slightly decreased if prevention was carried out, e.g. if nobody changed to a higher BMI category. Consequently, 26,000 (5%) new cases of osteoarthritis and 19,000 (2.5%) new cases of work disability could be prevented among men and women, when the Dutch working-aged population was followed for ten years. The preventable incidence of knee osteoarthritis and work disability was higher in women than in men. Weight gain prevention in subjects with a BMI <27.5 kg/m^2 and in subjects with a BMI ≥27.5 kg/m^2 leaded to similar proportions of prevented osteoarthritis. Weight gain prevention in men with a BMI <27.5 kg/m^2 was somewhat more effective in preventing work disability then weight gain prevention in men with a BMI ≥27.5 kg/m^2. In women more work disability could be prevented by weight gain prevention in women with a BMI ≥27.5 kg/m compared to weight gain prevention in women with a BMI <27.5 kg/m^2.

Osteoarthritis is one of the most important risk factors for disability.[16] Osteoarthritis is a non-inflammatory damage of the joint, especially of the cartilage tissue. The relation between obesity and osteoarthritis may be explained by increased pressure on weight bearing joints. The stronger relation of obesity to osteoarthritis of the knee than of the hips is compatible with this explanation.[5] There might also be a metabolic explanation for the relation between obesity and osteoarthritis because obesity is also related to an increased risk of osteoarthritis in the hands.[5] Other musculoskeletal disorders that are possibly related to obesity are low back pain, shoulder joint impairment and chronic neck pain.[17-19] Longitudinal data on this subject, however, are scarce. Osteoarthritis is more common in elderly populations than in the present study population aged 20-59.years We suppose that weight gain prevention to avoid osteoarthritis is particularly important in elderly.

Table 5.2.4 Number of new cases of work disability that could be prevented due to weight gain prevention in the Dutch working aged-population during a follow-up of ten years

	Category of subjects in whom weight gain prevention is carried out		
		Body mass index (kg/m^2)	
	All subjects	<27.5	≥27.5
Men			
five years after baseline	1,494	956	565
ten year after baseline	5,539	3,526	2,245
Women			
five years after baseline	3,703	955	2,752
ten year after baseline	13,050	3,333	9,787

Obesity is clearly related to work disability. This relation may be, at least in part, explained by obesity-related osteoarthritis. Nonetheless, more work disability is attributable to obesity than to osteoarthritis (chapter 5.1). Other explanations for a relation between obesity and work disability are disabilities due to coronary heart disease and diseases of the back.[10] In men somewhat more work disability was prevented if weight gain prevention was carried out in those with a BMI <27.5 kg/m^2, whereas in women more work disability was prevented if weight gain prevention was carried out in those with a BMI ≥27.5 kg/m^2. This difference between men and women could probably be explained by a relatively stronger relation between moderate overweight and work disability in men and a stronger relation between severe overweight do work disability in women. Since men tend to have more physically demanding jobs, overweight might lead to work disability earlier in men than in women. Obesity has large economic consequences because of loss of productivity. It has been calculated that 10% of productivity loss due to sick leave and disability was attributable to obesity, according to a Swedish population of obese women.[11] It should be noted that productivity loss is estimated being 10% lower if *all* obesity could be prevented. Our estimation of a preventable 2% of work disability in men and 3% in women is based on prevention of a small amount of weight gain.

Mathematical modelling is a powerful tool to learn about potential efficacy of intervention strategies, such as weight gain prevention programs, on the incidence of disease and disability at population level. Results of mathematical modelling, however, should be interpreted with caution, because several assumptions have to be made on uncertainties. Regarding the present study, it could be questioned whether input data on the BMI distribution from the MORGEN project 1993-1997 is

representative for the Dutch population. Data were collected in three cities only, Amsterdam, Doetinchem, and Maastricht. In addition, higher educational levels were over-represented in the MORGEN project. Body weight is generally lower in high educational categories compared to lower educational categories in western societies. It cannot be established whether selective participation by BMI was disproportional across age groups. Such disproportional participation could lead to a biased estimate of the increase in BMI due to increasing age. Furthermore, longitudinal increases in BMI according to the reference scenario were calculated from cross-sectional data on age-related increases in BMI. Different age categories are from different birth years and it is not clear how BMI increased within each birth cohort. Moreover, an extra increase in BMI due to a time-trend in mean BMI and prevalence of obesity has not been taken into account. The increase in BMI according to the reference scenario would have been somewhat larger if a time-trend was taken into account, especially in those with high initial BMI. The secular increase in levels of BMI among those with low initial BMI is reported to be considerably low.

Relative risks of obesity for osteoarthritis and work disability that are used in the Chronic Diseases Model are based on a small number of studies and could not be derived from Dutch studies. An advantage of the studies that were selected to derive input data for the Chronic Diseases Model is that internal validity of these studies was high. The relative risks of BMI-categories for osteoarthritis presented by Felson *et al.* were based on longitudinal data. BMI was measured and not reported, which might have leaded to underestimation of body weight, especially in the subjects with high BMI. Osteoarthritis diagnosis was based on radiographs.[4] It would be of value, however, to be able to compare these relative risks, with wide confidence intervals, to more other longitudinal studies with similar methodology. The relative risks that we used in the model are relatively low compared to the few other longitudinal studies and the cross-sectional studies reported in table 5.2.2. A possible explanation is that there might be an interaction between obesity and high levels of physical activity levels in causing osteoarthritis. Intense physical activity in the Framingham Study (age: 63-93 years) of which data were used as input for the Chronic Diseases Model is likely less common than in our study population aged 20-59 years. Our estimations of preventable osteoarthritis by weight gain prevention may therefore be conservative for the age group 20-59 years. Internal validity of the study on BMI and work disability by Rissanen and *et al.* is also high.[19] Data were derived from a large population based cohort study. BMI was measured and follow-up data on work disability were complete because data were linked to the national

register on work disability pensions. Relative risks presented by Rissanen *et al.* were lower than the relative risks for work disability pensions in the study by Narbro *et al.*,[11] but in that study relative risks were presented for severe obesity. The definition of work disability was somewhat different in Finland and the Netherlands. Subjects in Finland who received a work disability pension were 100% work disabled. Subjects in the Netherlands were 80-100% work disabled. It is not clear whether the relation between obesity and these two definitions of work disability would differ.

Prevented changes in BMI in the present study were small and may seem reasonably to achieve. The maximum increase in mean BMI to be prevented was 1.3 kg/m^2 over a follow-up of ten years, in women aged 45-49 years, which corresponds with 0.40 kg weight change per year for a person with average height (1.70 m). A weight change in this order of magnitude is correlated with a crudely estimated change in the energy balance of 50 kcalories per week. Examples of energy intake and energy expenditure being associated with 50 kcalories are, respectively, half a glass of beer and twelve minutes of bicycling per week.[20,21] Successful weight gain prevention programs with long-term success on prevention of weight gain, however, have not been presented. The future challenge will be to develop and implement weight gain prevention programs. Some authors have suggested that new prevention programs will have to take into account the 'obesogenic environment.'[22] It is argued that weight gain is the result of a normal physiologic reaction to a pathologic environment, rather than a pathologic reaction to the environment.[23]

Conclusion

The potential effects of prevention of small weight changes on the public health have been presented in the present study. These large potential effects on the preventable incidence of osteoarthritis and work disability are supportive to put effort in taking action in the field of weight gain prevention.

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Chapter 5.3

OVERWEIGHT, OBESITY AND UNHEALTHY LIFE YEARS IN ADULT FINNS. AN EMPIRICAL APPROACH

Abstract Overweight and obesity have important impact on the incidence of several chronic diseases and on work disability. It is presently unknown how many more unhealthy life years obese subjects have compared to normal weight subjects. To compare the number of unhealthy life years between categories of body mass index (BMI), a representative cohort of 19,518 Finnish men and women aged 20 to 92 years were followed for a maximum of 15 years. Participation rate was 83%. We measured BMI at baseline and classified subjects into World Health Organization categories of overweight. We linked baseline BMI to incidence of work disability, hospitalisation for cardiovascular diseases and use of medication due to chronic diseases by record linkage. Obese subjects had increased relative risks for morbidity and disability. These relative risks exceeded those for mortality, and were highest in the youngest age groups. During a maximum follow-up of 15 years, obese men (BMI $\geq$30.0 kg/m^2) aged 20-64 years had 0.5, 0.4, and 1.7 more years of work disability, cardiovascular diseases, and morbidity leading to long-term medication, compared to men with normal weight (BMI 18.5-24.9 kg/m^2). Obese women suffered respectively 0.5, 0.4, and 1.3 more years from these conditions, compared to women with normal weight. In subjects aged 65 years and older, obesity increased the number of unhealthy years due to morbidity leading to long-term medication. From this study, it is concluded that obesity has an important effect on unhealthy life expectancy.

Tommy LS Visscher, Aila Rissanen, Jacob C Seidell, Markku Heliövaara, and Paul Knekt. Submitted for publication.

Introduction

Obesity often runs a long and disabling course with important health and economic consequences.[1,2] It is now well accepted that obesity contributes to the total burden of disease due to its role in the onset of cardiovascular diseases and type 2 diabetes mellitus.[3-6] Furthermore, evidence is accumulating that obese subjects develop more often osteoarthritis, suffer more from disability and have a lower quality of life than normal weight individuals.[7-9]

The direct health care costs due to obesity have been estimated at around 6% of the total health care expenditure in the United States[10] and at 1 to 5% in western European countries, where the prevalence of obesity is lower than in the United States.[11] Allison *et al.*, however, argued that direct health care cost estimations of obesity are probably over-estimations, since obesity not only induces disease and disability, but also reduces longevity.[12]

Thompson and colleagues did take into account the relation between obesity and reduced longevity when they calculated lifetime risks and economic consequences of obesity.[1] They calculated that the lifetime costs for treatment of hypertension, hypercholesterolaemia, type 2 diabetes mellitus, coronary heart disease, and stroke, among men aged 45 to 54 years, were $29,600 and $36,500 among those with body mass index (BMI) being 32.5 and 37.5 kg/m^2, respectively, compared to $19,600 among those with BMI being 22.5 kg/m^2.

Oster *et al.* calculated that 10% weight loss could reduce the number of life-years with hypertension with 1.2 to 2.9 years and the number of life-years with type 2 diabetes mellitus with 0.5 to 1.7 years.[13] These calculations, however, were based on mathematical modelling, rather than on empirical data.

The purpose of the present study was to calculate the number of years that obese subjects suffered more from disease and disability than subjects with normal weight did. The authors used data from The Finnish Social Insurance Institution's Mobile Clinic Unit following 20,000 Finns to study the impact of obesity on cardiovascular disease, reimbursement of medication due to chronic diseases, and work disability.

Methods

Study population

Between 1973 and 1977, the Social Insurance Institution's Mobile Clinic Unit carried out multiphase health examinations in twelve municipalities in four geographical regions of Finland.[14] The main emphasis was on the risk factors for cardiovascular disorders. In each of the four regions, all inhabitants or a random sample of inhabitants of one rural municipality and one urban or semi-urban municipality as well as the employees of one factory were invited to attend the examination. A total of 19,518 men and women participated in the examinations. The mean age of participants was 45.0 years (range: 20-92 years). Participation rate was 83%.

Measurements

A questionnaire with items concerning educational level, medical history, smoking and physical activity was sent to the subjects together with the invitation to the medical check-up, for completion before the examination. The answers to this self-filled questionnaire were checked and completed, if necessary, by a specially trained nurse at the examination.

