DETERMINANTS OF RELATIVE WEIGHT AND BODY FAT DISTRIBUTION IN AN INTERNATIONAL PERSPECTIVE

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Determinanten van relatief gewicht en vetverdeling - een internationaal perspektief

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Chapter 5.3:

Molarius A, Seidell JC, Visscher TLS, Hofman A. Misclassification of high risk elderly subjects by using waist action levels established for young and middle-aged adults: results from the Rotterdam Study (submitted).

1. Introduction

Overweight can be defined as excess storage of body fat in an individual. In adult men with a "normal" weight, the percentage of body fat is about 15-20%. In women this percentage is higher, about 25-30%. In spite of the fact that differences in weight between individuals are only partly due to variation in body fat, indices based on relative weight (such as body mass index (BMI), defined as weight (kg) divided by the square of height (m^2)) are most often used to measure the degree of overweight. It has been shown that there is a very good correlation between BMI and the percentage of body fat in large populations [1], and therefore the use of BMI to measure the degree of overweight in populations is justified. Overweight is generally defined as BMI equal to or higher than 25 kg/m^2, and obesity as BMI equal to or higher than 30 kg/m^2. These cut-off points have been recently incorporated in the WHO Expert Committee recommendation for the classification of overweight [2]. The WHO report names the first as grade 1 overweight and the latter as grade 2 overweight, but these terms have not spread to a wider use. In the following, the term overweight will be used to refer both to overweight and obesity when not referring to obesity alone.

Overweight is independently related to the incidence of several chronic diseases, such as coronary heart disease, non-insulin-dependent diabetes (NIDDM) and stroke, both in men and women, as well as to overall mortality [3-8]. In addition, it is associated with an increased incidence of arthritis, gallbladder disease, sleep apnea and certain types of cancer (breast and endometrial cancer in women, colon cancer in men) [9]. Moreover, overweight is related to some other risk factors such as blood pressure, serum cholesterol and insulin resistance which add to the risk of chronic disease morbidity and mortality [9]. The relative risk of mortality associated with overweight is similar in men and women, whereas the absolute risk is much lower in women than in men. BMI in the range 25-30 kg/m^2 is responsible for the major part of the impact of overweight on diabetes mellitus and cononary heart disease mortality due to its high prevalence in affluent populations [4-8].

In addition to the degree of overweight, body fat distribution has been found to be related to health. Vague [10] concluded in the 1950s that the male pattern of fat distribution (android obesity) carried a greater health risk than the female pattern (gynoid obesity). Later the concept was further developed and a distiction between abdominal and gluteo-femoral obesity was made. Adbominal obesity was found to be more closely linked to the development of cardiovascular disease, NIDDM, stroke and mortality than the degree of overweight [11-14]. At the time, the underlying biological mechanism for this was largely unknown, whereas later research has indicated that the fat stored in the abdominal cavity (visceral fat) may be the major source of health risk [15]. Because the direct measurement of the different types of body fat is not feasible in large epidemiological studies, anthropometric indices have been used to measure abdominal obesity. The ratio of waist to hip circumference is the most often used indicator, but several other indices have also been used to measure abdominal obesity in epidemiological studies [16].

Overweight is a common condition in most industrialized countries and a growing problem also in many developing countries [17,18]. More than half of the population aged 35-64 in Europe is overweight [19]. Overweight is more common in middle-aged men than in women, whereas obesity is more common in women than in men. There are, however, large differences in the prevalence of overweight between populations. For example, the prevalence of obesity in the populations included in the WHO MONICA Project ranged from less than 10% (Beijing and Gothenburg) to over 40% (women in Kaunas, Lithuania) in the early 1980s. During the past decade, the prevalence of obesity has increased in most countries which have reliable data on trend estimates [19-23].

Most of the data on body fat distribution has been collected for the purpose to investigate the association between body fat distribution and disease and are rarely representative of the general population. Knowledge on fat distribution and prevalence of abdominal obesity in general populations is therefore scarse. Furthermore, the results are difficult to compare between populations because different studies have used different methods. Even less is known about trends over time in fat distribution measures within populations.

While public health efforts to reduce the level of such risk factors as smoking, blood pressure and serum cholesterol have been successful in many countries [24], overweight has emerged as an increasing public health problem. Intervention studies aimed at changing body weights in obese subjects have not been successful [25]. Therefore, primary prevention of overweight seems the only way to fight the problem. In many countries the health authorities have recognised the serious health burden of increasing prevalence of overweight in the population and have set national targets to reduce the prevalence of overweight. Likewise, the WHO has launched an International Obesity Task Force [26]. The prevention of overweight requires, naturally, knowledge about the aetiology of overweight.

Overweight in individuals in any population is the result of a long-term positive energy balance. However, very little is known about the factors that may explain the large differences in the prevalences of overweight between populations. Several epidemiological studies have shown that the following factors are associated overweight in a population [2, 19, 27].

Demographic factors:

- *Age*: Overweight increases with age at least up till age 50-60 years in men and women.
- *Gender*: Women have generally higher prevalence of obesity than men, especially when older than 50 years, whereas men usually have higher prevalence of overweight than women.
- *Ethnicity*: Large, usually unexplained, variations between ethnic groups have been observed.

Socio-cultural factors:

- *Socio-economic status*: In industrialized countries, the prevalence of overweight is higher in subjects with lower level of education and/or income compared to those with high socio-economic status, especially among women. In developing countries, the prevalence of overweight is usually higher in subjects with high socio-economic status, both in men and women.
- *Marital status*: Usually overweight increases after marriage.
- *Cultural norms*: In many societies overweight is considered as a sign of wealth and health, whereas in many others it is not. There are also differences between populations in what is considered as "ideal weight".

Behavioral factors:

- *Dietary intake*: Although it is clear that nutrition is of critical importance in establishing a positive energy balance, methodological errors in determining energy intake, confounding and increased underreporting of energy intake with increasing degree of overweight make it difficult to interpret the results.
- *Smoking*: Smoking is associated with lower body weight and stopping smoking often leads to an increase in weight.
- *Alcohol consumption*: The effect of alcohol consumption is unclear in most populations.
- *Physical activity*: Those who remain or become inactive are usually heavier than those who are physically active. Studies on physical activity suffer, however, from similar methodological problems as studies on nutrition intake, and confounding, biased reporting and measurement error make it difficult to interpret the results.

Genetic factors:

- Genetic factors play a role in the onset of obesity in two ways. First, there are genes or chromosomal abnormalities that are primary factors in the development of obesity. These are, however, rare in the general population. Second, there are genes that modulate the interaction with environmental factors such as diet and exercise (genetic predisposition for obesity).

Most of the determinants of overweight are also determinants of body fat distribution [28]. Smoking, however, while inversely associated with relative weight, is positively related to waist-hip ratio, meaning that even if smokers are leaner than non-smokers they have higher waist-hip ratio than non-smokers of similar weight [29-32]. Body fat distribution and relative weight are also interrelated, so that heavier individuals tend to have more abdominal obesity than leaner individuals [33-35].

Outline of the thesis

The objective of this thesis is to investigate some of the determinants of relative weight and body fat distribution mentioned above. The perspective is international, comparing the determinants and their associations with relative weight and body fat distribution among populations with widely different prevalences of overweight. First, a review on the selection of indicators and cut-off points of abdominal obesity is given (chapter 2). Next, the methods of this thesis are presented (chapter 3): the study populations are described and the quality assessment procedures applied in the WHO MONICA Project for the measurements of relative weight (weight and height) and body fat distribution (waist and hip circumferences) to quarantee the comparability of data between populations and within populations over time are presented. In chapter 4, the focus of attention is on the determinants of relative weight. Differences between populations in the effect of smoking on relative weight, the effect of educational level on this association, and the association between educational level and relative weight and changes in this association over a 10-year study period are explored. In chapter 5, the determinants of body fat distribution are discussed, concentrating especially on age and degree of overweight. The distributions of anthropometric measures of abdominal obesity (waist and hip circumferences and waist-hip ratio) in different populations are presented. In addition, the applicability of waist circumference cut-off points for abdominal obesity suggested by others is examined in the MONICA populations. Finally, the investigation of the applicability of the suggested waist circumference cut-off points is expanded to the elderly. In the general discussion (chapter 6), the main results of this thesis are summarized and some methodological aspects discussed. The chapter is closed by reflecting the impact of the results of this thesis on future research.

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2. Review on indicators of abdominal obesity

2.1 Introduction

Body mass index (BMI) is the most commonly used measure of relative weight. It was first introduced by Quetelet in the end of last century. Although the percentage of fat in an individual with the same value of BMI can vary, it has been shown that there is a very good correlation between BMI and the percentage of body fat in large populations [1]. It has also been shown that BMI is largely independent of height [2]. Although some studies have suggested that the interpretation of BMI may be different in some racial groups [3,4] and in the elderly [5-7], or that BMI is not completely independent of height, especially in women [8,9], there is a relative concensus in the research field that BMI is a useful measure of relative weight in adults.

Measures of body fat distribution, however, vary from study to study. Many antropometric indicators, such as waist-thigh ratio, waist-height ratio, sagittal abdominal diameter etc. have been used as measures abdominal obesity in the literature. The most commonly used measure of abdominal fatness is, however, the ratio of waist circumference to hip circumference. Other measures of body fat distribution include e.g. skinfold thickness ratios. No concensus exists in the field about an optimal indicator of body fat distribution.

Cut-off points for a health indicator are used to express the magnitude of health risks conveyed by the condition. Cut-off points are useful tools in public health recommendations giving guidelines when to start treatment or other medical intervention. International guidelines exist e.g. for such risk factors as hypertension and hypercholesterolemia [10,11]. Universal cut-off points enable also a comparison of the prevalence of the condition between populations and within populations over time, and thus facilitate the scientific research of the condition. Lately, the BMI cut-off points have been incorporated in the WHO Expert Committee recommendation on the classification of degree of overweight [7]. Similar cut-off points have been suggested in the literature for body fat distribution [12], but the topic remains controversial.

We will next concentrate on one specific area of body fat distribution: abdominal obesity. We will review the discussion in the literature on the selection of anthropometric indicators suggested as optimal indicators of abdominal fatness and the cut-off points based on these indicators as markers of elevated risk or guidelines for intervention.

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2.2 Selection of abdominal indicators for classification of abdominal fatness – a critical review

Abstract

In the literature, a variety of anthropometric indicators for abdominal obesity have been suggested. The criteria for their selection vary, and they have been justified mainly on the basis of being correlated with other risk factors, with morbidity and mortality or to be predictors of the amount of visceral fat. Many of the studies, however, suffer from methodological limitations: they are based on a small number of subjects, often derived from cross-sectional data, based on indirect measurement of risk or the indicators are complicated to interpret biologically or difficult to use in a public health context. The literature lacks a systematic evaluation of the proposed indicators taking into account possible differences between sexes, age categories and ethnic groups and different diseases and mortality.

Similar considerations relate to the cut-off points based on the indicators of abdominal obesity. The suggested cut-off points for waist-hip ratio have been based on rather arbitrary criteria, and the studies where cut-off points for waist circumference have been suggested have methodological shortcomings as well, such as being based on cross-sectional data and arbitrary cut-off points for other variables. It is also a reason for concern that so far all the suggested cut-off points for abdominal obesity have been based on results obtained in Caucasian populations. Moreover, they are based on the assessment of risk and their appropriateness in the use of intervention has not been evaluated. Therefore, no consensus about the appropriateness of the different cut-off points have been reached.

In conclusion, there is an apparent lack of consistency in the field and therefore a more scientifically and theoretically solid basis for the selection and use of anthropometric indicators of abdominal obesity and cut-off points based on them should be a high priority in this research field in the near future.

Introduction

The WHO Technical Report [1] on the use and interpretation of anthropometry from 1995 lists several objectives for the use of anthropometric indicators:

- *Identification of individuals and populations at risk,* in which case an indicator should reflect past or present risk.
- *Selection of individuals or populations for an intervention,* in which case an indicator should predict the benefit to be derived from the intervention.
- *Evaluation of the effects of changing nutritional, health or socio-economic influences, including interventions,* in which case an indicator should reflect the response to past and present intervention.
- *Excluding individuals from high-risk treatment, from employment or from certain benefits,* in which case an indicator should predict a lack of risk (which is not always the same as to predict a risk).
- *Achieving normative standards,* some indicators are used just to reflect "normality" in a population.
- *Research purposes that do not involve decisions affecting nutrition, health or well-being,* in e.g. biological, behavioural and epidemiological modelling.

The appropriateness of indicators thus depends on the specific objectives of their use. Up to now, anthropometric indicators, including those for body fat distribution, have usually been based solely on the first objective i.e. on the identification of individuals at risk for mortality or morbidity. Little is known about how the use of cut-off points for anthropometric indicators meets different objectives.

The importance of fat distribution, especially abdominal obesity, as a risk factor for several diseases such as cardiovascular diseases, hypertension, stroke and non-insulin-dependent diabetes (NIDDM), and mortality has been generally recognized during the last decades. It was Vague [2] who first about 50 years ago showed the importance of fat distribution in relation to various diseases. He described what he called 'android' and 'gynoid' types of obesity, later interpreted by Kissebah and colleagues [3] as upper body vs. lower body fat accumulation. During the following decades other classifications of fat distribution were developed based on determining the central vs. peripheral types of obesity. These were estimated from the skinfold patterns e.g. subscapular-to-triceps skinfold ratio.

From the 1980s onwards the importance of abdominal obesity was recognised and the distinction between abdominal and gluteo-femoral patterns of fat distribution was made. Increasingly, the importance of visceral fat accumulation was emphasized.

The recognition of visceral fat accumulation as a potential risk factor led to the development of techniques to measure directly the amount of intra-abdominal fat (i.e. computed tomography and magnetic resonance imaging). Because these techniques are laborious and expensive, their use in large epidemiological studies is usually not feasible. Instead, fat distribution can be estimated from simple anthropometric measures. In the literature, numerous anthropometric indicators have been suggested as best measures of different concepts of body fat distribution. In this short review the discussion is limited to anthropometric indicators proposed to measure abdominal obesity, describing their selection criteria and evaluating the objectives of their use.

Anthropometric indicators of abdominal obesity

Table 1 lists a number of different indicators suggested in the literature as best measures for abdominal obesity. Each of them have been developed as a response to different challenges to describe body fat distribution and different criteria have been used to justify their selection. In the late 1970s Ashwell et al. [4] developed a score based on waist to thigh diameters measured from photographs to classify subjects having android or gynoid type of obesity, and a few years later they developed a similar indicator from body circumferences [5]. In the beginning of 1980s two groups, one in Gothenburg [6] and another in Wisconsin [7], used waist-hip ratio to measure fat distribution. Both groups expressed the need to standardize the waist circumference for body build but used the hip circumference instead of the thigh circumference because the latter was not available. They argued that the waist-hip ratio as good as the waist-thigh ratio in identifying upper body vs. lower body obesity.

An important turning point was the recognition of computed tomography (Ashwell et al. 1985 [8]) to measure directly the amount of abdominal body fat and the differentiation of the roles between subcutaneous and visceral abdominal fat. Consequently, attempts were made to establish optimal anthropometric predictors of visceral fat. Abdominal sagittal diameter [9,10] and, later, waist circumference [10,11] have been shown to be good predictors of visceral fat. Also the ratio of waist to height has been used [12] and has been claimed to be a better predictor of visceral fat than waist-hip ratio [13] although this was not confirmed in subsequent studies [14].

Table 1. Historical overview of the introduction of anthropometric indicators of abdominal obesity suggested in the literature.

Indicator	Initially proposed by	Initial reason for use	(Claimed) advantages	Potential disadvantages
Waist-thigh ratio (WTR)	Ashwell et al. 1978 [4] and 1982 [5]	Classifies android vs. gynoid obesity	(Better correlate of visceral fat/risk factors than waist-hip ratio) [56, 57]	May reflect both muscle and fat distribution Ratio*
Waist-hip ratio (WHR)	Krotkiewski et al. 1983 [6] Hartz et al. 1983 [7]	Similar to waist/thigh ratio	Good predictor of mortality and morbidity Generally used i.e. comparable between studies	May reflect both muscle and fat distribution Ratio*
Abdominal diameter	Kvist et al 1986 [9]	High correlation with visceral fat observed by CT scan	Best correlate of visceral fat	More difficult to measure in public health context than waist circumeference
Waist-height ratio	Higgins et al. 1987 [12]	Lack of measurements of hip and thigh	(Better predictor of visceral fat than waist circumference or WHR) [13] Better predictor of mortality than WHR	Ratio* Height is inversely associated with morbidity/mortality independent of fat distribution
Conicity index	Valdez 1991 [15]	To standardize waist circumference for body shape	(Expected range, built-in adjustment of waist circumference for height and weight, does not require hip circumference) [58]	Complex to interpret
Abdominal diameter to midthigh girth ratio	Kahn et al. 1993 [16]	Better predictor of IHD and mortality from sudden coronary death than WHR	(Best simple index to predict morbidity and mortality) [59]	May reflect both muscle and fat distribution Ratio*
Waist circumference	Pouliot et al 1994 [10] Lean et al. 1995 [38]	Correlation with visceral fat Replacement of BMI and WHR	Simple interpretation Better correlate of visceral fat than WHR and WTR	High correlation with BMI

* Ratios are difficult to interpret biologically [17] and have limitations in relation to their use in statistical analyses [18].

In the beginning of 1990s other indicators of abdominal obesity, such as conicity index [15] and ratio of abdominal diameter to midthigh girth [16] have been developed based on a variety of criteria.

Following the introduction of these indicators, numerous studies have been published to show the advantage of a particular indicator in comparison with other indicators. Often these studies have shown differences too small to have any practical importance or they have been based on small samples, cross-sectional data or indirect measurement of risk (by other risk factors or amount of visceral fat). Consequently, instead of providing evidence for one single indicator this has led to a diversity of "competing" indicators.

All the proposed indicators have advantages and disadvantages in relation to their interpretation and use in public health context as listed in Table 1. Many of these indicators are specified as ratios in an attempt to control for some potentially confounding variable. Ratios are, however, difficult to interpret biologically and a change in body fat distribution may produce little or no change in the ratios [17]. Furthermore, ratios have limitations regarding to their use in statistical analyses and their use can introduce spurious correlations among the ratios and other variables [18].

For example, at the time waist-hip ratio was introduced the biological mechanism linking it to the development of disease was largely unknown. Since then more studies have been undertaken to explore this mechanism. With an increasing knowledge about potential mechanisms, it has become apparent that the waist-hip ratio is difficult to interpret biologically. The waist circumference measures predominantly visceral organs and abdominal - both subcutaneous and intra-abdominal - fat. The hip circumference may reflect different aspects of body composition i.e. muscle mass, fat mass and skeletal frame. When these two circumferences are combined in a ratio, it is difficult to interpret differences in the ratio between and within individuals. For instance, waist-hip ratio may be a good predictor of risk of NIDDM but that may not be solely due to abdominal fat accumulation but also the relative size of peripheral muscle [19]. In addition, a reduction in weight usually results in a reduction in both waist and hip circumferences and that will not necessarily result in a change in waist-hip ratio [20], and in turn, a decrease in waist-hip ratio may not necessarily be independently related to a reduction in cardiovascular risk factors [21].

Waist-height ratio is another example of an indicator with problems of interpretation. Statistically this ratio may be a better predictor of morbidity and mortality than waist-hip ratio and waist circumference, but this may be partly due to the contribution of short stature which is associated with increased morbidity [22]. Moreover, waist circumference is only very weakly correlated with height [23], so that the need to adjust waist for height is minimal.

The conicity index includes a built-in adjustment of waist circumference for weight and height. It is, however, too complicated to use in a public health context and difficult to interpret biologically. Abdominal sagittal diameter is more closely related to visceral fat volume than waist circumference or waist-hip ratio [24]. It is, however, more difficult to measure than waist circumference, particularly in the general population.

Waist circumference is strongly correlated with visceral fat areas and can be easily measured and interpreted. This makes it a suitable candidate for an optimal indicator of abdominal obesity. Some researchers have, however, argued that it may be an oversimplification to use waist circumference as a single measurement for cardiovascular risk [25]. Waist circumference is strongly correlated with BMI and the addition of waist to age and BMI adds little, especially in women, to the explanation of the variance in visceral fat [26]. This is puzzling because concerning some diseases, e.g. stroke [27], waist circumference seems to be a better predictor of risk than BMI. Waist circumference is also strongly related with abdominal subcutaneous fat, total abdominal fat and total body fat [28]. This raises the question whether visceral fat after all is the major risk factor for disease. In their review of the literature Seidell and Bouchard [29] concluded that the evidence linking visceral fat as the main determinant of diseases is largely circumstantial. The question whether it is visceral fat or general adiposity which causes increased risk of morbidity and mortality needs to be clarified. An additional explanation may be that visceral fat is more important for some diseases e.g. NIDDM [30] and stroke [27] while general adiposity may be more important factor for cardiovascular diseases [31] and mortality [32]. The relation might also be age-specific. Rimm et al. [31], for instance, found in a large prospective study of the US men that before the age of 65 years BMI was the best predictor of coronary heart disease, whereas in men 65 years or over waist-hip ratio was a better predictor of risk. Goodman-Gruen et al. [33] found that after the age of 80 waist-hip ratio is a poor method of assessing central or visceral adiposity and waist circumference is a better measure of fat distribution. Clearly, there is a need for clarification about the appropriateness of these indicators.

In practise, it may prove to be difficult to evaluate the independent effects of visceral fat, subcutaneous fat and general adiposity on morbidity and mortality, because it requires large prospective studies and the measurement of visceral fat, as mentioned earlier, is not feasible in a large number of subjects. One possibility is to measure anthropometric indices in the whole study population and to use predictive equations to estimate visceral fat, subcutaneus fat and total fat from the anthropometric measurements. CT scans in a random subsample of the study population can be used to develop these predictive equations. It has been suggested that estimates of body compartments obtained from such equations predict a change in cardiovascular risk factors better than anthropometric measurements [25]. Differences in the equations between sexes and age groups should be tested, and in general the validity and accuracy of these equations should be appropriately demonstrated [34] before their use.

Cut-off points based on anthropometric indicators of abdominal obesity

Criteria for selection of cut-off points

The literature concerning the definition of cut-off points of anthropometric indicators of abdominal obesity shows a large variety of (often arbitrary) criteria for classification. There are several criteria on which the cut-off points can be selected. These include:

- *Percentiles of distribution or standard deviation scores.* These are possible only if large datasets representative of the whole population are available. Percentiles have been used in various health recommendations e.g. in life insurance tables for desirable weight [35], the American National Center for Health Statistics classification of BMI [36], and Canadian Fitness Survey's recommendations for waist-hip ratio [37]. This approach has, however, several drawbacks. The choice of percentile cut-off points is always somewhat arbitrary, it assumes that the average in the population is desirable and the cut-off points are vulnerable to changes over time as the population distributions change. The population-specific percentile cut-off points also make it difficult to compare prevalences across populations.
- *Other classifications.* For example, waist circumference cut-off points to replace classification based on cut-off points for BMI and waist-hip ratio [38].
- *Relative or absolute health risk.* This can be done based on inspection of the association between the anthropometric indicator and an indicator of risk (incidence of disease or presence of risk factors) or on evaluation of sensitivity/specificity/positive predictive value (receiver operating characteristics (ROC) analysis [39,40]) for detecting high risk in individuals.

- *A "critical amount" of visceral fat in a reference population.* Also this can be done by inspection of the association between the anthropometric indicator and the amount of visceral fat (as in Lemieux et al. [41]) or by ROC analysis [42]. This is usually feasible only in a relatively small number of subjects and therefore the generalizability of the results is limited.

Cut-off points proposed in the literature

There is a relative consensus about the classification for general adiposity which is incorporated in the WHO recommendation based on categories of BMI [1]. Similar universal recommendation for abdominal obesity would be very helpful for the purposes of public health recommendations and comparisons between populations. Attempts have been made to derive such cut-off points, and in this review we will examine the cut-off points for abdominal obesity suggested in the literature based on a) waist-hip ratio and b) waist circumference. Table 2 lists some of the recommendations frequently cited in various studies and in health recommendations. The criteria behind their selection and the methods used to define them will be compared and their methodological strengths and limitations discussed.

The first recommendations on cut-off points for waist-hip ratio were given by Per Björntorp in the early 1980s [43]. He induced the cut-off points from the analysis of the prospective Gothenburg Studies in men and women. The earliest publications [44,45] did not mention these cut-off points and give only the risk of disease in quintiles and tertiles of waist-hip ratio (the cut-off points for which are not specified for the reader). Björntorp argued that "the risk of complicating disorders to obesity increase sharply at a waist-hip circumference ratio exceeding 1.00 in middle-aged men and 0.80 in middle-aged women" [46]. Thus these cut-off points were established based on visual inspection of the association between waist-hip ratio and relative risk of disease. They were derived from relatively small number (792) of middle-aged men all born in the same year and a larger sample (1462) of middle-aged women. Inspection of the association between waist-hip ratio and mortality and morbidity shows a gradual increase in risk and therefore these cut-off points were rather arbitrary. In addition, in men the hip circumference was measured at the level of iliac crest which is deviating from the current WHO recommendation [1]. Nevertheless, these cut-off points have since then been cited in numerous studies. In a public health context these cut-off points have, however, the advantage of being easily understood.

Table 2. Criteria and methods used to define cut-off points for need of weight management on the basis of fat distribution suggested in the literature.

	Criteria	Method	Age specific	Sex specific	Number of observations	Selection criteria	Age range	Population	Cut-off poits
Waist-hip ratio									
Björntorp 1985 [43]	Risk of CVD and death	(1	No	Yes	792 men 1462 women	Population -based	men: 54 women: 38-60	Caucasian (Swedish)	1.00 men 0.80 women
Bray 1987 [47]	Risk of CVD and death	(1	No	Yes	same as Björntorp				1.00 men 0.90 women
Dietary guidelines for Americans 1990 [48]	?	?	No	Yes	?	?	?	?	0.95 men 0.80 women
Lemieux et al. 1996 [41]	Absolute level of visceral fat	Regression analysis	No	Yes	213 men 190 women	Self-recruited	18-	Caucasian (Canadian)	0.94 men 0.88 women
Waist circumference									
Lean et al. 1995 [38]	Cut-off points for BMI and waist-hip ratio (2	Sensitivity and specificity	No	Yes	990 men 1216 women	Population -based	25-74	Caucasian (Scottish (3)	102 cm men 88 cm women
Lemieux et al. 1996 [41]	Absolute level of visceral fat	Regression analysis	Yes	No	213 men 190 women	Self-recruited	18-	Caucasion (Canadian)	100 cm $\leq$ 40 yrs 90 cm > 40 yrs

1) Both seem to induce their cut-off points from the reports of the Gothenburg Study [44, 45] although the original articles do not mention these cut-off points.
2) Later verified against cardiovascular risk factors [51].
3) Later verified in Dutch population [51].

Another often cited reference for waist-hip ratio cut-off points is the paper of Bray [47] where he recommend the cut-off points 1.00 for men and 0.90 for women. The interesting feature about this recommendation is that Bray seems to base it on the same original studies [45,46] of the Gothenburg group as Björntorp. Other cut-off points for waist-hip ratio have also been suggested, like the US Department of Agriculture 0.95 for men and 0.80 for women [48]. Some investigators have, however, raised the issue that the suggested cut-off points may not be appropriate in all age and ethnic groups [17,49].

As already mentioned, at the time waist-hip ratio was introduced in the literature, the biological mechanism behind it was largely unknown. Most researchers currently adhere to the view that the risk factor of disease is the visceral adipose tissue depot, although the evidence still is far from conclusive [29,50]. If true, however, waist circumference shows a higher correlation with visceral fat than waist-hip ratio and therefore qualifies as an attractive candidate as an indicator of risk. The use of such single measurement would simplify the interpretation of epidemiological data as well as health recommendations regarding weight management. Consequently, cut-off points for waist circumference have been suggested in the literature.

Lean et al. [38] have suggested two "action levels" for waist circumference. According to them men with waist circumference ≥ 94 cm and women with waist circumference ≥ 80 cm should gain no further weight (action level 1), and men with waist circumference ≥102 cm and women with waist circumference ≥ 88 cm should reduce their weight (action level 2). These cut-off points are based on cut-off points for BMI (≥ $25/m^2$ at action level 1, and ≥ 30 kg/m^2 at action level 2) and waist-hip ratio (0.95 for men and 0.80 for women at both action levels). The exact procedure which resulted in these cut-off points is not clear from the original paper, but the authors show a very high sensitivity and specificity (>90%) for these cut-off points in respect to the cut-off points for BMI and waist-hip ratio in their study population. The authors did not, however, follow the conventional way of defining true and false positives which would have resulted in a lower estimate of sensitivity. The study population was a relatively large sample of 990 men and 1216 women representative of the population aged 25-74 years in Glasgow. Later the same team has verified the cut-off points in a population based sample of Dutch citizens and have likewise shown a very high sensitivity and specificity in respect to cut-off points for BMI and waist-hip ratio but much lower sensitivities (27-71%) and specificities (56-92%) in identifying individual risk factors [51].