Baseline

Body height and weight were measured at baseline when subjects were wearing light clothing. Body mass index (BMI) was calculated as weight divided by height squared (kg/m^2). Four categories of body weight were defined according to the World Health Organization guidelines.[15] BMI under 18.5 kg/m^2 was considered underweight. Results are not presented for the underweight category because of too small numbers. BMI 18.5- 24.9 kg/m^2 was considered normal weight, BMI between 25.0-29.9 kg/m^2 as grade-I overweight, also referred to as moderate overweight and a BMI between 30.0 and 39.9 kg/m^2 as grade-II overweight, also referred to as severe overweight or obesity. Subjects who had a BMI above 40.0 kg/m^2 (grade-III overweight) were added to the grade-II overweight category, because of small numbers in this category. Four categories of smoking habits were defined: - never smokers, - those who quitted smoking in the past, those who smoked fewer then 20 cigarettes per day at baseline or cigars only, those who smoked 20 cigarettes or more per day at baseline. Education was classified in three categories: <9 years; 9-13 years; >13 years. The questionnaire inquired about average alcohol consumption of beer, wine and strong alcoholic beverages during the proceeding month. The overall alcohol consumption was then calculated by multiplying the average intake in each

category by the average alcohol content of each beverage. For this study four categories were then defined as follows: 0, < 100, 100-500, and 500 or more grams of ethanol per month. The subjects were asked to classify their leisure-time activity during the usual week into one of three categories: 1) none or little; 2) walking, cycling, or related light activities, at least 4 hours per week; 3) ball games, jogging, or related activities at least 3 hours per week or regular vigorous activities.

Follow-up

Subjects aged 20-64 years were followed regarding work disability, hospitalisation due to coronary heart disease, morbidity leading to long-term medication, and all-cause mortality for a maximum of 15 years, until age 65 years. Age 65 years is the general age of retirement in Finland. Subjects aged 65 years or older were followed for a maximum follow-up of 15 years for all endpoints, except work disability.

Work disability

Unhealthy life years due to work disability were calculated as the time between onset of work disability until death or the end of follow-up. Work disability is defined as having a work disability pension from the National Social Insurance Institution. Finns are being granted a disability pension if they are expected to be work disabled during the rest of their lifetimes. Subjects who were work disabled at baseline were excluded from the analyses on work disability. Both baseline and follow-up data on work disability were derived by linkage of data to the Finnish Social Insurance Institution.

Coronary heart disease

Unhealthy life years due to coronary heart disease were classified as the time between hospitalisation for coronary heart disease until death or end of follow-up. Data on hospitalisation were derived from the Social Insurance Institution. Subjects with a history of cardiovascular diseases were excluded from the analyses on hospitalisation due to coronary heart disease. Data on cardiovascular diseases at baseline were obtained using specific questions: "Have you ever had, according to a physician's diagnosis, myocardial infarction, coronary heart disease, arterial hypertension, or cerebral stroke?"

Morbidity leading to long-term medication

Unhealthy life years due to morbidity leading to long-term medication is defined as the number of years between the onset of first reimbursement of medication due to chronic diseases and death or end of follow-up. In Finland, reimbursed drug therapy is provided for a number of chronic diseases, including common complications of obesity. Eligibility requires a comprehensive medical certificate written by the attending physician, and the evidence must be verified by an advisory physician of the Social Insurance Institution. Participants in the Mobile Clinic Health Examination Survey who later developed such chronic diseases were identified by linking the survey data with the Social Insurance Institution's population register, using the unique social security code assigned to each Finnish citizen. Most chronic diseases entitled to specially reimbursed medication meet commonly applied criteria, and the specificity of data is very high. Subjects who had reimbursed medication at baseline were excluded from the analyses on morbidity leading to long-term medication. During the follow-up most reimbursed medication was due to arterial hypertension (41%), cardiac failure (13%) bronchial asthma (9%), coronary heart disease (7%), and to diabetes (5%). The rest (25%) was due to 35 different less common chronic diseases other.

Statistical analysis

Relative risks for the onset of work disability, hospitalisation due to coronary heart disease, morbidity leading to long-term medication, and all-cause mortality per category of BMI have been calculated by using the Cox proportional Hazards model (proc PHREG, SAS-version 6.12). Adjustments were made for age, smoking, education, and alcohol intake. Additional adjustments were made for leisure time, physical activity, diastolic blood pressure, serum cholesterol, and self-reported diabetes. Relative risks were calculated for all smoking categories combined as well as for those who never smoked separately. Relative risks were also calculated per age group.

In addition, the number of unhealthy life-years years divided by the number of subjects at baseline per BMI-category was calculated by use of the generalised linear model (proc GLM, SAS-version 6.12). Adjustments were made for age, smoking, educational categories, and alcohol intake. Unhealthy life years were calculated for all smoking categories combined as well as for those who never smoked separately.

Table 5.3.1 Baseline characteristics in Social Insurance Mobile Clinic Unit Study; Number of subjects (%)

	<65 years		≥65 years	
	Men	Women	Men	Women
Body mass index (kg/m^2)				
<18.5 kg/m^2	86 (1.0)	288 (3.5)	25 (2.6)	24 (1.8)
18.5-24.9 kg/m^2	4,600 (51.6)	4,489 (53.9)	426 (43.9)	379 (29.0)
25.0-29.9 kg/m^2	3,467 (8.9)	2,426 (29.1)	402 (41.4)	523 (40.1)
≥30.0 kg/m^2	755 (8.5)	1,124 (13.5)	117 (12.1)	379 (29.0)
Smoking category, number (%)				
Never smokers	2,599 (29.2)	6,239 (74.9)	308 (31.8)	1.251 (95.9)
Ex,- current or cigar smokers	6.309 (70.8)	2.088 (25.1)	62 (68.2)	54 (4.1)
Cases at baseline, number (%)				
Work disability	813 (9.1)	743 (8.9)	a	a
Coronary heart disease	1,283 (14.4)	1,380 (16.6)	429 (44.2)	707 (54.2)
Morbidity causing long-term medication	853 (9.6)	1,194 (14.3)	311 (32.1)	1 (53.0)

a Work disability is relevant for <65 years only, as 65 is the general age of retirement in Finland

Results

In table 5.3.1 it is shown that 8.5% of the men and 13.5% of the women aged 20-64 years were obese. Overweight and obesity were more common after age 65 years than in younger subjects. Work disability at baseline was more common among men than among women, whereas cardiovascular diseases and chronic medication at baseline were more common among women than among men. Smoking was uncommon among women at baseline between 1973 and 1977.

In table 5.3.2 it is shown that obesity was more strongly related to the onset of work disability, hospitalisation due to coronary heart disease, and morbidity leading to long-term medication, than to all-cause mortality. The applied adjustment for educational level, geographical region, and alcohol intake, had negligible effect on relative risks. Additional adjustment for levels of physical activity did not alter relative risks (data not shown). Further adjustment for diastolic blood pressure, serum cholesterol level, and baseline presence of diabetes leaded to somewhat lower relative risks but relative risks were still statistically significant, except for work disability (data not shown). In subjects who never smoked, similar relative risks were found as when all smoking categories were combined. Obesity, however, was not related to increased mortality in women who never smoked (data not shown).

Table 5.3.2 Relative risks of work disability, hospitalisation due to coronary heart disease, morbidity leading to long-term medication, and all cause mortality during a maximal follow-up of 15 years until age 65 years

Endpoint	Subjects	Events	Body mass index (kg/m²) 18.5-24.9 (reference)	25.0-29.9	≥30.0
Men					
Work disability	8,046	1,341	1	1.1 (1.0-1.3)	1.7 (1.5-2.0)
Coronary heart disease	7,579	905	1	1.2 (1.1-1.4)	1.6 (1.3-2.0)
Morbidity leading to long-term medication	8,008	1,734	1	1.5 (1.4-1.7)	2.5 (2.2-3.0)
All-cause mortality	8,853	580	1	1.0 (0.8-1.1)	1.3 (1.0-1.7)
Women					
Coronary heart disease	6,924	409	1	1.6 (1.3-2.0)	2.6 (2.0-3.4)
Morbidity leading to long-term medication	7,103	1,470	1	1.5 (1.4-1.7)	2.2 (1.9-2.6)
All-cause mortality	8,291	161	1	0.8 (0.6-1.2)	1.2 (0.8-1.9)

Adjusted for age, smoking, educational level, geographical region, and alcohol use
Subjects with the condition studied at baseline were excluded from the analyses
All smoking categories are combined

Relative risks of overweight and obesity were generally highest in the youngest men and women. In men aged 20-34 years relative risk of obesity for work disability was 2.6 (95% confidence interval (CI): 1.5-4.6), and in women aged 20-34 years 1.9 (95% CI: 0.9-4.3), compared to men and women aged 20-34 years with normal weight. Relative risks of obesity for hospitalisation due to coronary heart disease were 1.8 (95% CI: 0.9-3.4) in men and 2.9 (95% CI: 1.4-6.3) in women aged 20-34 years. Relative risks of obesity for morbidity due to chronic diseases were 3.3 (95% CI: 2.3-4.8) in men and 2.3 (95% CI: 1.3-3.5) among women aged 20-34 years.

In table 5.3.3, it is shown that overweight and obese subjects had more unhealthy life years than normal weight subjects during a maximum follow-up period of 15 years. Obese men had 0.5 more unhealthy life years due to work disability, 0.4 more years of coronary heart disease and 1.7 extra years morbidity leading to long-term medication compared to normal weight men. Obese women had 0.5, 0.4, and 1.3 years due to these respective conditions. Never smokers had fewer unhealthy life years than was observed in all smoking categories combined, but the difference in unhealthy life years between obese, overweight, and normal weight never smokers was similar to the differences observed in all smoking categories combined (figure 5.3.1). A difference in number of unhealthy life years between normal weight and obese subjects was present in all age groups (data not shown).

Table 5.3.3 Average number of unhealthy life years[a] in men and women aged 20-64 years during a maximal follow-up of 15 years until age 65 years

Unhealthy life years due to:	Number of subjects	Unhealthy life years[a] Body mass index (kg/m^2) 18.5-24.9 (reference)	25.0-29.9	≥30.0
Men				
Work disability	8,046	0.70	0.80	1.19
Coronary heart disease	7,579	0.48	0.67	0.83
Morbidity leading to long-term medication	8,008	0.83	1.45	2.52
Women				
Work disability	7,558	0.71	1.01	1.24
Coronary heart disease	6,924	0.24	0.45	0.67
Morbidity leading to long-term medication	7,103	0.99	1.67	2.32

a Adjusted for age, educational level, geographical region, and alcohol intake
Subjects with the condition at baseline were excluded from the analyses

Table 5.3.4 Relative risks[a] of unhealthy life years subjects aged 65 years and older who never smoked during a 15-years follow-up

Unhealthy life years due to:	Subjects	Events	Body mass index (kg/m^2) 18.5-24.9 (reference)	25-29.9	>30.0
Men					
Coronary heart disease	176	72	1	1.3 (0.8-2.1)	1.4 (0.6-3.3)
Morbidity leading to long-term medication	203	78	1	2.5 (1.5-4.4)	2.8 (1.2-6.1)
All-cause mortality	305	148	1	1.3 (0.9-1.8)	2.0 (1.2-3.3)
Women					
Coronary heart disease	558	248	1	0.8 (0.6-1.0)	0.8 (0.6-1.1)
Morbidity leading to long-term medication	568	301	1	0.7 (0.6-1.0)	1.3 (1.0-1.7)
All-cause mortality	1,221	583	1	0.9 (0.7-1.1)	0.9 (0.8-1.2)

a Adjusted for age, educational level, geographical region, and alcohol intake
Subjects with the condition at baseline were excluded from the analyses

Among subjects aged 65 years and older who never smoked, obesity was related to hospitalisation due to coronary heart disease, morbidity leading to long-term medication, and all-cause mortality in men, not in women (table 5.3.4). The relations between obesity, hospitalisation for coronary heart disease and morbidity leading to long-term medication were less strong in men when all smoking categories were combined, but still statistically significant. (data not shown).