Lemieux et al. [41] used a different approach and concluded that waist circumference cut-off point 100 cm should be used for subjects under age 40 years and 90 cm in subjects over 40 years, for both men and women. They based their calculation on the absolute amount of visceral fat, which was measured using a CT scan, and used the cut-off point 130 cm^2 as the reference value. Using regression models they calculated that the above-mentioned waist cut-off points best corresponded to the specified amount of visceral fat. Their study population was relatively small (213 men, 190 women). In the same study Lemieux et al. also looked at possible cut-off points for waist-hip ratio, and using the same approach found that the cut-off points 0.94 in men and 0.88 in women corresponded to the critical amount of 130 cm^2 of visceral fat.

Both these studies have several advantages. The most important strength is that at least the authors have tried to justify the recommended cut-off points with clearly stated criteria, which is an improvement to the early recommendations for the cut-off points for waist-hip ratio. There are, however, several limitations as well. The biggest drawback is, perhaps, that they are based on other arbitrary classifications, such as cut-off points for waist-hip ratio and visceral fat area. The objectives of the two studies differ. While the objective of Lean et al. [38] cut-off points is to select individuals for intervention, the objective of Lemieux et al. [41] is to assess visceral fat level related to increased cardiovascular risk factors. Yet both studies are based on cross-sectional data and the appropriateness of these cut-off points in relation to disease or as targeting subjects for intervention remains to be proven. Both studies have been based on Caucasian populations, and one should be cautious against generalizing their results in other populations. Some studies have suggested that the Lean et al. cut-off points may not be useful in other populations [52,53].

A closer look at the differences between the studies reveals choises that may cause methodological problems. Whereas the cut-off points for BMI Lean et al. [38] used are well established, the evidence for the cut-off points for waist-hip ratio (0.95 in men, 0.80 in women) is weaker. In fact of the references the authors cite to justify these cut-offs in the original paper, four of five are studies done only in women - of which one uses cut-off point 0.85 - and the only one including men applied the cut-off point 1.00. Several cut-off points for waist-hip ratio have been suggested in the literature and, obviously, a change in the waist-hip ratio cut-off point would change the cut-off points for waist circumference as well. Similarly, the critical level of 130 cm^2 for visceral fat [41] seems largely arbitrary. Moreover, Lean et al. recommend different cut-off points for men and women but have not explored potential age-specific cut-off points, whereas Lemieux et al. identified the same cut-off points for men and women. Lemieux et al. justified the use of the same cut-off points for men and women on the basis of absolute risk produced by elevated visceral fat. They proposed a 10 cm lower cut-off point for older subjects (over 40 years) compared to younger subjects. The relatively small number of subjects did probably not allow a narrower age stratification. Moreover, these different cut-off points by age may be statistically justified but, since waist circumference increases with increasing age, will be difficult to apply in a public health or health promotion context.

In addition to those based on waist-hip ratio or waist circumference, there is a variety of cut-off points based on other indicators of fat distribution suggested in the literature. Often these are based on combinations of other indicators, like waist/height combined with waist-hip ratio [54] or waist circumference combined with height [55], and are therefore more complicated to use in practise. The limitations related to the use of ratios and their interpretation mentioned for the indicators apply likewise to the cut-off points based on them.

Conclusions and recommendations

In the literature, a variety of anthropometric indicators for abdominal obesity have been suggested. The criteria for their selection vary, and they have been justified mainly on the basis of being correlated with other risk factors, with morbidity and mortality or to be predictors of the amount of visceral fat. Many of the studies, however, suffer from methodological limitations: they are based on a small number of subjects, often derived from cross-sectional data, based on indirect measurement of risk or the indicators are complicated to interpret biologically or difficult to use in a public health context. The literature lacks a systematic evaluation of the proposed indicators taking into account possible differences between sexes, age categories and ethnic groups and different diseases and mortality. The need for this kind of evaluation has been acknowledged already in the beginning of 1990s [17], but little has been done to achieve this aim. More effort should be put into derive an optimal indicator for abdominal obesity. Such an indicator should fulfil at least the following requirements:

- *must predict morbidity and mortality* at least as accurately as other indicators. This can only be assessed in prospective studies large enough to test possible differences between sexes, age categories and ethnic groups. The assessment should be done for each chronic disease and mortality separately.

- *must be biologically interpretable* i.e. there should be a plausible biological mechanism relating the indicator to the development of the disease,
- *must be amenable to change by lifestyle or other interventions* and a reduction in the indicator should predict a reduction in risk. This requires long-term intervention studies.
- *must be easily and accurately measured and interpreted* in a public health context.

Similar considerations relate to the cut-off points based on the indicators of abdominal obesity. The suggested cut-off points for waist-hip ratio have been based on rather arbitrary criteria, and the studies where cut-off points for waist circumference have been suggested have methodological shortcomings as well, such as being based on cross-sectional data and arbitrary cut-off points for other variables. It is also a reason for concern that so far all the suggested cut-off points for abdominal obesity have been based on results obtained in Caucasian populations. Moreover, they are based on the assessment of risk and their appropriateness in the use of intervention has not been evaluated. Therefore, no consensus about the appropriateness of the different cut-off points have been reached.

Several questions emerge from the methodological review of the recommended cut-off points for abdominal obesity:

- Is it possible to have cut-off points that are universal i.e. appropriate in all populations/ethnic groups?
- Should the cut-off points be age and/or sex-specific and if so what implications has this in practice?
- Should the cut-off points be disease-specific?
- Should the cut-off points be based on absolute or on relative risks? How big an increase in risk is enough to be defined as an "elevated" risk?

The selection of cut-off points is especially problematic because the risk of disease often increases gradually, although not necessarily linearly. Cut-off points are, however, extremely important for public health recommendations and also for comparisons between populations. Very elaborate sets of cut-off points (for each gender, age, ethnic group, and disease) may not be useful in practice, but the use of a simple set of cut-off points may be inappropriate if its validity is uncertain. A broader evaluation of possible cut-off points is needed before these questions can be answered and general public health recommendations can be given.

In summary, it is important to put the diversity of anthropometric indicators and cut-off points currently suggested in the literature and used in public health recommendations as optimal measures for body fat distribution into perspective. A more comprehensive assessment of possible indicators is needed to derive an optimal indicator for abdominal obesity. This requires a better understanding of the different roles of abdominal and general adiposity in the development of different diseases and a clarification of the contribution of visceral fat in this process, and of possible differences in this mechanism between sexes and age groups. This can only be assessed in large prospective studies. Similar requirements concern optimal cut-off points based on anthropometric indicators. The risk of morbidity or mortality should be assessed directly, possible differences between sexes, age categories and ethnic groups should be tested, and targeting individuals for intervention should be evaluated in long term intervention studies. Similarly, more attention should be paid to the pattern of the increase in risk with increasing value of the indicator. Thus, there is an apparent lack of consistency in the field and therefore a more scientifically and theoretically solid basis for the selection and use of anthropometric indicators of abdominal obesity and cut-off points based on them should be a high priority in this research field in the near future.

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3. Methods

3.1 Study populations

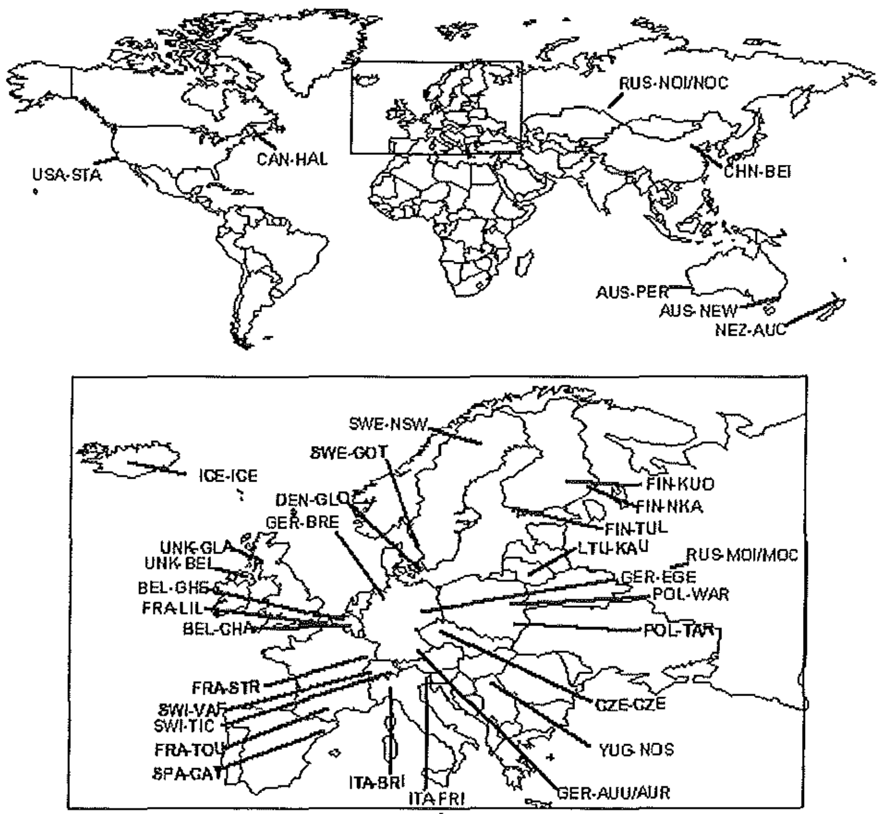
WHO MONICA Project

Most of the studies included in this thesis are based on the data from the WHO MONICA (MONItoring trends and determinants in CArdiovascular disease) Project. The WHO MONICA Project was designed to monitor the incidence and mortality from cardiovascular disease, and to assess the extent to which these trends are related to known risk factors [1]. The MONICA Collaborating Centres (MCCs) are funded locally, and the WHO is responsible for the coordination of the project. Several MCCs are monitoring more than one study population. The WHO MONICA Project comprise 54 study populations in 26 countries (see Figure 1). The populations are mainly concentrated in Europe but include some areas in the USA, Canada, China, Australia and New Zealand.

The risk factors in the WHO MONICA Project were monitored through two or three independent cross-sectional surveys scheduled in the beginning, the middle and in the end of the 10-year study period, ranging from the early 1980s to the 1990s. The surveys included random samples of at least 200 people in each gender and 10-year age group for the age range 35-64 years, and optionally 25-34 years. The middle survey was optional. The participation rates varied between 90% and 47% between populations, and were on average 3% lower in the final survey compared to the initial survey [2]. Event rates of myocardial infarction and stroke were determined by registering and validating all eligible events in defined populations over a 10-year period.

The WHO MONICA Project applied common standardized methods for data collection and analysis. This feature makes these data an invaluable source for comparisons between populations. The quality of the data was centrally assessed and any population with insufficient quality of data or response rate less than 50% was subsequently excluded from the collaborative analyses of the project. Further, there were large differences in the prevalence of overweight among the MONICA populations. The data are therefore especially suitable for investigating the determinants of these differences from an international perspective in a standardized and comparable way.

Figure 1. Populations of the WHO MONICA Project.



Monitoring Project on Cardiovascular Disease Risk Factors in The Netherlands

One of the studies included in this thesis is based on data from the Monitoring Project on Cardiovascular Disease Risk Factors in the Netherlands. The Project was carried out in 1987-91 in three towns (Amsterdam, Maastricht and Doetinchem) in the Netherlands [3]. The age range for this study was 20-59 years. Each year new random samples were selected from the municipal registries of these towns, and during the four years altogether about 36,000 men and women participated in the project. The average response rate was 50% for men and 57% for women.

A non-response survey was carried out among all non-respondents of the Monitoring Project in the period August-December 1991 to assess possible selection bias due to low response rate. The non-response survey indicated that a substantial proportion of the non-response was due to errors and non-currentness of the municipal population registration [3]. Also, no difference was found in the education level between respondents and non-respondents.

Rotterdam Elderly Study

One of the studies included in this thesis focused on the elderly. The study comprised data from the participants of the Rotterdam Study. The Rotterdam Study is a prospective single centre population-based study, designed to investigate determinants of selected chronic diseases and disabilities in the elderly [4]. The rationale of the study is based on the expectancy of an increasing number of elderly people with chronic diseases in many Western countries including the Netherlands. The focus of the study has been on neurogeriatric, cardiovascular, locomotor and opthalmologic diseases.

The cohort of the Rotterdam Study was defined as all inhabitants of Ommoord, a suburban district in Rotterdam, who were 55 years of age or older at 1 January 1990. All eligible participants were invited to participate, including those living in nursing homes. The baseline examinations started in May 1990 and continued until June 1993. Of the 10275 eligible subjects, 7983 (78%) agreed to participate. During a home visit, trained interviewers administered a questionnaire, covering socioeconomic background, smoking habits, alcohol consumption, dietary habits, medical history and medication use. This was followed by two extensive clinical examinations at the research centre. Those living in nursing homes or homes for the elderly, about 11% of the study population, were examined at their institutions.

Follow-up data on morbidity and mortality of the participants of the Rotterdam Study are obtained through automatized diagnosis registers of collaborating general practitioners and information on medication is provided by pharmacists. Information on vital status was also acquired at regular intervals from the municipal authorities of Rotterdam. Many of the examinations at the research centre were repeated using identical procedures by biennal examinations and were supplemented with questions addressing issues that are not part of the follow-up data provided routinely by the general practitioners.

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3.2 Quality of data on measurements of relative weight and body fat distribution in the WHO MONICA Project

When anthropometric measures are compared between study populations or within study populations over time, sufficient attention should be paid on the quality of data to ensure that the possible differences observed are not due to bias in the measurements. In multi-centre clinical trials the importance of standardization and quality control is well understood, but in other studies this part of the data analysis is often described very briefly in the literature. Reporting the use of standardized methods is however not adequate, it is important also to evaluate the extent these methods have been followed in the different study populations.

The anthropometric variables measured in the WHO MONICA Project were weight and height, and circumferences of waist and hip. In this chapter the assessment of the quality of data on measurements of weight and height, and waist and hip circumferences in the population surveys of the WHO MONICA Project are described, areas with potential influence on the validity and precision of results of these measurements are identified and standard methods for quality assessment are suggested by identifying quality items and defining quality scores. Three major areas are considered: survey procedures used, measures of quality assurance applied in the study centres to ensure high quality of data and quality indicators contained in weight, height, waist and hip value recordings. The analysis is qualitative rather than quantitative in terms of estimating the effects on survey results.