In figure 5.3.2, the number of unhealthy life years is presented for never smoking subjects over 65 years of age. The number of unhealthy life years due to coronary heart disease was not increased in obese subjects compared to their normal-weight counterparts. When smoking categories were combined, the number of unhealthy life years due to coronary heart disease was smaller than for never smokers alone. There was again no difference between the number of unhealthy life years due to coronary heart disease in obese and normal-weight elderly. The number of unhealthy life years due to morbidity leading to long-term medication was clearly elevated in never smoking obese men and women over 65 years of age compared to their normal weight counterparts. The number of unhealthy years due to morbidity leading to long-term medication was also smaller when smoking categories were combined, than when never smokers were analysed separately. Based on analyses for combined smoking categories, obese elderly men had 1.7 more years morbidity leading to long-term medication compared to normal weight counterparts. Obese elderly women had 1.4 more years morbidity leading to long-term medication then normal weight men and women, during a maximum follow-up of 15 years.

Discussion

Obesity predicted the onset of disease and disability most strongly in the youngest age-categories. Obesity was a stronger risk factor for disease and disability than for all-cause mortality. Consequently, obese subjects had more unhealthy life years than their normal weight counterparts. This is the first prospective study regarding the impact of obesity on number of unhealthy years. Comprehensive data on body weight, work disability, hospitalisation due to coronary heart disease, and the use of medication for chronic diseases were available from a representative cohort of Finns. This study clearly shows that obesity has great impact on relatively non-fatal outcomes, which is larger than the impact on mortality.

Relative risks of obesity for disease and disability were highest in the youngest age group. Large relative risks in young age groups and higher proportions of obesity in older age groups imply a large impact of obesity on disease and disability across all ages between 20-64 years. The obesity-related increase in unhealthy life years due to morbidity leading to long-term medication was larger than the obesity-related increase in unhealthy life years due to coronary heart disease. Two explanations could be given. First, relative risks of obesity were higher for morbidity leading to long-term medication than for hospitalisation due to coronary heart disease. Second, coronary heart disease is more often fatal than the various diseases that were combined in our definition of morbidity leading to long-term medication.

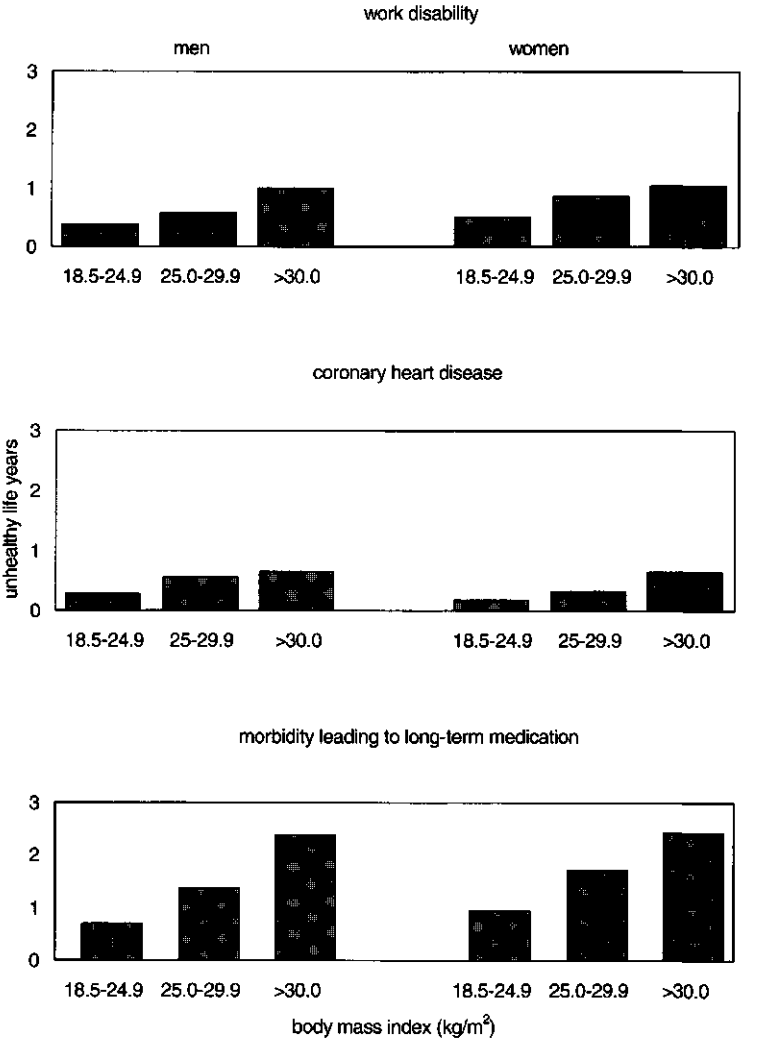

Figure 5.3.1 Average number of unhealthy life years due to work disability, coronary heart disease, and morbidity leading to long-term medication among never smokers aged 20-64 years during a maximum follow-up of 15 years until age 65 years
Subjects with the condition at baseline were excluded

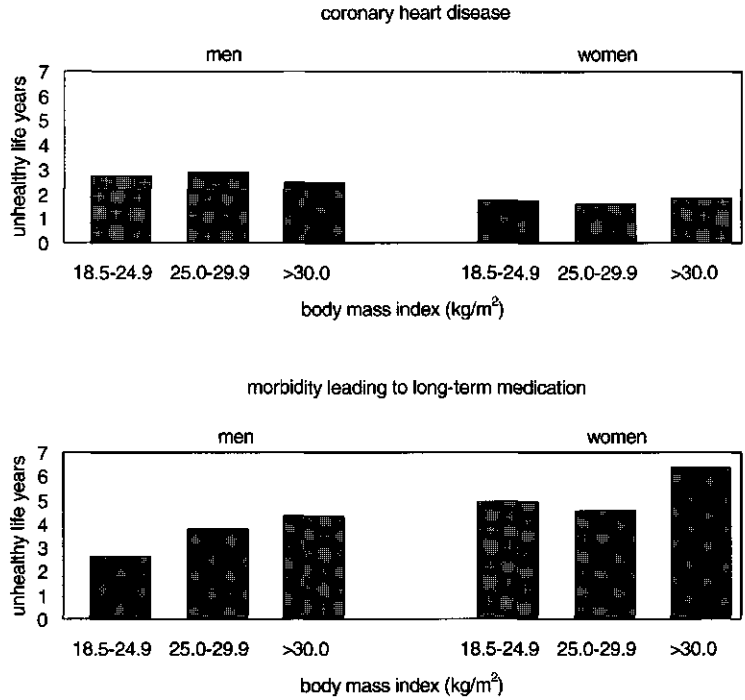

Figure 5.3.2 Average number of unhealthy life years due to coronary heart disease and morbidity leading to long-term medication among never smokers aged ≥65 years during a follow-up of 15 years Subjects with the condition at baseline were excluded

The latter possibly explains why obese subjects aged 65 years and older did not have more life years of coronary heart disease than normal weight subjects from this age, while the incidence of hospitalisation for coronary heart disease was clearly elevated in the obese. We suggest that this is explained by high mortality rates due to coronary heart disease in those aged 65 years and older. The absolute difference in years of morbidity leading to long-term medication between obese and normal weight subjects aged 65 years and older was much larger than the absolute difference in years of coronary heart disease.

The World Health Report reported from a study on 191 countries that life expectancy increased during the last decade and the number of healthy life years increased more strongly.[16] Fries argued earlier that postponement of death concurs with a stronger postponement of morbidity and labelled this phenomenon as 'compression of morbidity.'[17]Non-smoking alumni from the Pennsylvania State University had low BMI and were physically active, lived longer and reported onset

of disability at an older age than people with a high-risk profile. Moreover, the alumni with a low risk profile had less disability at any time.[18] From the present study, we hypothesise that a further increase in the prevalence of obesity will lead to an increase in nonfatal consequences of obesity.

Public health consequences of obesity have often been estimated by calculating economic costs of obesity. It has been estimated that 6% of the direct health care costs in the United States were attributable to obesity.[10] Allison *et al.* argued that such calculations are likely to be overestimations, because the relation between obesity and mortality was not taken into account.[12] Further studies on the costs of obesity should take into account the number of life years suffering from obesity-related consequences. We propose that costs due to obesity-related work disability highly depend on duration of work disability rather than on incidence of work disability. Work disability is an expensive consequence of obesity, because it is associated with persistent productivity loss and loss of income. Large obesity-related costs due to medication for chronic diseases are also mainly explained by the number of unhealthy life years. We conclude that increases in the prevalence of obesity will lead to further increase in the obesity attributable health care costs due to large extra number of unhealthy life years due to nonfatal conditions. For smoking, for instance, the opposite is true. It has been estimated that smoking is relatively cheap for the public health, as smokers die early and are prevented from long-term health care.[19] In the present study we indeed found lower number of unhealthy life years in elderly smokers, then in elderly never smokers.

This study has some important methodological strengths. We measured body weight in a representative sample of Finns. Participation rate was high. Follow-up data was complete because of the unique personal identity code, which is used in all health registers in Finland. Obesity is associated with other risk factors of disease and disability. Only the adjustment for diabetes, diastolic blood pressure and serum cholesterol lowered the relative risks. Adjustment for these risk factors, however, is not appropriate as they are in the causal chain between obesity and coronary heart disease and all-cause mortality.[20] It should be noted that persons with disease or disability at baseline were already excluded from the analyses. Therefore, we suggest that most part of the difference in unhealthy life years between obese and normal weight subjects that are presented in this study could be directly attributed to obesity.

A drawback of the analyses on number of unhealthy life years is that it was not possible to calculate confidence intervals, because of their severely skewed distributions. Log-transformation in order to approach a normal distribution on the log-scale could not be done, because the majority of subjects had no unhealthy life year. It is unlikely, however, that the difference in unhealthy life years between normal weight and obese subjects was a chance finding. A dose response relation between BMI and number of unhealthy life years was noted, and analyses were based on more than 100,000 person-years for men and women separately. A second drawback of the present analyses may be that we defined disease and disability duration as time between onset and end of 15-years follow-up. Regarding work disability we know that Finns will be work disabled for the rest of their life, if they receive a disability pension by the Social Insurance Institution. Regarding coronary heart disease and medication for chronic diseases, one might argue that a small proportion of subjects may recover from coronary heart disease or stop using medication. If this argument is valid, however, we hypothesise that this would be more the case in diseased subjects with normal weight than in diseased overweight and obese subjects. We may have underestimated the difference in unhealthy life years between normal weight subjects and subjects with overweight or obesity. We cannot explain why obesity was relatively weakly associated with mortality in subjects aged 20-59 years. Some large studies reported that relative risks of obesity for mortality are higher in the younger than in older age groups. Obesity was related to mortality in men aged 65 years and older. Also, in this category obese subjects had more unhealthy life years due to morbidity leading to long-term medication than normal weight men. Obesity was not related to mortality in elderly women. Especially for the elderly, it would have been of value having data on the waist circumference. Waist circumference may be a better measure of body fatness and indicator of disease in the in the elderly than the body mass index.[21] To indicate health risk due to body fatness in the elderly it may be valuable to link measures of waist circumference to disease and disability outcome.

Conclusion

The present study shows that obesity is somewhat related to increased mortality, but more strongly to disability and morbidity. Obese subjects have more unhealthy life years due to work disability, coronary heart disease, and morbidity leading to long-term medication. The present study provides empirical evidence that obesity is related to an increase in the number of unhealthy life years. We hypothesise from these findings that a further increase in the prevalence of overweight and obesity will lead to an increase in the number of unhealthy life years.

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Chapter 6

General discussion

6.1 Introduction

The prevalence of obesity (severe overweight) has increased dramatically during the last few decades of the 20th century.[1] Therefore, an increasing attention for the public health impact of obesity is warranted. Large epidemiological studies have shown that obesity is related to mortality, morbidity, and disability.[2] Most of these studies used levels of body mass index (BMI), calculated as body weight divided by height squared (kg/m^2) to define the degree of overweight and obesity.

The relation between obesity and mortality is less strong in elderly than in younger populations.[3-5] One explanation is that BMI is not the best measure of body fatness in the elderly. An alternative explanation is that low BMI is also indicative of low lean body mass, which is related to health impairment.[6] Other measures of body fatness than the BMI are probably better predictors of mortality in the elderly.[7] A possible cohort effect and selective survival may be other explanations for a weaker BMI-mortality relation in older compared to younger age groups.[8]

It is clear that obesity is related to morbidity, such as cardiovascular diseases and type 2 diabetes mellitus.[9-13] Relatively few studies have reported a relation between obesity and disability, such as work disability and difficulties in performing everyday activities.[14,15] The role of musculoskeletal disorders, which are possible intermediates in the causal chain between obesity and disability, has not been systematically evaluated.

Public health impact is not only evaluated in terms of relative risks and population attributable fractions, but also in terms of costs. It is estimated that direct costs of obesity are about 6% of the total health care expenditure in the US.[16] In Europe, estimates vary between 1 and 5%.[17] Costs due to obesity-related sick leave and work disability are estimated at about 10% of the total morbidity-related productivity loss.[18] Weight loss could reduce the number of life years with hypertension and type 2 diabetes mellitus.[19] Empirical data on the number of unhealthy life years in obese, overweight and normal weight subjects are not available in the literature.

This thesis aimed at studying long-term and recent increases in the prevalence of obesity in the Netherlands and at elucidating the role of obesity in mortality, morbidity, disability, and unhealthy life-years. In this general discussion, methodological aspects of the studies presented and other studies are considered. Also, implications of the results are discussed regarding future obesity research.

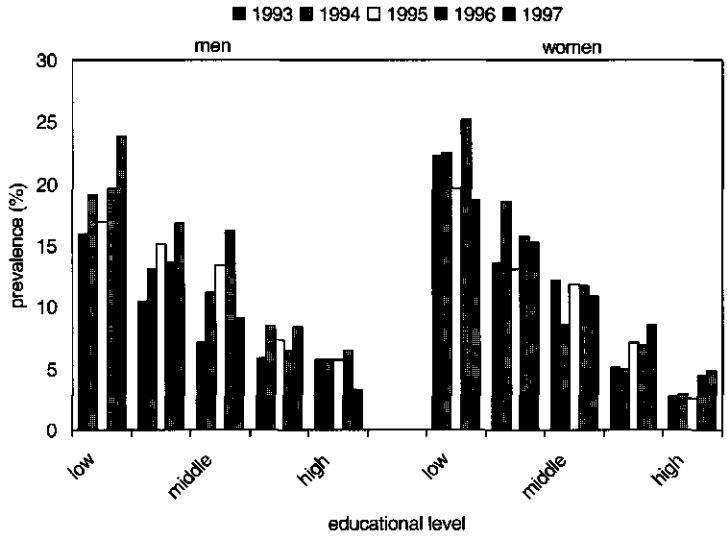

Figure 6.1 Prevalence of obesity (body mass index ≥30.0 kg/m^2)[a] per category of educational level in Dutch men and women aged 20-59 years:
MORGEN project 1993-1997 (see chapter 3.1.1)
a standardised to the five years age distribution in the Netherlands in 1995

6.2 Main findings

The prevalence of obesity (BMI ≥30.0 kg/m^2) increased steadily in the Netherlands between 1976 and 1997, from 5 to 9% in men and from 6 to 9% in women aged 37-43 years (**chapter 3.1**). Between 1993 and 1997, the prevalence of obesity was about 9% in men and 10% in women aged 20-59 years. During this period, the prevalence of obesity increased most strongly in men with a relatively low level of education. In contrast, a time trend in women was most pronounced in those with a relatively high educational level (figure 6.1). The prevalence of abdominal obesity was about 20% in men (waist circumference ≥102 cm) and about 25% in women (waist circumference ≥88 cm) (**chapter 3.2**). The increase in the prevalence of abdominal obesity per year was somewhat stronger than the increase in the prevalence of obesity (BMI ≥30.0 kg/m^2) between 1993 and 1997. Seasonal variation (increase in winter and decrease in summer) was more clearly seen for levels of waist circumference than for levels of BMI (**chapter 3.2**).

In **chapters 4.1 and 4.2**, it is reported that obesity (BMI ≥30.0 kg/m^2) was related to mortality in elderly men who had never smoked, but not in men who were smokers and not in women.[5,20] A possible cohort effect did not explain the somewhat lower

relative risks of obesity for mortality in elderly compared to younger populations. Overweight (BMI 25.0-29.9 kg/m^2) was not related to increased mortality. Waist circumference was more clearly related to mortality than was BMI in elderly men who had never smoked (**chapter 4.2**).[20]

Obesity was related to the presence of knee and hip osteoarthritis at baseline, which are important risk factors for disability (**chapter 5.1**).[21] Moreover, obesity was associated with difficulties in activities of daily living at baseline and to onset of work disability during follow-up. These associations were found in both the presence and absence of osteoarthritis. Obesity was also associated with chronic low back pain, shoulder joint impairment, and neck pain in women, although to a lesser extent than to osteoarthritis. In men, overweight (BMI 25.0-29.9 kg/m^2) was, but obesity (BMI ≥30.0 kg/m^2) was not associated with the presence of these musculoskeletal disorders.

It was estimated that prevention of little weight gain (less than 0.5 kg per year) could prevent about 26,000 new cases of osteoarthritis of the knee and 19,000 new cases of work disability in the Dutch working-aged population during a period of ten years (**chapter 5.2**). That is 5% and 2.5%, respectively, of the number of new cases of osteoarthritis and work disability that would occur in Dutch working-aged men and women, when no weight gain prevention was carried out.

The relation between obesity and work disability, hospitalisation due to coronary heart disease, and morbidity leading to long-term medication was strongest in young adults within the age range 20-64 years (**chapter 5.3**). Obesity was more strongly related to morbidity and disability than to mortality. Obese Finns had more unhealthy life years than their normal weight counterparts (**chapter 5.3**).

6.3 Methodological considerations

In this thesis, the prevalence of obesity and its impact on the public health is studied by use of epidemiological, observational studies. In epidemiological research, the exposure must be clearly defined. Knowledge on potential biases is needed, because they may harm internal and external validity of studies. Also, definitions of different measures of outcome should be taken into account.

6.3.1 Exposure assessment

The amount of body fat is best measured by Magnetic Resonance Imaging (MRI) techniques, Computer Tomography (CT)-scanning, or, more indirectly, by densitometry. Such techniques, however, are too expensive and time-consuming for large epidemiological studies. For health promotion purposes, proxy measurements of body fat are needed so that individuals themselves can assess their risk status.

Body mass index

The body mass index (BMI), which was developed by the Belgian mathematician Quetelet in the 19th century, is the most commonly used measure of body fatness independent of body height. The World Health Organization defined cut-off points for overweight (BMI 25.0-29.9 kg/m^2) and obesity (BMI ≥30.0 kg/m^2) as they reflect increased risk of morbidity and mortality.[22] Moreover, universal classifications of degrees of overweight and obesity are useful for comparisons of prevalence of overweight and obesity within and between countries. It has been argued that different BMI cut-off points should be used in different ethnic groups in order to assess the risks of morbidity and mortality.[23] Asian persons for instance have a generally higher absolute risk of type 2 diabetes mellitus than Caucasians at the same level of BMI.[24]

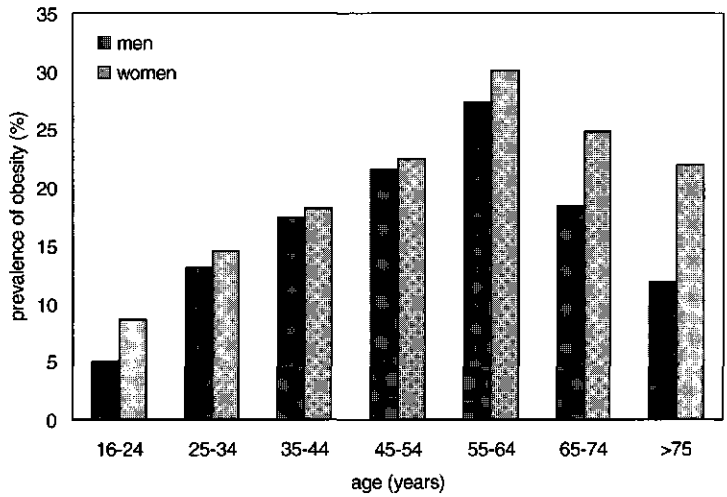

Figure 6.2 Prevalence of obesity (body mass index ≥30.0 kg/m^2) by age in men and women in the United Kingdom 1997 (Health Survey for England 1997)[46]
Figure adapted from Seidell and Visscher[8]

BMI is not an optimal indicator of body fatness in the elderly.[7] Average body weight and the prevalence of BMI ≥30.0 kg/m^2 increase until age 60-70 years and decline after this age (figure 6.2).[25] The reduced body weight, and consequently the reduced BMI, however, in the elderly is explained by a decrease in lean body mass and a loss of muscle mass, rather than a loss of fat.[26-29] Thus, a certain level of BMI indicates a higher level of fatness in older than in younger people.[30] Lean body mass slowly but progressively decreases during adulthood in men, and in women after menopause.[28]

Waist circumference

Although the majority of studies report on body fatness measured by BMI, waist circumference may be a better measure of excess fat than the BMI, because of several reasons. Waist circumference is a measure for the amount of abdominal fat as well as the amount of total body fat. Abdominal obesity is recognised as the most important risk factor for type 2 diabetes and among the major determinants of coronary heart disease.[9,31,32] An advantage for health promotion is that individuals can easily measure the waist circumference themselves. Waist measurements are cheap, reliable and do not need adjustment for body height, at least for middle-aged populations.[33] Action levels have been proposed by Lean *et al.* to define cut-off points for large waist circumferences (table 6.1).[34]

In chapter 3.2 of this thesis, it is concluded that waist circumference is a better indicator of changes in energy balance and energy balance related behaviour than BMI. This conclusion is based on the observation that the time-trend and seasonal variation was more pronounced for waist circumference than for BMI. Greater changes in waist circumference than in BMI may be explained by changes in physical activity patterns. Physical activity is associated with smaller waist circumference and relatively stable BMI. Fat mass is decreased but lean mass (muscles) is increased because of increased physical activity.[35]

Table 6.1 Waist circumference action levels a suggested by Lean *et al.*[34]

	Men	Women	Clinical implication
Action level 1	94 cm	80 cm	Abdominal overweight:
			Losing weight generally not necessary
Action level 2	102 cm	88 cm	Abdominal obesity:
			Losing weight generally urged

Especially in the elderly, waist circumference may be a better indicator of risk than BMI, as it better indicates body fatness. Large waist circumference was related to increased cardiovascular risk factors as hypertension and hypercholesterolaemia in subjects aged 55 years and older from the Rotterdam Study, but age-specific waist action levels are not available.[36] It is important to elucidate the relation of waist circumference to mortality, morbidity, and disability, especially in the elderly.