Compared with most other measurements in the MONICA population surveys, like serum cholesterol or blood pressure, weight, height, and waist and hip circumferences can be measured more easily, provided that the standard measurement procedures are being followed and the observers have been trained properly. However, if the standard procedures and/or training have been neglected, the measurements are vulnerable to various biases. Potential sources of bias for weight and height measurements are inadequate measurement devices, incorrect calibration of the measurement devices, inappropriate clothing or position of the subject during measurement, and wrong position of the observer. For waist and hip circumferences, potential sources of bias include incorrect anatomical level of measurement, too heavy clothing or wrong position of the subject and applying incorrect tension to the tape measure.

Since all three surveys were not carried out in all study populations, the number of study populations differed by survey. Weight and height were measured in all study populations in all surveys. 54, 43 and 41 study populations in the initial, middle and final survey respectively were assessed for weight and height. The measurement of waist and hip circumference was introduced in 1990 in MONICA. Hence, waist and hip circumferences were not measured in the initial survey, and they were optional in the middle survey. 22 populations in the middle and 34 in the final survey measured waist and hip circumferences.

The standard procedures to measure weight and height were originally described in the Manual of Operations of the WHO MONICA Project [1]. The same procedures were repeated in the different versions of the MONICA Manual (1986 [2], 1990), until a more detailed description concerning the recommendation for scales and the procedures for checking the scales was given in the version of March 1992 [3] . The following standard procedures were stipulated to measure weight and height:

* The participants are in standing position without shoes and heavy outer garments.
* The use of balance scales to measure weight is recommended.
* The scales should be tested daily.
* Weight is measured to the nearest 200g and height to the nearest 1 cm.
* Use of self-reported data in ambulatory subjects is not allowed.

The following instructions were given in the Manual (November 1990) to measure waist and hip circumferences:

* The measurement of waist should be recorded at the level midway between the lower rib margin and the iliac crest, rounded to the nearest .0 or .5 cm.
* The circumference should be measured on subjects without heavy outer garments in standing position. The contents of all pockets should be removed. All tight clothing, including the belt, must be loosened. The participant should stand with the feet fairly close together (about 12-15 cm) with weight equally distributed on each leg. Participants should be asked to breath out gently at the time of the reading of the measurement to prevent them from contracting their muscles or from holding their breath.
* The tape should be held firmly in a horizontal position.
* Hip should be measured at the maximum circumference over the buttocks, rounded to the nearest .0 or .5 cm.

The quality items considered for weight and height measurements were: removal of clothes, type of scale, accuracy of weight measurement, accuracy of height measurement, use of self-reported data, measurer training, checking of scales, procedures with incorrect data, proportion of missing data, within cohort trends in height between surveys and distribution of terminal digits. For waist and hip measurements the following quality items were assessed: adherence to the protocol, observer training, availability of observer code, removal of clothes, accuracy of measurement, proportion of missing data and distribution of terminal digits. Results of these assessments are reported in detail in separate publications [4,5].

To summarize the quality of data on weight and height measurements quality scores were defined.

Weight score was defined as:

- 2 (no indication of a problem) if the proportion of terminal zeros was <= 30% and there were <= 13% zeros in the second last digit;
- 1 (some concern) if not 2 or 0;
- 0 (major concern) if the proportion of terminal zeros was >60% or there were >14% zeros in the second last digit.

Scale score was defined as:

- 2 if balance scales were used (this was the recommendation);
- 1 if digital scales were used;
- 0 if bathroom scales were used.

Height score was defined as:

- 2 if the proportion of terminal zeros was <= 13%;
- 1 if not 2 or 0;
- 0 if the proportion of terminal zeros was > 14%.

A summary score for weight and height measurements was derived using the sum of weight score, scale score and height score. The score was 2 if the sum was 5 or 6; 1 if the sum was 3 or 4; and 0 if the sum was 0, 1 or 2 or the quality of some items was very bad even though the sum was more than two.

Waist score and hip score were defined as:

- 2 (no indication of a problem) if the proportion of terminal zeros was between 30% and 70%,
  and there were <= 13% zeros in the second last digit,
  and the proportion of missing data was <= 30%;
- 1 (some concern) if not 2 or 0;

0 (major concern) if there were >14% zeros in the second last digit or the proportion of missing data was >30%.

The score was also '1' when the measurement level was not standard but clearly defined (applies to one population which measured waist at the level of umbilicus). A summary score was derived using the sum of waist and hip scores. The score was 2 if the sum was 3 or 4; 1 if both waist score and hip score were 1; and 0 if waist score was 0 or hip score was 0.

The distributions of the summary scores for data on weight and height and waist and hip circumferences by survey in the WHO MONICA Project are presented in Table 1. The results of the quality analysis show that there were no major concerns of the quality of data on weight, height, and circumferences of waist and hip in most of the MONICA study populations. 51 study populations had satisfactory quality of data for weight and height measurements in the initial survey, 42 in the middle survey and 40 in the final survey. Only one to three populations in each survey showed such quality problems in weight and height measurements that these populations cannot be included in the collaborative analyses of the WHO MONICA Project. The analysis also revealed that there was an improvement in the quality of weight and height measurements, especially regarding last digit preferences and accuracies of measurement, from the initial to the middle and final surveys.

Nineteen populations had satisfactory quality of data for waist and hip circumferences in the middle survey and 32 in the final survey. Two populations in both surveys showed such quality problems in measurements of waist and hip circumferences that these populations cannot be included in the collaborative analyses of the WHO MONICA Project.

The summary scores for both weight and height and waist and hip measurements were mainly based on the actual data available, not on information on survey procedures used and measures of quality assurance applied in the MCCs even though quality items of these areas were investigated in the analysis. This may be seen as a limitation of the method used. The reason to base the summary scores on the data quality items was that all the information on survey procedures and quality assurance measures was self-reported. Self-reported data are often susceptible to a so-called 'desirability-bias', and the many discrepancies between the reported and actual measurement accuracies observed among the populations of this study support the view that the information on survey procedures and quality assurance measures should be used with reservations.

Table 1. Distribution of summary scores for data on weight and height and measurements of waist and hip circumferences in the MONICA surveys.

Weight and height

Survey	Optimal (2)	Satisfactory (1)	Unsatisfactory (0)	Total
Initial	28	23	3*	54
Middle	33	9	1	43
Final	34	6	1	41

Waist and hip

Survey	Optimal (2)	Satisfactory (1)	Unsatisfactory (0)	Total
Middle	8	11**	2	22
Final	17	15	2	34

* One study population had a summary score zero even though the sum was more than 2. In this population 24% of the subjects had their weights recorded to the full 10 kg.

** One population measured waist at the level of umbilicus. In another population the mean hip was surprisingly low and the MCC was asked to check the data, but there was no indication of problems with the measurements or the data.

For weight and height, the quality assessment based on the data is probably good in identifying the populations where the measurers were not trained properly. However, it is less good in detecting errors in the calibration of the scales and height rules. In many populations the calibration was not checked regularly. In such populations an undetected bias due to calibration error is possible. For height measurements serious calibration problems could be reflected in large fluctuations in mean height within the birth cohorts. The accuracy of height measurement is especially important for calculating BMI, because the relative bias induced by height to BMI is approximately twice the bias of height. The results of the analysis of height within birth cohorts supports the view that relatively few problems occurred in the measurement of height.

For waist and hip circumferences, it is especially important that the measurements are standardized across the study populations because small differences in the anatomical measurement level can result in large fluctuations in the population estimates based on these measurements [6]. Even though some reports have shown very high inter-observer correlations of these measurements [7], the effect of inter-observer differences cannot totally be ruled out, even if the standard methods were applied, when comparisons are made between the study populations of the WHO MONICA Project.

In conclusion, even with a common study protocol appropriate measurement quality cannot be taken for granted in multi-centre studies but should be evaluated before data are used for comparative analyses. Standardized assessment methods of weight, height, waist and hip measurements proposed in this study can be used in such an assessment.

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4. Relative weight

4.1 Smoking and relative body weight - an international perspective from the WHO MONICA Project

Abstract

Study objective: To investigate the magnitude and consistency of the associations between smoking and body mass index (BMI) in different populations.

Design: Cross-sectional study.

Setting and participants: About 69,000 men and women aged 35-64 years from 42 populations participating in the first WHO MONICA survey in the early and mid 1980s.

Main results: Compared to never smokers, regular smokers had significantly ($p<0.05$) lower median BMI in 20 (men) and 30 (women) out of 42 populations (range -2.9 to 0.5 kg/m^2). There was no population in which smokers had a significantly higher BMI than never smokers. Among men, the association between leanness and smoking was less apparent in populations with relatively low proportions of regular smokers and high proportions of ex-smokers. Ex-smokers had significantly higher BMI than never smokers in 10 of the male populations but in women no consistent pattern was observed. Adjustment for socioeconomic status did not affect these results.

Conclusions: Although in most populations the association between smoking and BMI is similar, the magnitude of this association may be affected by the proportions of smokers and ex-smokers in these populations.

Introduction

Numerous epidemiological studies have shown a consistent inverse relationship between smoking and body weight: smokers weigh relatively less than non-smokers [1-11] and smoking cessation often leads to weight gain [1-3,5,7,10,12-14]. It has been demonstrated that this is mainly because smoking increases energy expenditure [15]. Moreover, the inverse relationship between smoking and relative body weight becomes stronger with age [4] which can be explained by longer duration of smoking [5,16].

Among smokers a U-shaped relationship between the number of cigarettes smoked and relative body weight has been found in several studies - those smoking 10-20 cigarettes per day being the leanest [1-5,7,9,17,18]. Although this seems paradoxical given the metabolic effects of smoking, it has been suggested that heavy smokers may weigh more because of clustering of other unhealthy habits such as high intake of saturated fat, heavy use of alcohol and little exercise. Indeed, a study in Finland found that a change in the association between smoking and body weight had occurred in the 1980s: smoking was no longer associated with leanness in this population but rather it was positively related to BMI, especially among younger middle-aged men [16].

Most studies of the relationship between smoking and relative body weight have looked at single populations or cohorts. Therefore we considered it important to examine whether associations are similar in populations with different histories of smoking habits and changes in body weight. We investigated this among men and women in 42 populations participating the WHO MONICA Project.

Given the findings of the Finnish study on changes in the relationship between smoking and relative body weight, it could be hypothesized that the "classical" inverse association between smoking and relative body weight might hold in populations with high prevalence of smoking and comparatively few anti-smoking activities, while a "new" positive association between smoking and relative body weight may be more typical in populations with a previously high but currently falling prevalence of smoking due to anti-smoking programmes. While our data do not allow us to test this hypothesis directly, we will mainly focus on determining whether there are populations with the "new" association to warrant pursuing such a hypothesis.

Subjects and methods

The WHO MONICA Project was designed to measure trends in incidence and mortality from cardiovascular disease, and to assess the extent to which these trends are related to changes in known risk factors in 49 study populations in 26 countries. Risk factors in the WHO MONICA Project are monitored through up to three independent cross-sectional population surveys [19-20]. The surveys included random samples of at least 200 people in each gender and ten-year age group, for the age range 35-64 years, and optionally 25-34 years. This study presents data from the baseline surveys. The survey periods range from May 1979 to February 1989 and are mostly concentrated in the early and mid 1980s. In this study, only the age range from 35 to 64 years is considered. The overall participation rates for the surveys varied from 54% to 89%. The population sizes, participation rates and survey periods have been described in more detail elsewhere [21].

Height and body weight were measured with participants standing without shoes and heavy outer garments. Body mass index (BMI) was calculated as weight divided by height squared (kg/m^2) as a measure for relative weight. BMI categories were formed according to the WHO guidelines [22] except for using 21 kg/m^2 instead of the WHO recommendation of 18 kg/m^2 as a cut-off point for the leanest category. This cut-off point was selected to ensure a sufficient number of subjects in each category and because of its use in some other studies [23]. The subjects were classified as follows:

* Lean persons: BMI less than 21 kg/m^2
* Persons of normal weight: BMI equal to or more than 21 but less than 25 kg/m^2
* Overweight persons: BMI equal to or more than 25 but less than 30 kg/m^2
* Obese persons: BMI equal to or more than 30 kg/m^2.

Data on smoking were obtained with a standard questionnaire [24]. In the analysis respondents were classified as follows:

* Regular cigarette smokers, those reporting smoking cigarettes every day. They were further classified in concordance with several other studies [2,3,8,9] as
    a) light to moderate smokers, those smoking 1-19 cigarettes per day, and
    b) heavy smokers, those smoking 20 or more cigarettes per day.
* Other current smokers, those reporting smoking cigarettes occasionally or at least 1g of pipe tobacco per week or at least one cigar per week.
* Ex-smokers, those reporting smoking cigarettes regularly in the past but not currently.

* Never smokers, those who were not current smokers and had never smoked cigarettes regularly.

The age group of the subject was obtained from the sampling frame at the time of sample selection. Tertiles of years of schooling within each population were used as a measure of socioeconomic status (SES). Years of schooling were obtained by asking: "How many years did you spent at school or in full-time study?". Tertiles of years of schooling were calculated for men and women in each 10-year age group separately.

The quality of data on weight, height, smoking behaviour and years of schooling has been centrally assessed. Any population with unsatisfactory quality of data or response rate lower than 50% for any of the items has been omitted from this study. This left 42 populations, except for analyses involving years of schooling, where only a subset of 34 populations with full data was included.

Statistical methods

In the first phase of data analysis, population level (ecological) data were analyzed to estimate the strength of association between smoking and relative body weight. Pearson correlation coefficients between the proportions of regular cigarette smokers and the means and percentiles of BMI were calculated for men and women for each 10-year age group. Correlations of age standardized values are given for the age group 35-64. Age standardized values were calculated using the World Standard Population [25] as the reference population with weights 12, 11 and 8 for the 10-year age groups 35-44, 45-54 and 55-64 respectively.

In the second phase, individual data were used to examine the consistency and magnitude of the relation between smoking and BMI at the individual level. All analyses were carried out separately for men and women. Two types of analyses were performed: firstly, comparing medians or means of BMI between different categories of smoking, and secondly, comparing proportions of regular smokers between different categories of BMI within populations. Differences were reported to be statistically significant if the p-value was less than 0.05.

To compare the levels of BMI between smoking categories, medians instead of means of BMI were used because of the distributions of BMI were skewed to the right. Confidence intervals for the differences in median BMIs in categories of smokers, compared to the never smoker category, were calculated using the Normal approximation as described by White et al. [26]. Linear regression was used to control for potential confounding by SES. Mean BMIs and differences in mean BMIs by smoking category were calculated using the general linear model (GLM) procedure of SAS statistical software [27], adjusting for age group and population as categorical covariates. To assess the confounding effect of SES, regression analyses were performed both with and without adjusting for population specific tertiles of years of schooling. Confidence intervals for the estimates were calculated from the standard errors of the regression coefficients assuming that the sampling distributions of the coefficients were normal. The results of the linear regression were also used to give an overall estimate of the differences in the mean BMIs between smoking categories summarizing the results across all populations. In addition, the same overall estimates were calculated using non-parametric methods to confirm that the estimates based on the regression analysis did not differ from the estimates based on medians.

To compare the prevalence of regular cigarette smoking between BMI categories, age standardized proportions of regular cigarette smokers were calculated for the age group 35-64 using the same method for age standardization as described above. The differences in the proportions of smokers between BMI categories within populations were tested by fitting a logistic regression model with regular cigarette smoking as the binary dependent variable and age group as the independent variable, with and without adjustment for indicator variables for BMI categories.

To estimate the overall difference in the age standardized proportions of regular cigarette smokers between BMI categories the mean of the differences and a 95% confidence interval for this mean were calculated summarizing the results across all study populations. The normal weight category (BMI=21.0-24.9 kg/m^2) was used as the reference category when comparing proportions of regular smokers. The confidence intervals were calculated from standard errors of the means using t-distribution with the number of populations minus one for the degrees of freedom.

Results

Table 1 gives the number of subjects, age standardized proportion of regular cigarette smokers and age standardized prevalence of obesity (BMI $\geq$ 30 kg/m^2) in each population. The table shows considerable variation both in prevalence of regular smoking and obesity across the study populations. The prevalence of regular cigarette smoking ranged from 24% to 59% in men and from 3% to 50% in women. In general, among men the prevalence of smoking was highest in some Eastern European (Poland, Russia) populations and lowest in

Table 1. Number of subjects, age-standardized proportion (%) of regular cigarette smokers and age-standardized prevalence of obesity (BMI≥30 kg/m²) in first MONICA population survey. Men and women aged 35-64 years.

			MEN			WOMEN		
Population	Country	Abbreviation	N	% smokers	% obese	N	% smokers	% obese
Newcastle	Australia	AUS-NEW	1218	34	15	1241	24	16
Perth	Australia	AUS-PER	631	33	9	661	22	11
Ghent	Belgium	BEL-GHE	539	43	11	495	25	15
Luxembourg Province	Belgium	BEL-LUX	989	43	13	959	18	18
Beijing	China	CHN-BEI	619	51	3	641	16	9
Czech Republic	Czech Rep.	CZE-CZE	948	44	21	990	21	32
Glostrup	Denmark	DEN-GLO	1456	45	11	1361	44	10
Kuopio Province	Finland	FIN-KUO	968	34	18	981	10	19
North Karelia	Finland	FIN-NKA	1125	30	17	1212	9	24
Turku/Loimaa	Finland	FIN-TUL	1194	30	19	1270	17	17
Lille	France	FRA-LIL	641	39	14	530	11	19
Strasbourg	France	FRA-STR	666	34	22	714	14	23
Toulouse	France	FRA-TOU	678	36	9	645	17	11
Augsburg rural	Germany	GER-AUR	846	30	20	857	12	22
Augsburg urban	Germany	GER-AUU	712	36	18	679	18	15
Bremen	Germany	GER-BRE	633	45	14	656	29	18
Cottbus County	Germany	GER-COT	460	31	17	543	11	23
Halle County	Germany	GER-HAC	816	38	18	859	14	27
Karl-Marx-Stadt County	Germany	GER-KMS	813	37	14	926	15	19
Rest of DDR-MONICA	Germany	GER-RDM	763	37	17	822	24	21
Rhein-Neckar Region	Germany	GER-RHN	1170	31	13	1266	23	12
Iceland	Iceland	ICE-ICE	657	26	11	704	40	11
Area Brianza	Italy	ITA-BRI	618	44	11	639	18	15
Friuli	Italy	ITA-FRI	719	35	16	724	26	19
Kaunas	Lithuania	LTU-KAU	728	38	22	735	4	45
Auckland	New Zealand	NEZ-AUC	1018	29	8	567	25	9
Tarnobrzeg Voivodship	Poland	POL-TAR	1250	58	13	1472	11	32
Warsaw	Poland	POL-WAR	1309	59	18	1337	33	26
Bucharest	Romania	ROM-BUC	524	38	20	632	15	31
Moscow control	Russia	RUS-MOC	770	48	13	645	12	33
Moscow intervention	Russia	RUS-MOI	1163	46	12	1234	9	35
Novosibirsk control	Russia	RUS-NOC	1061	59	15	1054	3	44
Novosibirsk interv.	Russia	RUS-NOI	601	53	13	646	3	43
Catalonia	Spain	SPA-CAT	993	47	9	994	7	24
Gothenburg	Sweden	SWE-GOT	517	33	7	557	34	9
Northern Sweden	Sweden	SWE-NSW	640	24	11	611	26	14
Ticino	Switzerland	SWI-TIC	781	38	20	769	24	15
Vaud/Fribourg	Switzerland	SWI-VAF	627	32	13	568	21	13
Belfast	UK	UNK-BEL	927	34	11	925	33	14
Glasgow	UK	UNK-GLA	502	52	11	480	50	16
Stanford	USA	USA-STA	427	40	10	516	36	15
Novi Sad	Yugoslavia	YUG-NOS	592	49	17	555	27	29

some Nordic (Sweden, Iceland) populations. Among women, however, smoking was relatively more common in some Western European populations and less common in Eastern Europe. There were more female than male smokers only in Iceland (where 22% of men smoked pipes or cigars) and in Sweden. The prevalence of obesity ranged from 3% to 22% in men and from 9% to 45% in women and was relatively more common in populations with low prevalence of smoking, especially among women.

Table 2. Pearson correlation coefficients between proportion (%) of regular cigarette smokers and mean and percentiles of body mass index (BMI) for 42 populations in the first MONICA survey.

	MEN		WOMEN	
Age group	r	95% CI	r	95% CI
MEAN				
35-44	-0.07	(-0.36, 0.24)	-0.45	(-0.66,-0.17)
45-54	-0.37	(-0.61,-0.08)	-0.65	(-0.79,-0.43)
55-64	-0.30	(-0.55, 0.01)	-0.63	(-0.79,-0.41)
age stand. 35-64	-0.25	(-0.52, 0.05)	-0.59	(-0.76,-0.35)
MEDIAN				
35-44	0.00	(-0.30, 0.30)	-0.46	(-0.67,-0.18)
45-54	-0.34	(-0.59,-0.04)	-0.62	(-0.78,-0.39)
55-64	-0.30	(-0.55, 0.00)	-0.64	(-0.79,-0.41)
age stand. 35-64	-0.22	(-0.49, 0.09)	-0.57	(-0.75,-0.33)
10th PERCENTILE				
35-44	-0.16	(-0.44, 0.15)	-0.47	(-0.68,-0.19)
45-54	-0.54	(-0.73,-0.29)	-0.63	(-0.79,-0.41)
55-64	-0.50	(-0.70,-0.23)	-0.58	(-0.75,-0.33)
age stand. 35-64	-0.43	(-0.65,-0.14)	-0.56	(-0.74,-0.31)
90th PERCENTILE				
35-44	0.04	(-0.27, 0.34)	-0.37	(-0.61,-0.08)
45-54	-0.22	(-0.49, 0.09)	-0.58	(-0.75,-0.33)
55-64	-0.10	(-0.39, 0.21)	-0.60	(-0.76,-0.36)
age stand. 35-64	-0.08	(-0.37, 0.23)	-0.54	(-0.72,-0.28)

Table 2 presents Pearson correlation coefficients between the proportion of regular cigarette smokers and BMI. These are ecological correlations where each population represents one observation. For women, smoking was significantly inversely related to BMI for all four measures: 10th percentile (leanness), mean and median BMI (average weight) or 90th percentile (obesity). For men, the age-standardized prevalence of smoking was significantly inversely related to the 10th percentile only. For both men and women the weakest correlations were observed in the age group 35-44 years.

Figures 1.1 and 1.2 show differences in median BMI between never smokers and regular cigarette smokers. In almost all populations smokers were leaner than never smokers: the difference was statistically significant in 20 out of 42 populations for men and in 30 out of 42 populations for women. The differences ranged from -2.4 to 0.5 kg/m^2 in men and from -2.9 to -0.1 kg/m^2 in women. When translated into kilograms for an average height of 1.72 m and 1.60 m for men and women, respectively, they correspond to the range from -7.1 to1.5 kg for men and from -7.4 to -0.3 kg for women. The largest differences were observed in populations with relatively high smoking rates (e.g. in some Eastern European populations).

To elucidate further the difference between the populations where the smokers were considerably leaner than never smokers in comparison to populations where they were not, we compared the proportion of regular smokers in the 14 populations with the largest differences in BMI to the 14 populations with the smallest differences in BMI between smokers and never smokers with a non-parametric (Wilcoxon rank sum) test (Table 3). Among men, there were significantly more regular smokers in the populations with the largest differences in BMI than in the populations with the smallest differences. In addition, the proportions of ex-smokers were statistically significantly lower in these populations. For women, however, there were fewer smokers in the group of populations with the largest differences in BMI than in the populations with the smallest differences but the difference in smoking prevalences was not statistically significant. The prevalence of ex-smokers was significantly lower in the populations with large differences in BMI.

Figures 2.1 and 2.2 show the difference in median BMI between never smokers and ex-smokers. Ex-smokers had higher BMI than never smokers in 37 (and significantly so in 10) out of 42 populations among men, whereas for women there were differences in both directions but few were statistically significant. No systematic differences in BMI were observed between heavy and light smokers in most populations (data not shown).

Figure 1.1 Difference in median BMI between regular cigarette smokers and never smokers. First MONICA survey, men aged 35-64.

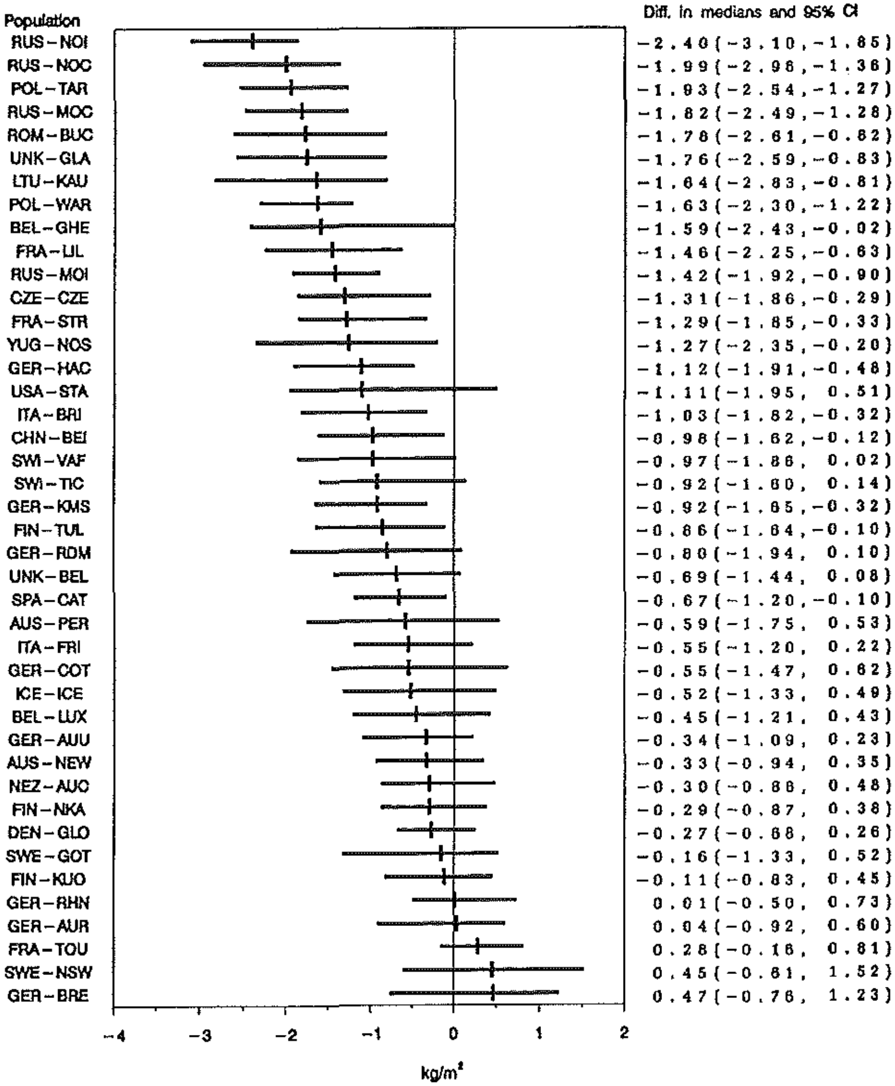

Figure 1.2 Difference in median BMI between regular cigarette smokers and never smokers. First MONICA survey, women aged 35-64.

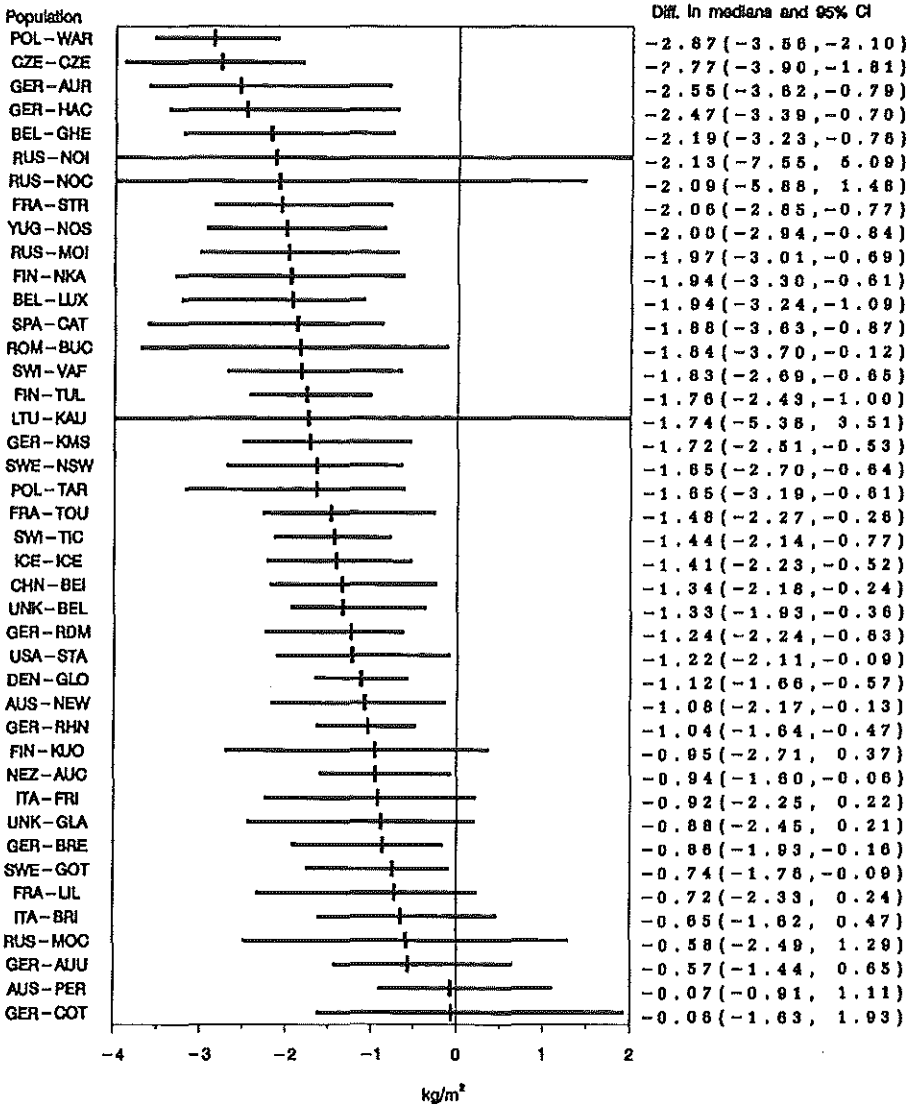

Table 3. Proportions of regular smokers and ex-smokers in 14 populations with the largest difference in BMI between smokers and never smokers compared with 14 populations with the smallest difference. First MONICA survey, men and women aged 35-64.