Waist-hip ratio

The waist-hip ratio reflects the distribution of fat, rather than the absolute amount of fat. Several cut-off points for waist-hip ratio have been presented in the literature, but classifications for categories of waist-hip ratio so far were dichotomous on which no consensus has been reached.[37,38] Recently, new light has been shed on the discussion whether low hip circumference is associated with increased mortality risk.[39,40] It has been suggested that a low hip circumference is an indicator of increased risk for morbidity and mortality.[40] Further studies should measure both waist and hip circumference and analyse them separately.

6.3.2 Prevalence and time trends

The prevalence and time trend in obesity has been presented in chapter 3.1 of this thesis. External validity is of importance when study results are used to estimate the prevalence and trend in obesity in the Dutch population.

Prevalence of obesity

The prevalence of obesity in the Netherlands was assessed from data of the MORGEN project 1993-1997 (chapter 3.1). It could be questioned, however, whether these data are representative for the Dutch population. Data were derived from three cities in the Netherlands, Amsterdam, Doetinchem, and Maastricht, and participation rate was low (45%). Persons with a relatively high educational level, in which obesity is less common than in low educational categories, were overrepresented. An advantage of the MORGEN project, regarding the internal validity, is that data are based on measured body weight and height. The prevalence of obesity reported in chapter 3.1 could be compared to data from Statistics Netherlands, which had different methodological advantages and disadvantages compared to the MORGEN project. Statistics Netherlands had a higher response rate (60%) and covered all regions in the Netherlands.[41] The main disadvantage of the data was that they were based on self-reported body weight and height.

The prevalence of obesity is likely to be underestimated when estimations are based on self-reports.[42] The magnitude of underestimation could be studied by comparing reported body weight and measured body weight from persons who participated in both Statistics Netherlands and the Regenboog project. The Regenboog project is a recent monitoring study, carried out at the National Institute of Public Health and the Environment in co-operation with Statistics Netherlands. Prevalence estimations based on self-reported body weight underestimated the prevalence of obesity with 2-4 percentage points.[43]

Statistics Netherlands reported a somewhat lower prevalence of obesity (about 6% in men and 8% in women) than the MORGEN project, for the period 1993-1997. After comparing data from the MORGEN project and Statistics Netherlands, with different above described methodological advantages, it can be concluded that our estimated prevalence of obesity, being 9% in Dutch adult men and 10% in women, for the period 1993-1997 is likely to be close to the true prevalence.

Time trends of obesity

In chapter 3.1, it was furthermore concluded that the prevalence of obesity increased between 1993 and 1997. Response rates in the MORGEN project, however, decreased between 1993-1997 from about 50% to 40%. It could be questioned whether the reported increase in the prevalence of obesity is due to selective participation being different over time.

Time trends have been studied within educational categories partly because participation rates in the MORGEN project differed across educational categories. The prevalence of obesity increased most strongly in men with a relatively low level of education. In contrast, time trends were most pronounced in women with a relatively high level of education (figure 6.1). Furthermore, the estimated time-trend in the MORGEN project can be compared with two national studies, one on adults (Statistics Netherlands)[41] and one on children.[44,45] Both studies showed a clear increase in the prevalence of obesity that was of a similar magnitude as the time trend reported from the MORGEN project. Thus, the different designs of the study and methodology of body weight assessment lead to different prevalence estimates of obesity but still in the same order of magnitude. These methodological differences had less or no influence on the estimates of time trends obesity.

6.3.3 Potential sources of bias

The relation between obesity and different health outcomes may be subject to various sources of biases. For example, if a factor is associated with obesity, but also with the studied disease occurrence, then this may lead to spurious relations between obesity and health. Statistical methods can account for various sources of bias, but are not always appropriate. Some potential sources of bias in the relation between obesity and disease occurrence are discussed below.

Confounders

A potential confounder in the relation between obesity and disease occurrence is a factor that is associated with obesity, causally or not causally, and also directly related to the disease, and which is, at least in part, responsible for an observed association between obesity and disease. Age is an important example of a confounder in the relation between obesity and most disease occurrences. Body weight increases until age 60-70 years after which it declines.[46] Diseases such as coronary heart disease are more common in older than in younger populations. Adjustment for age should therefore always be made when age differs between individuals of the study population. Other potential confounders are behavioural determinants of obesity. The quantity and quality of the diet and the amount of physical activity for example may determine the onset of obesity and are related to diseases such as coronary heart disease. Adjustment for these determinants, however, is difficult because obese subjects tend to underestimate their food intake and overestimate their physical activity pattern.[47]

Intermediate risk factors

If a factor is in the causal chain between obesity and health outcome, it is inappropriate to adjust for that factor. Relative risks of obesity for the health outcome will then be underestimated. Examples of intermediate risk factors are high blood pressure and high serum cholesterol that are in the causal chain between obesity and for example cardiovascular morbidity and mortality.[48]

Effect modifiers

When the effect of obesity on disease occurrence is modified by a third factor, i.e. when the effect of obesity is different in strata of this factor, analyses have to be performed in each of the strata separately. A known effect modifier in the relation between obesity and mortality is smoking.[7,49] In this thesis, for example, obesity was

related to mortality in men who had never smoked, but not in men who smoked in the Seven Countries Study and the Rotterdam Study (chapters 4.1 and 4.2).[5,20] One explanation for this effect modification is that obesity adds little risk to smokers, possibly because of the high mortality risk associated with smoking.

Cohort effect

Relative risks of obesity for mortality seem to decline with ageing (figure 6.3).[3-5] Different age groups often come from different birth cohorts. The people in these different birth cohorts grew up during different time periods and thus may have experienced different body weight developments. If mortality rates are also different between birth cohorts, different relative risks of obesity for mortality between age groups may be partially explained by a cohort effect. In chapter 4.1, a cohort effect has been avoided by following a cohort of men twice for a period of 15 years, but with a different age at baseline.[5]

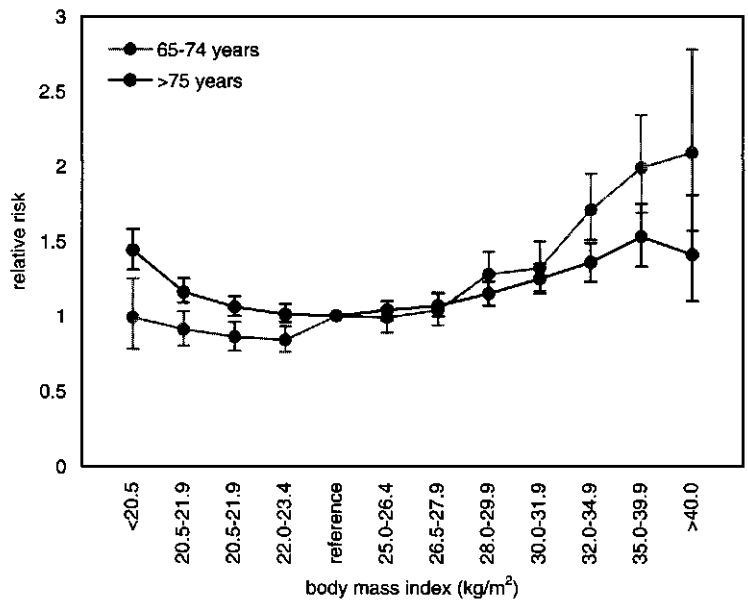

Figure 6.3 Relative risks (95% confidence intervals) of mortality from all causes among healthy women aged 65-74 years and ≥75 years. Adapted from Calle *et al.*.[3]

Disease induced weight loss

Some diseases with a relatively high fatality rate may also lead to weight loss, possibly giving rise to spurious associations between low BMI and such diseases.[48,50] This bias would then be an example of reverse causation of health outcome and BMI.[48,51] It has been suggested to take weight loss prior to mortality into account by excluding the first five years of mortality.[48] Excluding the first five years of mortality in the Seven Countries Studies lead to somewhat lower relative risks of underweight for mortality. Relative risks of overweight and obesity, however, were not affected by the exclusion of the first five years of mortality. This effect is compatible with the conclusion from Allison's meta-analysis who concluded that excluding early mortality will lead to negligible effects on the relative risks of obesity for increased mortality.[52] In a recent study it has been suggested that those who die early after the start of follow-up might have lost more weight than persons who died later in the follow-up. The authors recommended that only the first year of mortality should be excluded.[50] It is unclear whether exclusion of the first year of mortality is sufficient when assessing the relation between obesity and other health outcomes than mortality.

6.3.4 Measures of effect

This thesis reports on the public health impact of obesity. The impact of obesity on health outcome can be expressed in different ways. Different measures of effect have different meaning in clinical medicine and in community medicine. In the following section, different measures of effect are discussed.

Absolute risk

The absolute risk is synonymous with incidence and means the rate of disease occurrence.[53] Incidence can be expressed as incidence proportion (i.e. events per number of subjects), or incidence rate (i.e. events per total person years).[54] It is the basic rate from which the relative risk is derived.[53] The absolute risk is more often used in clinical medicine than in community medicine. The interpretation of the relative effect depends on the absolute effect.[54] An intervention may not be warranted in an individual when the relative risk of disease occurrence for exposure is high, but the absolute risk is very low. The probability that the individual will develop the disease is then low, irrespective of exposure. Conversely, same relative risks for two populations could correspond with differing absolute effects.[54] In that case, the absolute risk measure could be useful in community medicine to study the impact of exposure on disease occurrence. In chapter 5.2, for example, weight gain

prevention could potentially prevent 5% of new cases of osteoarthritis in men and 6% of new cases in women. If absolute risk of osteoarthritis would be ignored, one might conclude that the impact of weight gain prevention on the incidence of osteoarthritis is similar in men and women. The absolute risk of osteoarthritis, however, was different in men and women. Due to the higher absolute risk in women more new cases of osteoarthritis were expected in women (320,000 new cases) than in men (175,000 new cases), during a period of ten years, if no weight gain prevention would be carried out. Thus, the number of new cases of osteoarthritis that could be prevented by weight gain prevention was 9,000 in men and 18,000 in women. Taking the absolute risk calculation into account, it can be concluded that weight gain prevention has more impact on the incidence of osteoarthritis in women than in men.

Relative risk

The relative risk is the ratio of the incidence (proportion or rate) in the exposed to the incidence in the non-exposed.[53,54] In clinical medicine, the relative risk is used to indicate how much the risk is increased in a person who represents the exposed category, without indicating the absolute risk.[53] In community medicine, relative risks can be used to indicate populations effects of exposure on disease occurrence.[54] In this thesis, for example, the relative risk was used to compare the impact of obesity on mortality, morbidity, and disability (chapters 2.1 and 5.3). Since relative risks for obesity of morbidity and disability generally exceeded the relative risk of mortality, it was concluded that the impact of obesity on morbidity and disability is higher than its impact on mortality (figure 6.4).

Population attributable fraction

The population attributable fraction indicates the fraction of cases that would not have occurred if exposure had not occurred.[54] In community medicine, the population attributable fraction is more informative than the relative risk alone when studying the impact of exposure on occurrence of different diseases, because it is derived from both the relative risk and the proportion of exposed subjects. It does not indicate an absolute number of cases that could be avoided if exposure had not occurred. In this thesis, the population attributable fraction was used to compare the impact of high BMI and large waist circumference on all-cause mortality in men aged 55 years and older who never smoked (chapter 4.2).