	Range for diff. in BMI between smokers and never smokers (kg/m²)	Median % of regular smokers	p-value	Median % of ex-smokers	p-value	N
MEN						
Big diff.	-2.4, -1.3	47	<0.001	23	0.03	14
Small diff.	-0.5, 0.5	33		29		14
WOMEN						
Big diff.	-2.9, -1.8	14	0.07	7	0.02	14
Small diff.	-1.1, -0.1	22		10		14

Regression analysis was used to examine the potential confounding effects of SES using population specific tertiles of years of schooling as an indicator. The unadjusted (for SES) analysis was performed first for all populations and then for a subset of 34 populations, for which data on years of schooling were available, and then the SES-adjusted analysis was performed for the 34 populations (Table 4). The results were very similar whether adjusted for tertiles of years of schooling or not, indicating that SES had hardly any confounding effect on this association.

The mean BMI in the never smoking category was 26.6 kg/m^2 for men and 26.8 kg/m^2 for women when adjusted for age group and population. In men, regular cigarette smokers were on average 0.9 kg/m^2 leaner than never smokers, which implies that a male smoker of average height of 1.72 m weighed 2.7 kg less than a never smoker of the same height. Male ex-smokers had 0.5 kg/m^2 higher BMI than never smokers indicating that an ex-smoker of average height weighed 1.5 kg more than never smoker. In women, regular cigarette smokers were on average 1.1 kg/m^2 leaner than never smokers which implies a difference of 2.8 kg for a woman of average height of 1.60 m, but there was no significant difference between never and ex-smokers. For women, but not for men, light smokers had significantly lower BMIs than heavy smokers thus showing a U-shaped relationship between smoking and BMI.

Figure 2.1 Difference in median BMI between ex-smokers and never smokers. First MONICA survey, men aged 35-64.

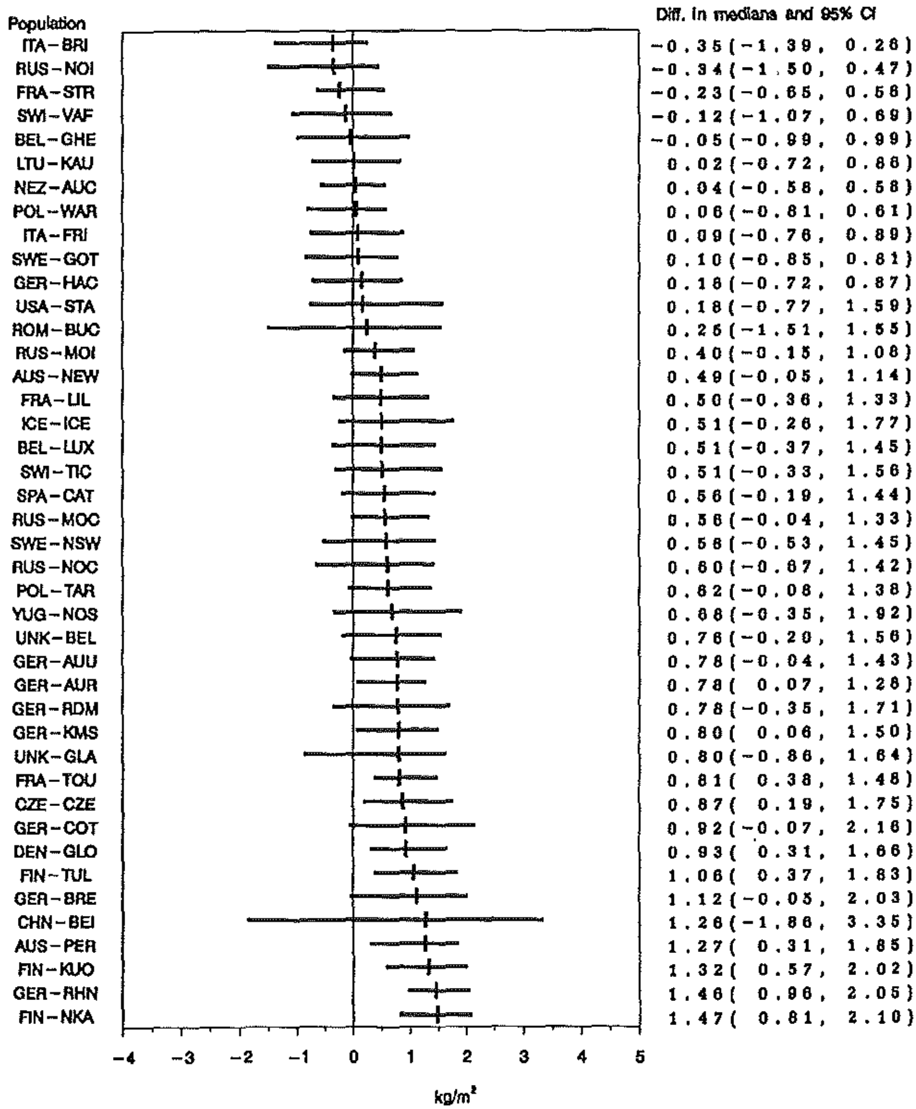

Figure 2.2 Difference in median BMI between ex-smokers and never smokers. First MONICA survey, women aged 35-64.

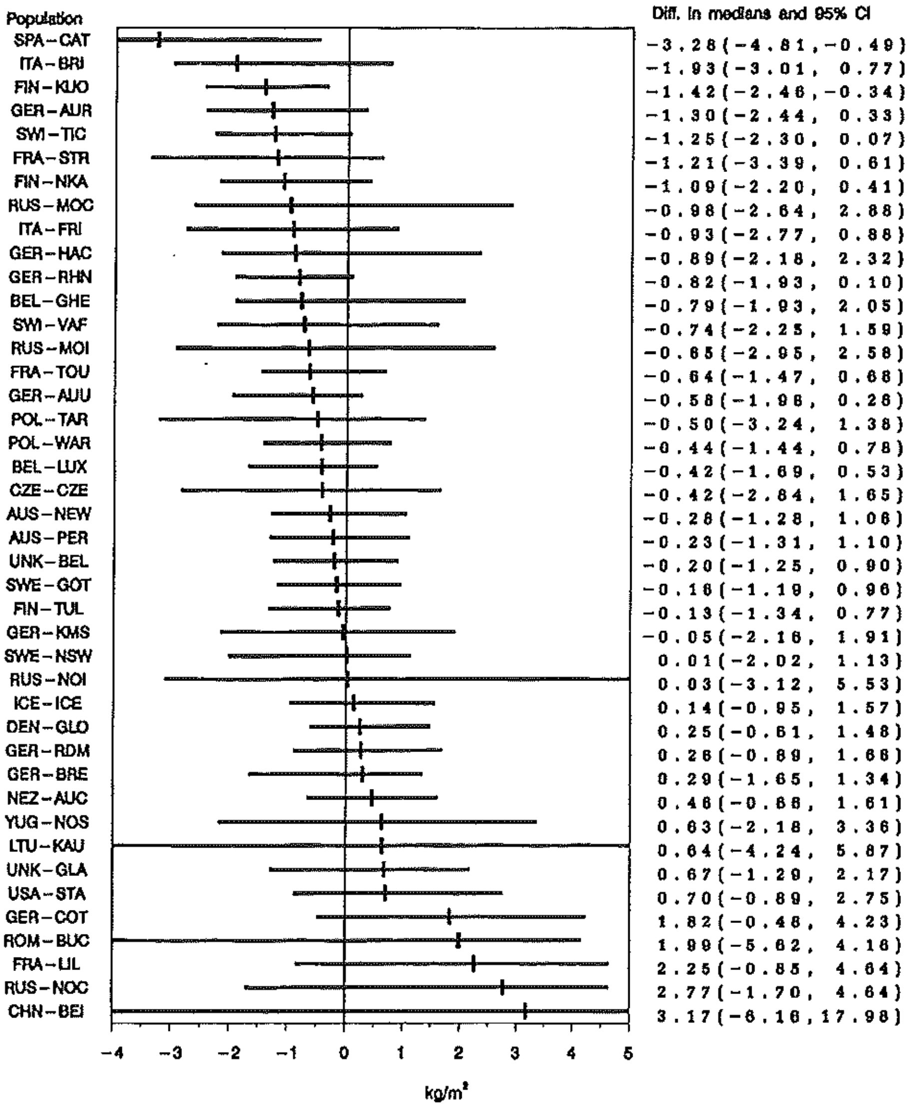

Table 4. Summary measures of BMI by smoking category. Results from regression analysis. First MONICA survey, men and women aged 35-64.

MEN

	Mean BMI (and 95% CI) adjusted for age group and population					
	unadj. for SES *		unadj. for SES **		adj. for SES **	
Never smokers	26.6	(26.5,26.6)	26.6	(26.5,26.7)	26.6	(26.5,26.7)
Difference between never smokers and						
Regular cigarette smokers	-0.9	(-1.0,-0.8)	-0.9	(-1.0,-0.8)	-1.0	(-1.1,-0.9)
Light smokers	-0.9	(-1.0,-0.7)	-0.9	(-1.0,-0.8)	-0.9	(-1.1,-0.8)
Heavy smokers	-0.9	(-1.0,-0.7)	-0.9	(-1.1,-0.8)	-1.0	(-1.1,-0.9)
Ex-smokers	0.5	(0.4,0.6)	0.5	(0.4,0.6)	0.5	(0.4,0.6)

WOMEN

	Mean BMI (and 95% CI) adjusted for age group and population					
	unadj. for SES *		unadj. for SES **		adj. for SES **	
Never smokers	26.8	(26.7,26.9)	26.9	(26.9,27.0)	26.9	(26.8,26.9)
Difference between never smokers and						
Regular cigarette smokers	-1.1	(-1.3,-1.0)	-1.2	(-1.4,-1.1)	-1.2	(-1.3,-1.0)
Light smokers	-1.3	(-1.4,-1.1)	-1.4	(-1.5,-1.2)	-1.3	(-1.5,-1.1)
Heavy smokers	-0.8	(-1.0,-0.6)	-0.9	(-1.1,-0.7)	-0.9	(-1.1,-0.7)
Ex-smokers	-0.03	(-0.2,0.2)	-0.05	(-0.3,0.2)	0.1	(-0.1,0.3)

SES measured with population, gender and age group specific tertiles of years of schooling
* based on data from 42 populations
** based on data from 34 populations

The overall estimates of the differences in BMI between smoking categories were also calculated using non-parametric methods. The estimates based on medians were very similar to those produced by the regression analysis. Only the median BMIs for never smokers (26.3 and 26.1 kg/m^2 for men and women respectively) were somewhat lower than the means, especially for women, due to the skewness of the distributions.

The age standardized proportion of regular smokers decreased consistently with increasing BMI category (Table 5). The difference between BMI categories was significant in 35 out of 42 populations among men and in 26 among women. In men the differences were larger than in women. Some exceptions to the general pattern were observed, for example among men in Auckland, Gothenburg, Toulouse and Northern Sweden there were more smokers in the obese than in the normal weight category, but the exceptions were usually not statistically significant.

On the basis of these results one could group the populations into two categories. In most populations for men and almost all for women the "classic" inverse association between smoking and BMI was observed. In some populations, there was no clear association. These include at least Auckland, Gothenburg, Toulouse and Northern Sweden for men and perhaps Cottbus County and Perth for women.

Table 5. Age-standardized prevalence of regular cigarette smoking by BMI category based on data from 42 populations. First MONICA survey, men and women aged 35-64.

MEN

BMI category	Proportion (%) of smokers	95% CI
Lean (BMI<21.0)	61.8	(56.4, 67.2)
Normal weight (BMI=21.0-24.9)	45.6	(41.8, 49.3)
Overweight (BMI=25.0-29.9)	35.2	(32.8, 37.6)
Obese (BMI>=30.0)	31.8	(29.5, 34.1)

WOMEN

BMI category	Proportion (%) of smokers	95% CI
Lean (BMI<21.0)	30.0	(26.0, 34.0)
Normal weight (BMI=21.0-24.9)	22.8	(19.3, 26.4)
Overweight (BMI=25.0-29.9)	18.0	(14.8, 21.2)
Obese (BMI>=30.0)	13.9	(11.3, 16.5)

Discussion

The association between smoking and relative body weight is an important health issue because both smoking and increased body weight are independent risk factors for cardiovascular disease and quitting smoking is known to lead to weight gain. In addition, smoking is a potential confounder in the relationship between relative body weight and mortality [8,23]. Therefore the recent suggestion that the relationship might be changing from a negative association to a positive one [16], especially among men, prompted us to explore this association in a wide range of populations. The data collected through the WHO MONICA Project population surveys provided a unique opportunity to look at this relationship in a large number of populations from different parts of the world, based on common standardized survey methods for data collection and quality assurance, and centralized data analysis.

Our results show that the generally accepted finding that smokers weigh less than never smokers [12] still prevails in most populations. This was especially true for women. Also a U-shaped relationship between BMI and number of cigarettes smoked was found among women but not among men, whereas earlier investigations have generally found a stronger relationship in men [4,9,16,18]. This could be partly explained by the fact that we only used two categories for numbers of cigarettes smoked.