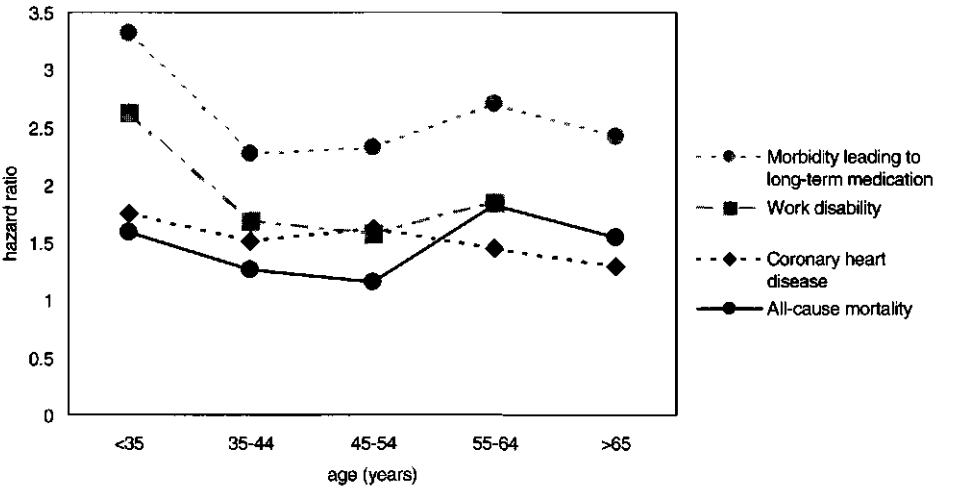

Figure 6.4 Hazard ratio of obesity versus normal weight for various end-points among men aged 20-92 years in the Social Insurance Institution's Mobile Clinic Study (see chapter 5.3.3)

Although comparison of relative risks indicated higher impact of high BMI than large waist circumference on all-cause mortality, comparisons of population attributable fractions indicated a clearly higher impact of large waist circumference than a high BMI on all-cause mortality. The relative risk of BMI ≥30.0 kg/m^2 (relative risk: 2.6) for mortality was higher than the relative risks of waist circumference above action level 1 (relative risk: 1.7) and waist circumference above action level 2 (relative risk: 1.6) for mortality. The proportion of men with waist circumference above action level 1 or action level 2 (0.49), however, was larger than the proportion of men with high BMI (0.07). From the relative risks and the proportions of men with large waist circumference and high BMI, it was calculated that the proportion of mortality attributable to a large waist circumference (0.28) was nearly three times higher than the proportion of mortality attributable to a high BMI (0.10).[20] In chapter 5.3, it was concluded from high relative risks for obesity of morbidity and disability in the youngest age group (20-34 years) and higher proportions of obesity in older age groups (until age 65 years), that obesity has large impact on morbidity and disability in all age groups (figure 6.4).

6.3.5 Outcome measures

The term 'public health' has to be specified when studying the 'public health' impact of obesity. Several public health outcome measures are discussed below.

Mortality

The impact of obesity on increased mortality rates has been known since the first report of actuarial studies in the early 1950's.[55] The relation between obesity, defined as BMI $\geq$ 30.0 kg/m^2, and mortality in elderly populations is topic of recent debates.[8] Obesity, BMI $\geq$30.0 kg/m^2, was related to increased mortality in elderly men who had never smoked. Relative risk of obesity for mortality, however, is lower in elderly than younger populations (figure 6.3).[3-5,20] Moreover, overweight, BMI 25.0-29.9 kg/m^2, was not related to mortality in elderly men who never smoked (chapters 4.1 and 4.2).[5,20] It can be concluded that the BMI level at which minimal mortality occurs, increases with ageing. As discussed earlier, large waist circumference identified more men who never smoked aged 55 years and older from the Rotterdam Study with increased mortality risk than did high BMI (chapter 4.2).[20]

Obesity was not related to mortality in women aged 55 years and older from the Rotterdam Study (chapter 4.2),[20] or in women aged 65 years and older from the Finnish Social Insurance Institution's Mobile Clinic Study (chapter 5.3). It was suggested that a redistribution of fat after menopause may be responsible for the absence of a relation between large waist circumference and increased mortality.[56,57] As a consequence of the change from a gluteal to a more abdominal distribution of fat following menopause, duration of abdominal obesity may have been shorter in women than in men. Furthermore, levels of bioavailable endogenous estrogens are relatively increased in postmenopausal women with abdominal obesity.[56,58] Although speculative, these levels of endogenous estrogens may favourably influence cardiovascular risk, and thereby all-cause mortality risk. Further studies with longer follow-up or more complete baseline data on disease status should assess whether absence of a relation between waist circumference and mortality among women can be confirmed.

Morbidity and disability

The effect of obesity on mortality can largely be explained by the relation between obesity and chronic diseases such as cardiovascular diseases and type 2 diabetes mellitus. Obesity is currently recognised as major risk factor for type 2 diabetes mellitus and cardiovascular diseases. Obesity is also related to some types of cancer, respiratory diseases, such as asthma, sleep apnoea, and shortness of breath, and to various musculoskeletal disorders.[2] A large waist circumference has been shown to indicate impaired levels of cardiovascular risk factors, shortness of breath and difficulties in everyday activities.[59]

In chapter 5.1, obesity is linked to osteoarthritis, low back pain, shoulder joint impairment, and chronic neck pain, although based on cross-sectional analyses. It is not clear what came first: obesity or the musculoskeletal disorders. It may well be that patients with musculoskeletal disorders become less physically active and thereby gain weight. Some studies, however, report longitudinal relations between obesity and these musculoskeletal disorders, providing stronger evidence for a causal relation.[60,61,62] Obesity is less clearly related to low back pain, shoulder joint impairment and chronic neck pain, than to knee- and hip osteoarthritis.[63] Longitudinal studies are needed to further explore the relation between obesity and these musculoskeletal disorders.

The relation between obesity and morbidity is important from a public health point of view. Obesity-related morbidity is not only associated with increased mortality, but also with increased disability, affecting one's quality of life.[15,64] Both morbidity and disability, in particular work disability, imply large obesity-related health care costs.[18]

Unhealthy life years

The relation between obesity and morbidity is now widely reported.[2,65] Evidence for a relation between obesity and disability is accumulating. The number of unhealthy life years in obese, overweight and normal weight persons, however, is unknown. Data on increased number of unhealthy life years in obese persons are needed to improve health care planning and calculating obesity-related health care costs.

Oster et *al.* calculated that 10% weight loss would lead to 1.2-2.9 fewer life years suffering from hypertension and to 0.5-1.7 fewer years of suffering from type 2 diabetes mellitus, depending on age-category (between 35 and 64 years) and initial BMI.[19] These calculations are based on mathematical modelling, requiring assumptions regarding the relations between obesity, morbidity, and mortality.

In this thesis, it is reported that obesity is related to both mortality and an increased number of unhealthy life years that were due to work disability, coronary heart disease, and morbidity leading to long-term medication (chapter 5.3). To our knowledge, this is the first attempt to make such calculations using empirical data. An advantage of using empirical data from one cohort of subjects is that all relations between obesity, morbidity and mortality and fatality rates of diseases studied are taken into account. Because the distribution of unhealthy life years was

severely skewed, confidence intervals could not be calculated, which require a normal distribution of the variables of interest. Log-transformation of the data was not possible, since the majority of subjects experienced zero unhealthy life years due to work disability, coronary heart disease and morbidity leading to long-term medication. It is unlikely, however, that our results are due to chance. Clear dose-response relations were observed and analyses were based on more than 100,000 person-years in men and women. It is hypothesised from these findings that a further increase in the prevalence of obesity will lead to an increase in the number of unhealthy life-years.

6.4 Public health implications

From this thesis, it can be concluded that an increase in the prevalence of obesity will lead to an increase in the number of unhealthy life-years due to increased non-fatal morbidity and disability. Thus, the recently reported increase in the prevalence of obesity and the expected further increase in the prevalence of obesity in the near future will lead to increased health care costs due to obesity.

An increase in body weight is due to a positive energy balance: increased energy intake and/or decreased energy expenditure. Small daily changes in energy intake and physical activity will have a large impact on the change in body weight in the long run. Small increases in body weight in the population will have a large impact on the prevalence of overweight and obesity and the number of unhealthy life-years attributable to weight gain.[22,66]

The prevalence of overweight and obesity has been increasing at a particular high rate since the last decades, while the 'gene pool' hardly changed. Consequently, causes of the average weight gain are largely environmental, although genes are potentially very important in individual cases of obesity. Gene-environment studies are needed to elucidate the interaction between genes and the environment. Changes in energy intake and in the physical activity patterns at school, work and during leisure time are often mentioned as causes of weight gain.[67,68] Egger and Swinburn suggested to approach the obesity epidemic as a normal response to the pathologic 'obesogenic environment', in which choices are easily made to increase food intake and decrease physical activity.[69]

It is of public health importance to develop weight gain prevention programs. It has been calculated that prevention of weight gain has more potency to reach public

health care goals than treatment of obesity.[70] Minor changes in energy intake or energy expenditure (in order of magnitude of half a glass of beer or twelve minutes bicycling per week) had a potentially important effect on changes in the prevalence of obesity and consequent changes in incidence of osteoarthritis and work disability (chapter 5.2). Only a few prevention programs, however, have been evaluated and results were generally disappointing.[71-74]

A possibly important explanation for the failure of weight gain prevention programs is that those programs aimed too much at individual behaviour modification. The 'obesogenic environment' could have an overriding influence on people's overall behaviour.[69] Possibly, altering the 'obesogenic environment' is critical for successful weight gain prevention, but determinants of failure to cope with these environmental (social, physical, and economic) circumstances are unknown. These determinants of behaviour must be studied to prevent obesity effectively.

New weight gain prevention programs should probably focus on the balance between food intake and physical activity. Determinants of weight gain are multifactorial.[75] Hill and Peters suggested from their review on the environmental contributions to the obesity epidemic that traditionally neglected aspects of energy balance should be considered in future weight gain prevention programs. They suggest that food availability and portion size are important determinants of weight gain, in a society in which 'super sizing' of food proportions is commonplace. Energy density should be studied in relation to energy intake, although reductions in fat intake may be the most effective way to reduce energy intake. Their third suggestion to improve weight gain prevention is to make the environment more conducive to physical activity.[76] One explanation for a relatively low prevalence of obesity in the Netherlands compared to the United States and England is the high number of people who use bicycles for transportation in the Netherlands.

6.5 Conclusions

Obesity is a major determinant of impaired health in all ages including the elderly. The results presented in this thesis confirmed that the relation of obesity with morbidity and disability is stronger than the relation of obesity with mortality. Based on empirical data, it is clearly shown that obese subjects have more unhealthy life years than normal weight subjects. This thesis provides evidence based on large cohort studies, that there is an urge for the development, implementation, and evaluation of new weight gain prevention programs. Recently, the World Health

Report showed that the healthy life expectancy increased substantially during the last century in 193 countries.[77] If the prevalence of obesity will further increase, it is reasonable to expect that the healthy life expectancy may be unfavourably affected in the next decades in societies with a high prevalence of obesity.

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Summary

The prevalence of obesity (severe overweight) has increased dramatically in western societies during the last decades of 20th century. There is therefore a need to study the public health consequences of obesity. The aim of this thesis is to study the increase in the prevalence of obesity in the Netherlands, and to elucidate different aspects of the relations between obesity and mortality, morbidity and disability.

In a literature review in **chapter 2**, it is described that the prevalence of obesity has been increasing in affluent countries, and recently also in developing societies. In affluent countries, obesity is most prevalent among those with relatively low socio-economic status. It is concluded that body composition is changing with ageing. Body mass index (BMI) might not be the best indicator of body fatness in elderly populations. In addition, it became clear that the relation between obesity and mortality is less strong than the relations between obesity, morbidity, and disability. The number of unhealthy years due to morbidity and disability in obese and normal weight subjects, however, is unknown. Based on the findings from this review, it is hypothesised that obese populations have higher mortality rates but also have more unhealthy life years.

In **chapter 3** of this thesis, the long-term and recent time trend in BMI levels in the Netherlands are addressed, with special reference to educational level. In addition, the recent time trend and seasonal changes in BMI and waist circumference are compared. Between 1976-1980 and 1993-1997 the prevalence of obesity (BMI ≥30.0 kg/m^2) increased from 5% in to 9% among men and from 6 to 9% among women, aged 37 to 43 years. Analyses were based on measured body weight and height from 29,141 men and women, who participated in one of three consecutive multicentre monitoring studies of the National Institute of Public Health and the Environment, Bilthoven, the Netherlands. These monitoring studies were carried out in 1976-1980, 1987-1991 and in 1993-1997. In the period 1993-1997, data were also collected from 21,926 men and women aged 20 to 59 years. The average prevalence of obesity during period 1993-1997 was estimated to be 9% among men and 10% among women aged 20-59 years. Within this period the prevalence of obesity increased with 0.54 (95% confidence interval (CI): 0.13-0.96) percentage points per year among men and with 0.35 (95% CI: -0.03;0.73) percentage points per year among women, adjusted for age, town of examination and educational category. The recent increase in the prevalence of obesity was strongest among men with a relatively low educational level and, in contrast, among women with a high educational level. Among men, the prevalence of abdominal obesity (waist circumference ≥102 cm) was 20% and increased with 0.70 (95% CI: 0.15-1.24)

percentage points per year between spring 1993 and autumn 1997. Among women, the prevalence of abdominal obesity (waist circumference ≥88 cm) was 25% and increased with 1.33 (95% CI: 0.79;0.87) percentage points per year. Seasonal variation (increases in winter and decreases in summer) was most clearly present for abdominal obesity.

In **chapter 4**, the relation between obesity and mortality is described with special reference to elderly populations. Data on measured BMI was used in a cohort of men aged 40-59 years and who were followed for 15 years regarding all-cause mortality. The same cohort was measured again in 1970, when the men were aged 50-69 years, and followed again for 15 years. Analyses were based on 7,985 European men who took part in the Seven Countries Study. The relative risks of obesity for mortality was 1.8 (95% CI: 1.2-2.8) for men aged 40-59 years who never smoked, and 1.4 (95% CI: 1.0-1.9) for men aged 50-69 years who never smoked, with normal weight as the reference. Among current smokers, obesity was not related to increased mortality, possibly because of the high mortality risk in smokers. Overweight (BMI 25.0-29.9 kg/m^2) was not related to increased mortality rates in any smoking category. In the Rotterdam Study, waist circumference showed a more continuous and steeper relation with all-cause mortality than the BMI, again in men who never smoked only. The Rotterdam Study comprised data regarding 6,296 men and women aged 55 to 102 years. Mean follow-up period was 5.4 years. Waist-hip ratio (ratio of waist circumference over hip circumference) was not clearly related to increased all-cause mortality. The proportion of mortality among elderly men who never smoked that was attributable to a large waist circumference, was three times higher than the proportion of mortality that was attributable to a high BMI.

In **chapter 5**, the relation of obesity with morbidity and disability in the Mini-Finland Health Survey is addressed. This Finnish population based cohort study consists of data regarding 5,625 men and women aged 30 to 64 years in 1978-1980. Body weight and several musculoskeletal disorders were assessed during a health examination. Disability was defined as being granted a work disability pension during a 15-year follow-up period, and as the experience of difficulties in everyday activities at baseline. Work disability data were obtained by linkage to the Finnish national pension register. Obesity was more strongly associated with knee osteoarthritis than with hip osteoarthritis. Osteoarthritis, in turn, was associated with disability. Obesity was also related to disability independently from osteoarthritis. The relations between obesity and disability were found among both

subjects with and without osteoarthritis. When both obesity and osteoarthritis were present, the odds ratio for difficulties in everyday activities was 7.9 (95% CI: 4.4-13.9) compared to normal weight subjects without osteoarthritis. Relative risk of developing work disability during follow-up was 2.4 (95% CI: 1.3-4.3) for subjects with both obesity and osteoarthritis compared to normal weight subjects without osteoarthritis. Obesity was furthermore related to chronic low back pain, shoulder joint impairment and neck pain at baseline in women. In men overweight (BMI 25.0-29.9 kg/m^2) was associated, but obesity (BMI ≥30.0 kg/m^2) was not associated with the presence of these musculoskeletal disorders.

In addition, in **chapter 5**, the potential effects of a weight gain prevention program on the incidence of osteoarthritis and work disability are described that have been calculated by means of the mathematical Chronic Diseases Model. It was calculated that partial prevention of little weight gain (less than 0.5 kg per year) would prevent an increase in the prevalence of obesity with 3.5 percentage-points. Concurrently, 26,000 new cases of knee osteoarthritis and 19,000 new cases of work disability in the Dutch working-aged population could be prevented by weight gain prevention at population level during a period of ten years.

Finally, relative risks for and unhealthy life years due to work disability, coronary heart disease, and morbidity leading to long-term medication are presented per BMI-category. For this purpose data of another Finnish population based cohort study, the Social Institution's Mobile Clinic Unit, were used. In this study, body weight was measured in about 17,000 Finnish men and women aged 20-64 years at baseline in 1973-1978. Subjects were followed with respect to incidence of work disability, hospitalisation due to coronary heart disease, and morbidity leading to long-term medication during a maximum follow-up period of 15 years until age 65 years. Relative risks of obese versus normal weight subjects for morbidity and disability exceeded those for mortality and were highest in the youngest age categories. During a maximal follow-up of 15 years, obese men (BMI ≥30.0 kg/m^2) had 0.5, 0.4, and 1.7 extra years of work disability, coronary heart disease, and morbidity leading to chronic medication, respectively. Obese women suffered respectively 0.5, 0.4, and 1.3 extra years from these conditions, compared to normal weight women.

In **chapter 6**, the results of this thesis are summarised and discussed in the context of the literature. The prevalence of obesity has increased recently in Dutch adults. Results of cohort studies reported in this thesis confirm that obesity is related to

mortality, morbidity, and disability. Relative risks of obesity for morbidity and disability exceeded relative risks for mortality. As hypothesised in the literature review in **chapter 2**, empirical data showed that obese persons not only live shorter, but also had more unhealthy life years due to work disability, coronary heart disease, and morbidity leading to long-term medication.

In the last part of **chapter 6**, the potential importance of new, innovative weight gain prevention programs is discussed. Prevention programs are in theory more efficient than weight loss programs in stopping the increase in obesity prevalence rates. So far, no major effect of weight gain prevention has been reported in large population based prevention programs. Recently, it has been suggested that obesity is a result of normal behaviour to a pathogenic environment, entitled the 'obesogenic environment.' New weight gain prevention studies should therefore aim at understanding the environment affecting the community's behaviour. Altering the 'obesogenic environment' is probably critical for successful weight gain prevention programs.

Obesity, as measured by high BMI, has an impact on the public health across the whole age-span. The effect of obesity on health in the elderly, however, is possibly better captured by the waist circumference rather than the commonly used BMI. This thesis provides new evidence, based on both epidemiological data from large population based cohort studies and mathematical modelling, that the expected increase in the prevalence of obesity will lead to an increase in mortality, morbidity, and disability in the community. Weight gain prevention programs should get high priority on both the scientific and political agenda.

Samenvatting

SUMMARY IN DUTCH

Obesitas (ernstig overgewicht) komt steeds vaker voor in westerse landen. Vanwege de enorme toename gedurende de afgelopen decennia is het belangrijk de gevolgen van obesitas op de volksgezondheid te bestuderen. Het doel van dit proefschrift was het beschrijven van de toename van obesitas in Nederland en het verder ophelderen van de relatie tussen obesitas, sterfte en het optreden van ziekte en lichamelijke beperkingen.

In een literatuuroverzicht (**hoofdstuk 2**) werd beschreven dat obesitas wereldwijd is toegenomen in de meeste landen met een hoog welvaartspeil en sinds kort ook in veel ontwikkelingslanden. In welvaartslanden komt obesitas het meest voor bij mensen met een relatief lage sociaal-economische status, in ontwikkelingslanden juist bij mensen met een relatief hoge sociaal-economische status. De lichaamsamenstelling verandert met ouder worden en de body mass index (BMI), waarbij het gewicht wordt gedeeld door lengte in het kwadraat (kg/m^2) is wellicht niet de beste maat om de hoeveelheid lichaamsvet te bepalen bij oudere populaties. Naar aanleiding van het literatuuroverzicht is de hypothese geformuleerd dat sterftecijfers weliswaar hoger zijn in groepen mensen met obesitas, maar dat zij ook meer ongezonde levensjaren doormaken dan groepen mensen met een normaal gewicht.

In **hoofdstuk 3** van dit proefschrift werd de lange termijn en de recente toename in BMI in Nederland beschreven, met speciale aandacht voor opleidingsniveau. Daarnaast zijn de recente tijdstrend en de seizoensvariatie in BMI en buikomvang met elkaar vergeleken. Tussen 1976-1980 en 1993-1997 steeg het vóórkomen van obesitas (BMI $\geq$30,0 kg/m^2) van 5% tot 9% bij mannen en van 6% tot 9% bij vrouwen in de leeftijd 37-43 jaar. Gemeten lengte en gewicht was beschikbaar voor 29.141 mannen en vrouwen die deelnamen aan één van de drie multicenter monitoringstudies van het RIVM. Deze monitoringstudies zijn uitgevoerd in 1976-1980, 1987-1991 en 1993-1997. Voor de periode 1993-1997 waren ook gegevens beschikbaar voor 21.926 mannen en vrouwen in de leeftijd 20-59 jaar. Tussen 1993 en 1997 kwam obesitas voor bij 9% van de mannen en bij 10% van de vrouwen in de leeftijd van 20-59 jaar. Gedurende deze periode steeg na correctie voor leeftijd, stad en opleidingsniveau het vóórkomen van obesitas bij mannen met 0,54 percentagepunten per jaar (95% betrouwbaarheidsinterval (BI): 0,13-0,96) en bij vrouwen met 0,35 percentagepunten per jaar (95% BI: -0,03-0,73). De stijging in het vóórkomen van obesitas tussen 1993 en 1997 was het grootst bij mannen met een relatief laag opleidingsniveau en, omgekeerd, bij vrouwen met een hoog opleidingsniveau. Abdominale obesitas (buikomvang $\geq$102 cm) kwam voor bij 20%

van de mannen en dit percentage steeg met 0,70 (95% BI: 0,15-1,24) percentagepunten per jaar. Bij vrouwen kwam abdominale obesitas (buikomvang ≥88 cm) voor bij 25% van de individuen. Dit percentage steeg met 1,33 (95% BI: 0,79-0,87) percentagepunten per jaar. Seizoensvariatie (stijging in de winter en daling in de zomer) was duidelijker waarneembaar voor buikomvang dan voor BMI. De buikomvang lijkt dus beter bruikbaar dan de BMI om veranderingen in energiebalans en lichaamssamenstelling te detecteren.