Among men, in some of the study populations there was no association between smoking and BMI and in these populations there were in general fewer smokers and more ex-smokers than in populations where smokers were considerably leaner than never smokers. This finding suggests that the magnitude of the inverse association between smoking and body weight may be related to the prevalence of smoking in the population. It also partly supports the original hypothesis that the "classical" inverse association might no longer be found in populations with extensive anti-smoking activities and reduced prevalence of smoking e.g. in Australia, Finland, Sweden, the USA. However, no statistically significant positive association was found in any of these populations. Therefore it would be premature to draw any definitive conclusions about a change in the direction of the relationship, especially because this study was based on cross-sectional data and reflects the situation in the early and mid 1980s. More recent data, covering a longer time period, will allow this hypothesis to be tested directly.

One mechanism by which the change from inverse to positive correlation between smoking and BMI observed in the Finnish study [16] might act is through selection among smokers. As an increasing proportion of light smokers tend to quit smoking when smoking becomes regarded as socially undesirable behaviour, the group of smokers consists increasingly of heavy smokers, who on one hand have more difficulties in quitting [17] and who on the other hand have higher BMIs than light smokers [1,3,9,17]. The change in the association from inverse to positive would therefore be only an ecological change at the population level since the relative body weight of the heavy smokers at individual level need not have changed. The lack of an inverse association between smoking and BMI is more often seen among younger men than among older men or women. This might be partly explained because the decline in body weight is a long-term affect of smoking, whereas the slightly higher BMI observed in heavy smokers may be unrelated to the duration of smoking. This is, in fact, in agreement with the findings of the Finnish study where, in spite of the overall positive association, years of smoking was confirmed as a significant inverse predictor of BMI [16]. The effect of duration of smoking on body weight can however be an indirect one; it is better recognised in older people whose weights have a bigger range than in the young. The reasons for higher BMI of heavy smokers remain unclear. Clustering of unhealthy habits [16] and use of smoking as a way to control body weight among obese people [4] have been suggested as potential explanations, but no studies have been conducted specifically to explore this phenomenon.

When looking at the prevalence of smoking between different BMI categories, the most consistent inverse association was found in relation to leanness, especially among men. This is supported by earlier research [8] and suggests that even if, in some populations, average body weight might be positively associated with smoking, leanness remains inversely associated with cigarette smoking. Our data did not allow us to investigate the association between BMI and duration of smoking. This might have further elucidated the differences between populations, because mean age of starting to smoke may differ among populations and this, too, could affect the distribution of BMI.

Some studies have found ex-smokers to be heavier than never smokers [4,10], whereas others have not [3,5]. Our findings suggest that, among men, ex-smokers tend to have higher BMI than never smokers, but not among women and this finding is supported by one earlier study [11]. Also Flegal et al. [14] found that male ex-smokers were heavier than never smokers, but among women only those ex-smokers who had stopped smoking less than 10 years ago. The category of occasional cigarette smokers, pipe and cigar smokers was not compared with never smokers in this study because of the small number of observations.

Socioeconomic status (SES) is a potential confounder in the relationship between smoking and body weight. Persons with lower SES tend to smoke more [9,28] and to have higher BMIs [9,11,18] than those with higher SES, the latter especially among women. The associations found in this study were not explained by the effects of SES measured in tertiles of years of schooling. This is consistent with the results of several other studies [3,5,9,18]. We did not measure such potential confounders as physical activity, caloric intake and alcohol use, but in several studies they have not been found to be actual confounders [3,5,8] for the BMI-smoking relationship.

This work is one example how large international multi-centre studies can be used to obtain an overview strengthened by standardized methods of data collection and quality assurance. One should, however, be cautious in applying quantitative measures obtained by combining data from heterogenous populations. Nevertheless, the consistency of associations observed among a large number of different populations gives considerably more weight to the findings than results based only on one cohort or study population which cannot be directly generalized to other populations.

In summary, in populations of the WHO MONICA Project covering a wide range of smoking habits and prevalence of overweight, men and women who smoked generally had lower BMIs than never smokers. Among men, the difference was more pronounced in populations where smoking was relatively more common. Heavy smokers did not generally have lower BMIs than light smokers. Among men, but not among women, those who had stopped smoking had higher BMIs than those who never smoked. These results confirm that smoking is associated with relative body weight in individuals as well as in populations but that differences in smoking habits in a population can influence the magnitude of this association.

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4.2 Differences in the association between smoking and relative body weight by educational level: Monitoring Project on Cardiovascular Disease Risk Factors in the Netherlands

Abstract

Objective: To investigate differences in the association between smoking and relative body weight by sex, age group and level of education.

Design: Cross-sectional study.

Subjects: About 36,000 men and women who participated in the Monitoring Project on Cardiovascular Disease Risk Factors in the Netherlands in 1987-91.

Results: The association between smoking and relative body weight differed by level of education. This difference was more pronounced among men than among women. Male heavy smokers had statistically significantly ($p<0.05$) higher mean BMI than never smokers at high educational level, whereas they had a significantly lower mean BMI than never smokers at low educational level. In addition, ex-smokers had significantly higher mean BMI than never smokers in men with high education but not in men with low education nor in women. The difference in the association between smoking and relative body weight by educational level could not be explained by physical activity, fat intake or alcohol consumption nor by factors related to smoking behaviour.

Conclusion: The association between smoking and relative body weight may differ between subgroups within one population. Therefore adjustment for these subgouprs, for example for educational level, may be inappropriate in studies of the BMI-smoking relationship. Also, stopping smoking may have different effects on weight in these subgroups.

Background

Numerous epidemiological studies have shown that smokers have relatively lower body weights than non-smokers [1-11] and smoking cessation often leads to weight gain [1-3,5,7,10,12-14]. This is mainly due to the effects of smoking on metabolic rate: smoking increases energy expenditure [15], and the effect of nicotine is especially strong during light activity [16]. Moreover, the inverse relationship between smoking and relative body weight seems to become stronger by increasing age [4] which can be explained by longer duration of smoking [5,17].

Among smokers a U-shaped relationship between number of cigarettes smoked and relative body weight has been found in several studies, those smoking 10-20 cigarettes per day being leaner than those smoking less than 10 and those smoking more than 20 cigarettes per day [1-5, 7, 9, 18, 19]. Although this seems paradoxical given the metabolic effects of smoking, it has been suggested that heavy smokers may weigh more because of clustering of other unhealthy habits such as high intake of saturated fat, heavy use of alcohol and little exercise. Indeed, a study in Finland found that smoking was no longer inversely but positively related to body mass index, especially in younger middle-aged men [17]. These findings suggest that the association between smoking and relative body weight may differ between men and women and also between different age groups. Besides the effect of age, any relationship between smoking and relative body weight may be confounded by socioeconomic status (SES), as persons with lower SES tend to smoke more [9,19,20] and to have higher BMI [9,11,20] than those with higher SES. Other lifestyle factors which may effect body weight are also related to SES.

We studied the association between smoking and relative body weight in the Dutch population using data from the Monitoring Project on Cardiovascular Disease Risk Factors assigning special attention to the possible variation in this relationship between men and women and between different age groups and socioeconomic categories.

Subjects and methods

The Monitoring Project on Cardiovascular Disease Risk Factors was carried out in the Netherlands from 1987 to 1991. The aim of this project was to monitor major risk factors for cardiovascular diseases, e.g. blood pressure, plasma cholesterol, smoking habits and relative body weight. The project was carried out by the municipal health services in three towns in the Netherlands: Amsterdam, Doetinchem and Maastricht. Each year new random samples of men and women aged 20-59 years were selected from the municipal registry of each town and invited to participate in the study. To obtain equal numbers in each age category, the sampling was stratified by gender and 5-year age classes. The overall participation rate for these years was 50% for men and 54% for women [21]. From 1987 till 1991 about 36,000 men and women were examined.

The respondents were weighed wearing indoor clothing after they had taken off their shoes and emptied their pockets. Weight and height were measured to the nearest 0.1 kg and 0.5 cm respectively. Body mass index (BMI) was calculated as weight divided by height squared (kg/m^2) as a measure for relative weight. Current cigarette smoking was estimated from the questions 'Do you smoke?' as well as 'How many cigarettes do you smoke per day?' Former smoking was estimated from the following question: 'Have you ever smoked cigarettes regularly?' In addition some further questions concerning smoking history were asked of all subjects : 'At what age did you start cigarette smoking?', 'Do you smoke cigars now?', 'Do you smoke pipe now?' In the analysis respondents were classified as follows:

* Regular cigarette smokers reported smoking cigarettes every day. They were further classified into

    a) light to moderate smokers, those who smoked 1-19 cigarettes per day, and

    b) heavy smokers, those who smoked 20 or more cigarettes per day.

* Other current smokers reported smoking cigarettes occasionally or smoking pipe or cigar currently. Due to small number of subjects (430 men, 72 women) this category was excluded from the analyses.

* Ex-smokers reported smoking cigarettes regularly in the past but not currently.

* Never smokers had never smoked cigarettes regularly.

In addition, information was obtained about education, physical activity during leisure time, alcohol consumption and energy intake. Education was used as a measure for socioeconomic status. It was categorized into three levels: low, medium and high. Low education was defined as primary school, lower occupational education or less, medium as secondary level education and high education as university, higher occupational or corresponding education. Physical activity was dichotomized into inactive and active. Active was defined as exercise during leisure time for at least 4 hours per week. Alcohol consumption was obtained by asking the number of alcohol containing beverages in glasses per week and then divided by 7 to get the average number of drinks per day. The usual dietary intake was assessed by using a short (70 food items) self-administered semi-quantitative food frequency questionnaire [22]. The questionnaire was constructed to be able to assess the intake of energy and nutrients of interest in cardiovascular disease epidemiology. The food frequency questionnaire was validated in a subsample of 203 subjects. Unfortunately, it is known that there is increasing underreporting of energy intake by increasing levels of overweight [23] (usually there is a negative association between energy intake and BMI although it is known from controlled studies that the association should be positive). Therefore, percentage of fat in total energy intake was used in the analyses instead of total energy intake. After excluding pregnant women (n=306) there remained all together 35,657 subjects in the study.

To assess the possible selection bias, a non-response survey was carried out among 1 620 subjects who had been approached between August and December 1991 [21]. In 1992 they were approached for a second time by telephone (75%) or by mail for those who did not have a telephone (25%). The response was 61%, 23% could not be reached and 16% refused to participate. Respondents and non-respondents were similar with respect to educational level. In men, but not in women, the percentage of smokers was 15% higher among the non-respondents than among the respondents. The percentage of alcohol users was about 10% lower among the non-respondents compared with the respondents.

Statistical analyses

For crude analysis of the relationship between smoking and BMI, we compared mean BMIs in different smoking categories across age groups and levels of education. Since educational level, but not age, emerged as an important modifying factor in the crude analysis, multiple regression analysis was used for calculating mean BMIs in different categories of smoking adjusted for age and stratified by level of education. Mean BMIs by smoking category were calculated using the general linear model (GLM) procedure of SAS statistical software [24]. Confidence intervals for the estimates were calculated from standard errors of the regression coefficients assuming that the sampling distributions of the coefficients were normal. To test the significance of effect modification by education, we performed a regression analysis with BMI as the dependent variable and age, smoking status and educational level as independent variables together with an interaction term between educational level and smoking status. Since the results for medium education category were intermediate to those of low and high education and to keep the comparison as simple as possible, only high and low educational levels were included in this analysis. To test whether the interaction could be explained by lifestyle or by factors related to smoking behavior, we added variables measuring these factors to the model containing the interaction term, first "lifestyle variables" alone, then "smoking factors" alone and finally all together. To evaluate possible clustering of unhealthy lifestyle habits in heavy smokers, we compared the proportion of physically active, alcohol users and mean percentage of fat in total energy intake in heavy, light, never and ex-smokers stratified by educational level.

Results

Table 1 gives the mean BMI, mean age and proportion of subjects with high education in different categories of smoking. In both sexes, light smokers were the leanest. Differences between the smoking categories in age and educational level were observed. Overall, heavy smokers weighed slightly more than never smokers among men but slightly less than never smokers among women. Ex-smokers weighed more than never smokers among men but not among women. As reported already earlier [21], the mean BMI increased with age in both sexes and was inversely associated with educational level. This was more pronounced in women than in men. The prevalence of regular cigarette smokers was 42% and 39% in men and women respectively.

Mean BMI by smoking category was calculated for different age groups and different levels of education. The association between smoking and BMI was similar in all age groups (not shown) although more pronounced with advancing age. The association differed, however, by level of education. Figures 1.1 and 1.2 show the relationship between smoking and BMI stratified by educational level when adjusted for age. Among men, heavy smokers weighed more than light smokers at all levels of education. In the low education category, heavy smokers weighed significantly less than never smokers whereas they weighed significantly more than never smokers in the high education category. Ex-smokers weighed significantly more than never smokers at high and medium educational level whereas there was no difference in BMI between never and ex-smokers at low educational level. There was a bigger difference in BMI among never smokers across educational level than among heavy smokers who tended to have a "similar" BMI regardless of education. Among women, smokers usually weighed less than never smokers, but the difference was more pronounced,

Table 1. Monitoring project on Cardiovascular Disease Risk Factors in the Netherlands. Mean BMI (SD in parenthesis), mean age and proportion of subjects with high education by smoking status, men and women aged 20-59 years.

	Mean BMI (SD)	Mean age (SD)	% high educat.	N (%)
MEN				
Never smokers	25.0 (3.4)	37.6 (11.1)	24.6	4648 (28)
Light smokers	24.7 (3.3)	40.3 (11.1)	16.4	3924 (24)
Heavy smokers	25.3 (3.6)	42.8 (9.8)	12.5	2939 (18)
Ex-smokers	26.0 (3.3)	45.0 (9.7)	22.4	5147 (31)
WOMEN				
Never smokers	25.2 (4.5)	41.7 (11.9)	15.7	7536 (40)
Light smokers	24.1 (3.9)	40.2 (11.0)	12.7	4775 (25)
Heavy smokers	24.6 (4.3)	41.4 (10.0)	9.8	2669 (14)
Ex-smokers	24.8 (4.0)	42.0 (10.0)	19.2	4019 (21)

and significant, at low educational level. Also ex-smokers weighed less than never smokers at low educational level whereas there was no difference between them and never smokers at other levels of education.

The interaction between smoking and educational level described graphically in Figures 1.1 and 1.2 is presented as results of regression analysis in Table 2. Never smokers with low education were used as the reference category. The modifying effect of level of education (the interaction term) was statistically significant for both sexes in all categories of smoking. The table shows that, among men, at low educational level heavy smokers weighed 0.67 kg/m^2 (2.1 kg at height 1.75 m) less than never smokers, whereas at high educational level heavy smokers weighed 0.50 kg/m^2 (1.5 kg at height 1.75 m) more than never smokers. Among women, heavy smokers weighed 1.16 kg/m^2 (3.3 kg at height 1.70 m) less than never smokers at low educational level, and 0.28 kg/m^2 (0.8 kg at height 1.70 m) less than never smokers at high educational level.