In **hoofdstuk** 4 werd de relatie tussen obesitas en sterfte beschreven met speciale aandacht voor oudere populaties. BMI was berekend uit gemeten gewicht en lengte van 7.895 Europese mannen die meededen aan de Zeven Landen Studie in de leeftijd 40-59 jaar. Zij werden vanaf 1960 gedurende maximaal 15 jaar gevolgd. Gekeken werd welke mannen overleden in deze periode. Tien jaar later, toen de mannen de leeftijd 50-69 jaar hadden bereikt, werd de BMI nog eens gemeten en zijn de overlevende mannen nog eens 15 jaar gevolgd. Het relatieve risico van obesitas op sterfte was 1,8 (95% BI: 1,2-2,8) voor mannen die nooit rookten in de leeftijd 40-59 jaar en 1,4 (95% BI: 1,0-1,9) voor mannen die nooit rookten in de leeftijd van 50-69 jaar, met normaal gewicht (BMI: 18,5-24,9 kg/m^2) als referentiecategorie. Bij mannen die rookten was obesitas niet gerelateerd aan een sterftetoename, mogelijk door het hoge sterfterisico dat rokers sowieso hebben door het roken zelf. Overgewicht (BMI 25,0-29,9 kg/m^2) was niet gerelateerd aan sterfte. In de Erasmus Rotterdam Gezondheid en Ouderen (ERGO) studie werden de BMI, de buikomvang en de ratio van buikomvang en heupomvang (buik-heup ratio) vergeleken als indicator voor verhoogde sterftecijfers. Het ERGO onderzoek omvat gegevens van 6,296 mannen en vrouwen in de leeftijd van 55 tot 102 jaar. De gemiddelde periode dat deelnemers zijn gevolgd was 5,4 jaar. Bij de 424 mannen die nooit rookten was de buikomvang meer continu en sterker gerelateerd aan de kans op overlijden dan de BMI. De buik-heup ratio was niet duidelijk gerelateerd aan de kans op overlijden. Het deel van de sterfte dat was toe te schrijven aan een grote buikomvang was driemaal zo groot als het deel van de sterfte dat was toe te schrijven aan een hoge BMI.

In **hoofdstuk** 5 werd het verband van obesitas met aandoeningen van het bewegingsapparaat en lichamelijke beperkingen in het Mini-Finland gezondheidsonderzoek behandeld. Deze Finse populatiestudie omvatte gegevens van 5.625 mannen en vrouwen in de leeftijd van 30-64 jaar die zijn gemeten in 1978-1980. Het hebben van lichamelijke beperkingen was gedefinieerd als het ontvangen van een werkloosheidsuitkering tijdens het 15-jarige vervolgonderzoek of het moeite

hebben met algemeen dagelijkse levensverrichtingen bij de start van het onderzoek. Gegevens over arbeidsongeschiktheid werden verzameld door het koppelen van gegevens aan het Finse nationaal register voor arbeidsongeschiktheidsuitkeringen. Het verband tussen obesitas en artrose in de knie was sterker dan het verband tussen obesitas en artrose in de heup. Artrose was gerelateerd aan lichamelijke beperkingen. Obesitas was ook onafhankelijk van artrose gerelateerd aan lichamelijke beperkingen. Het verband van obesitas met werkloosheid en moeilijkheden in algemeen dagelijkse levensverrichtingen werd zowel bij de groep mensen met artrose als bij de groep mensen zonder artrose gevonden. De groep mensen met zowel obesitas als artrose had 7,9 (95% BI: 4,4-13,9) zo vaak moeilijkheden met algemeen dagelijkse levensverrichtingen dan de groep mensen zonder obesitas en zonder artrose. In de groep Finnen met obesitas en artrose trad arbeidsongeschiktheid 2,4 (95% BI: 1,3-4,3) keer vaker op dan in de groep Finnen die geen obesitas en geen artrose hadden. Verder was obesitas gerelateerd aan chronische lagerugpijn, chronische pijn in het schoudergewricht en chronische nekpijn bij de start van het onderzoek in de groep vrouwen. In de groep mannen was overgewicht (BMI 25,0-29,9 kg/m^2) wel en obesitas (BMI ≥30,0 kg/m^2) niet gerelateerd aan deze aandoeningen van het bewegingsapparaat.

Verder werden in **hoofdstuk 5** de potentiële effecten beschreven van een gewichtsbeheersingsprogramma op het optreden van artrose en arbeidsongeschiktheid in de Nederlandse bevolking. Voor het berekenen hiervan is gebruik gemaakt van het chronische ziektenmodel. Het was berekend dat preventie van een gewichtsstijging (minder dan 0,5 kg per jaar) een toename in obesitas van 3,5 percentagepunten zou voorkómen. Hierdoor zouden 26.000 nieuwe gevallen van artrose en 19.000 nieuwe gevallen van arbeidsongeschiktheid worden voorkómen in de gehele Nederlandse bevolking van werkbare leeftijd door preventie van gewichtsstijging op populatieniveau gedurende een periode van tien jaar.

Tenslotte, werden relatieve risico's op en ongezonde levensjaren door arbeidsongeschiktheid, coronaire hartziekte en medicatiegebruik voor chronische aandoeningen gepresenteerd per BMI categorie. Hiervoor is data gebruikt van een tweede Finse populatiestudie, de Mobiele Kliniek Studie van het Finse sociale verzekeringsinstituut. In deze studie is lichaamsgewicht en lengte gemeten bij ongeveer 17.000 mannen en vrouwen in de leeftijd van 20-64 jaar bij de start van het onderzoek in 1973-1978. Deelnemers aan de studie zijn gedurende maximaal 15 jaar, tot leeftijd 65 jaar, gevolgd voor wat betreft het optreden van arbeidsongeschiktheid, ziekenhuisopname voor coronaire hartziekte, en ziekten die

leiden tot langdurig medicijngebrek. Relatieve risico's voor obesitas ten opzichte van normaal gewicht op het optreden van arbeidsongeschiktheid, coronaire hartziekte, en ziekten die leiden tot chronisch medicijngebruik waren groter dan de relatieve risico's op sterfte. Relatieve risico's waren het hoogst in de jongste leeftijdscategorieën. Tijdens het vervolgonderzoek van maximaal 15 jaar leefden obese mannen respectievelijk 0,5 0,4 en 1,7 meer jaren met arbeidsongeschiktheid, coronaire hartziekte, en ziekte leidend tot langdurig medicijngebruik dan mensen met een normaal gewicht. Obese vrouwen leefden respectievelijk 0,5 0,4 en 1,3 jaren meer met deze aandoeningen dan vrouwen met een normaal gewicht.

In **hoofdstuk 6** werden de resultaten van dit proefschrift samengevat en bediscussieerd binnen de context van de literatuur. Het vóórkomen van obesitas is recentelijk gestegen in Nederlandse volwassenen. De resultaten van cohort studies die in dit proefschrift worden gerapporteerd, bevestigen dat obesitas is gerelateerd aan het optreden van sterfte, ziekte en lichamelijke beperkingen. Relatieve risico's van obesitas voor het optreden van ziekte en lichamelijke beperkingen waren groter dan het relatieve risico van obesitas op sterfte. Volgens de hypothese die is gesteld in **hoofdstuk 2**, is met behulp van empirische gegevens aangetoond dat personen met obesitas niet alleen korter leven, maar ook meer ongezonde levensjaren doormaken door arbeidsongeschiktheid, coronaire hartziekte, en ziekte die leidt tot langdurig medicijngebruik.

In het laatste deel van **hoofdstuk 6** werd ingegaan op het potentiële belang van nieuwe, innovatieve gewichtsbeheersingsprogramma's. Preventieprogramma's zijn theoretisch efficiënter dan afvalprogramma's in het terugdringen van de stijging in het vóórkomen van obesitas. Er zijn slechts enkele grote populatiestudies uitgevoerd die waren gericht op de preventie van gewichtsstijging. Het is recentelijk geopperd dat obesitas het gevolg is van een normale reactie op een pathologische omgeving, de zogenaamde 'obesogene omgeving', in plaats van een pathologische reactie op een normale omgeving. Daarom zouden nieuwe gewichtsbeheersingsprogramma's als doel moeten hebben om meer te weten te komen over de omgevingsfactoren die het gedrag van mensen beïnvloeden. Het veranderen van de 'obesogene omgeving' is waarschijnlijk van groot belang voor het succes van gewichtsbeheersingsprogramma's.

Obesitas, gemeten met de BMI, heeft een grote invloed op de volksgezondheid, op alle leeftijden. De gezondheidsinvloed van obesitas bij ouderen is waarschijnlijk beter te bestuderen door het gebruik van de buikomvang dan door het gebruik van

de BMI. De epidemiologische populatiestudies en rekenkundige modellen die beschreven zijn in dit proefschrift, suggereren dat de verwachte toename in het vóórkomen van obesitas zal lijden tot een toename in sterfte, maar ook tot een toename in het aantal jaren van ziekte en lichamelijke beperkingen in de bevolking. De nieuwe gegevens in dit proefschrift tonen aan dat gewichtsbeheersingsprogramma's hoge prioriteit verdienen op zowel de wetenschappelijke als op de politieke agenda.

List of abbreviations

AF_p	Population Attributable Fraction
BI	Betrouwbaarheidsinterval
BMI	Body Mass Index
CHD	Coronary Heart Disease
CI	Confidence Interval
CVD	Cardiovascular Diseases
ERGO	Erasmus Rotterdam Gezondheid en Ouderen
HR	Hazard Ratio
MONICA	Monitoring trends and determinants in cardiovascular disease
MORGEN	Monitoring project on risk factors for chronic diseases
NC	Not Calculated
NHANES	National Health and Nutrition Examination Survey
OA	Osteoarthritis
OR	Odds Ratio
REF	Reference category
RR	Relative Risk
WCRF	World Cancer Research Fund
WHO	World Health Organization
WHR	Waist-Hip Ratio

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BFrisBee2's, if a ball dreams, it dreams it's a frisbee. En terecht.

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Curriculum vitae

TOMMY LEONARDUS SEBASTIANUS VISSCHER

Tommy was born in Veghel, Noord-Brabant, on December 29th 1971. His birth weight was 3,250 grams. In 1991 he passed secondary school (Gymnasium β) at Zwijsen College Veghel. In the same year he started studying Biomedical Health Sciences at the Catholic University Nijmegen, which he finished with a major in Epidemiology in the year 1996. During his study, Tommy visited the EURODIAB lab at the Department of Public Health and Epidemiology at University College London and the Department of Medical Informatics, Epidemiology, and Biostatistics at the Catholic University Nijmegen. In 1996, he started working on the present thesis as a PhD-student from research school n i h e s. At this research school from Erasmus University Rotterdam, he obtained a second MSc in epidemiology. Tommy was based at the Department of Chronic Diseases Epidemiology at the National Institute for Public Health and the Environment (RIVM). He visited the Department of Epidemiology and Biostatistics of Erasmus University Rotterdam, and the Department of Health and Disabilities of the National Public Health Institute, Helsinki, Finland. In June 2000, Tommy attended a World Health Organization meeting on 'Evidence of the impact of gender inequality on health' in Geneva, Switzerland, as special advisor for the WHO. In the final year of the PhD project, he prepared a study proposal for research school VLAG, which is funded by the Netherlands Heart Foundation. Tommy is now employed as a postdoc at the RIVM to work on this research program entitled '*Sustained behavioural changes in order to prevent weight gain: An integrated approach to develop and evaluate weight gain prevention programs by changing both food intake and physical activity.*' His current body weight is about 90 kilograms.

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