***Figure 1.1** Mean BMI by smoking category in men aged 20-59 years, stratified by educational level and adjusted for age.*

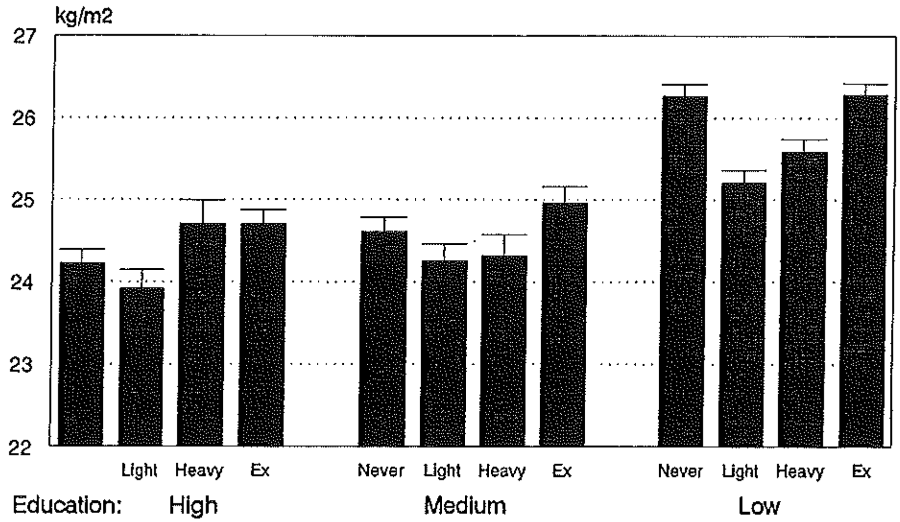

***Figure 1.2** Mean BMI by smoking category in women aged 20-59 years, stratified by educational level and adjusted for age.*

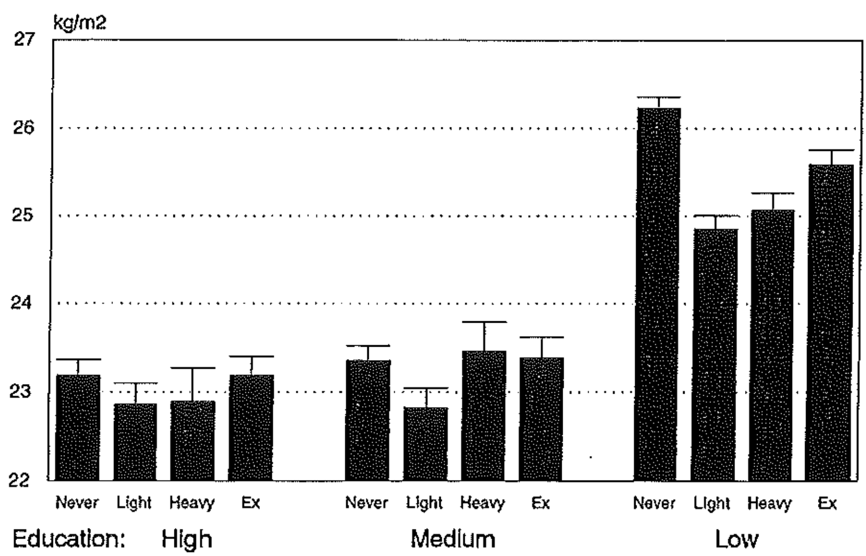

Table 2. Monitoring Project on Cardiovascular Disease Risk Factors in the Netherlands. Regression coefficients (β) for testing the interaction between education and smoking status in explaining mean BMI (kg/m²).

MEN	ß	s.e.	p-value
Intercept	22.93	0.134	.0001
Age (yrs)	0.08	0.003	.0001
Education [1]			
High	-1.83	0.118	.0001
Smoking [2]			
Light	-1.05	0.095	.0001
Heavy	-0.67	0.100	.0001
Ex	0.02	0.093	.86
Education*Smoking			
High Light	0.76	0.186	.0001
High Heavy	1.17	0.219	.0001
High Ex	0.49	0.164	.0029

N=12925 R^2=0.109

WOMEN	ß	s.e.	p-value
Intercept	21.60	0.157	.0001
Age (yrs)	0.11	0.003	.0001
Education [1]			
High	-2.46	0.133	.0001
Smoking [2]			
Light	-1.38	0.092	.0001
Heavy	-1.16	0.107	.0001
Ex	-0.64	0.100	.0001
Education*Smoking			
High Light	1.05	0.221	.0001
High Heavy	0.88	0.296	.0028
High Ex	0.59	0.211	.0054

N=15356 R^2=0.133

[1] compared to low education level
[2] compared to never smokers

Clustering of unhealthy lifestyle habits among heavy smokers was evaluated by comparing some characteristics across smoking categories stratified by level of education (Table 3). Heavy smokers were more often alcohol users and less physically active than light or never smokers. This was more pronounced among men with high education, among whom heavy smokers weighed more than light or never smokers. But it was also true for men with low

Table 3. Monitoring Project on Cardiovascular Disease Risk Factors in the Netherlands. Some charachteristics (mean and SD or proportion) of heavy, light, never and ex-smokers stratified by education.

MEN	High education			
	Heavy smokers	Light smokers	Never smokers	Ex-smokers
N	366	641	1142	1150
Age (yrs)	41.3 (8.8)	39.7 (8.8)	37.6 (9.3)	43.5 (9.1)
Duration of smoking (yrs)	22.9 (9.1)	19.6 (9.9)	-	14.6 (8.7)
Alcohol users (≥3 gl/day)	38%	22%	10%	20%
Physically active	52%	64%	73%	71%
% fat of total energy intake	37.7 (5.8)	38.5 (5.1)	39.2 (4.6)	38.3 (4.9)
	Low education			
	Heavy smokers	Light smokers	Never smokers	Ex-smokers
N	2032	2461	2241	2888
Age (yrs)	43.8 (9.8)	41.9 (11.3)	40.6 (11.2)	46.5 (9.3)
Duration of smoking (yrs)	26.7 (10.1)	23.4 (11.4)	-	18.5 (10.1)
Alcohol users (≥3 gl/day)	29%	16%	10%	17%
Physically active	53%	64%	68%	70%
% fat of total energy intake	39.4 (6.1)	40.1 (5.3)	40.2 (5.2)	39.7 (5.1)

WOMEN	High education			
	Heavy smokers	Light smokers	Never smokers	Ex-smokers
N	260	604	1179	769
Age (yrs)	39.3 (8.3)	37.2 (8.7)	37.9 (10.3)	40.0 (8.4)
Duration of smoking (yrs)	20.4 (7.8)	16.8 (8.4)	-	11.7 (7.4)
Alcohol users (≥3 gl/day)	18%	8%	2%	5%
Physically active	57%	69%	69%	69%
% fat of total energy intake	38.3 (5.0)	38.9 (4.4)	39.8 (4.4)	39.3 (4.4)
	Low education			
	Heavy smokers	Light smokers	Never smokers	Ex-smokers
N	2026	3289	4728	2494
Age (yrs)	42.6 (9.9)	42.7 (10.5)	45.4 (10.5)	44.0 (9.8)
Duration of smoking (yrs)	24.6 (9.5)	22.8 (10.2)	-	15.0 (9.6)
Alcohol users (≥3 gl/day)	8%	2%	1%	2%
Physically active	48%	62%	63%	67%
% fat of total energy intake	41.2 (5.6)	41.4 (4.9)	41.2 (4.8)	40.8 (4.6)

education and for women. The percentage of fat in total energy intake varied only little across the smoking categories and was slightly inversely associated with heavy smoking. Heavy smokers were also older and had smoked longer than light smokers. Ex-smokers were similar to light smokers with respect to alcohol intake but similar to never smokers with respect to physical activity.

To test whether the effect modification of education could be explained by lifestyle or by factors related to smoking behavior, we added variables measuring these factors to the model containing the interaction term (Table 4). BMI was significantly inversely associated with physical activity, alcohol use (positively in men, inversely in women) and percentage of fat in total energy intake (positively in men only), but these factors did not explain the interaction between smoking and education. Factors related to smoking behavior, such as duration of smoking, number of cigarettes smoked, number of cigarettes smoked during the smoking period (ex-smokers) and duration since stopping smoking (ex-smokers) did also not explain the interaction. In men, duration of smoking and duration since stopping smoking were significantly inversely associated with BMI, while number of cigarettes smoked (borderline) and number of cigarettes smoked during the smoking period were significantly positively associated with BMI. In women, only the duration of smoking and number of cigarettes smoked during the smoking period (ex-smokers) were statistically significant. The coefficients for the smoking status and for the interaction terms were somewhat reduced but still significant after adding the lifestyle and smoking behavior variables into the model. The proportion in the variation of BMI explained by these factors was 12% in men and 15% in women.

Discussion

It has been suggested that socioeconomic factors such as education might at least partly explain the greater body weight of heavy cigarette smokers, because in most developed countries low SES is strongly associated with higher prevalence of cigarette smoking and with higher prevalence of obesity, although this relationship is stronger among women than among men. In studies which have taken SES into account it has not been an important confounder and has not explained the greater body weight of heavy smokers [3,5,9,19]. In accordance with the general notion, low education was strongly associated with smoking and

Table 4. Monitoring Project on Cardiovascular Disease Risk Factors in the Netherlands. Multiple regression coefficients (ß) for testing whether the interaction between education and smoking status can be explained by differences in lifestyle or in smoking habits.

MEN	ß	s.e.	p-value
Intercept	22.08	0.310	.0001
Age (yrs)	0.09	0.004	.0001
Education [1]			
High	-1.75	0.118	.0001
Smoking [2]			
Light	-0.74	0.176	.0001
Heavy	-0.59	0.246	.0164
Ex	-0.18	0.213	.41
Education*Smoking			
High Light	0.67	0.187	.0004
High Heavy	1.09	0.218	.0001
High Ex	0.54	0.164	.0010
Physical activity	-0.53	0.061	.0001
Alcohol (≥ 3gl/day)	0.17	0.084	.0414
% fat in tot. energy [3]	0.17	0.060	.0042
Duration of smoking [4]	-0.10	0.025	.0001
Number of cigs/day [5]	0.14	0.076	.0692
Dur. since stopping [6]	-0.12	0.038	.0014
Past number of cigs/day [7]	0.47	0.046	.0001

N=12838

WOMEN	ß	s.e.	p-value
Intercept	21.08	0.356	.0001
Age (yrs)	0.12	0.004	.0001
Education [1]			
High	-2.28	0.134	.0001
Smoking [2]			
Light	-0.85	0.202	.0001
Heavy	-0.87	0.297	.0033
Ex	-0.79	0.261	.0026
Education*Smoking			
High Light	0.93	0.224	.0001
High Heavy	0.81	0.296	.0065
High Ex	0.49	0.213	.0214
Physical activity	-0.83	0.068	.0001
Alcohol (≥ 3gl/day)	-0.43	0.194	.0282
% fat in tot. energy [3]	0.08	0.070	.23
Duration of smoking [4]	-0.12	0.028	.0001
Number of cigs/day [5]	0.13	0.100	.19
Dur. since stopping [6]	-0.06	0.050	.27
Past number of cigs/day [7]	0.58	0.079	.0001

N=15253

[1] compared to low education level
[2] compared to never smokers
[3] per each 10 % of fat in total energy intake
[4] per each 5-year class of duration
[5] per each 10 cigarettes per day
[6] per each 5-year class of duration since stopping smoking
[7] per each 10 cigarettes on average per day during smoking period (ex-smokers)

higher BMI in our study population, the latter being more pronounced among women. But instead of being a confounder, education was found to be an effect modifier.

Our main finding was that in a study population containing almost 36,000 Dutch men and women aged 20-59 years during 1987-1991 the association between smoking and relative body weight differed by level of education. Heavy smokers weighed more than never smokers at high educational level, whereas they weighed less than never smokers at low educational level when adjusted for age. This modifying effect of education was more pronounced in men than in women. Also ex-smokers weighed more than never smokers among men with high education but not among men with low education nor among women.

Lifestyle factors such as physical activity, alcohol consumption and percentage of fat in total energy intake were associated with BMI, but did not explain the modifying effect of education observed in the present study. Likewise, factors related to smoking history such as duration of smoking and number of cigarettes smoked per day, duration since stopping smoking (ex-smokers) and number of cigarettes smoked during the smoking period (ex-smokers) did not explain the variation in the association by education.

Some differences in the association between smoking and relative body weight were observed between men and women. For men, the association was opposite at low and high educational level whereas, for women, the association was to the same direction but stronger at low educational level. Also the percentage of fat in total energy intake was significantly related to BMI among men but not among women. Moreover, alcohol consumption was positively associated with BMI among men but inversely associated with BMI among women. Even though this is in agreement with the findings of several studies, the evidence for the relationship between alcohol consumption and weight remains somewhat inconsistent in the literature which might be due to validity problems in measuring alcohol consumption [25,26]. In our study population alcohol consumption was more frequent at high than at low educational level.

Age was a positive predictor of BMI whereas duration of smoking was inversely associated with BMI when adjusted for age. This finding is supported by previous research [5,17]. Also in accordance with other studies is our finding that the number of cigarettes smoked per day was positively associated with BMI [9,17,19]. The fact that the number of cigarettes smoked per day was not statistically significantly related to BMI is probably due to that the division into heavy and light smokers was enough to cover the effect of amount of smoking. For ex-smokers, number of cigarettes smoked per day during the smoking period was positively associated with BMI which is supported by studies in which heavy smokers have been found to gain more weight than light smokers after stopping smoking [13]. Duration since stopping smoking was inversely related to BMI which agrees with the findings of Chen et al. [10] who demonstrated that weight gain after cessation of smoking levelled off after some years, and with the findings of Flegal et al. [14] who found that those who stopped smoking less than 10 years ago gained more weight than never smokers while those who had stopped smoking more than 10 years ago did not.

We found some evidence for clustering of unhealthy lifestyle habits such as physical inactivity and heavy alcohol use among heavy smokers compared to light and never smokers in men and women. In women, alcohol use was inversely associated with BMI and therefore only physical inactivity remains to explain the greater body weight of heavy smokers. Heavy smokers were also older and had smoked longer than light smokers. These factors may have cancelled out each other's effect to some degree since age was a positive and duration of smoking a negative predictor of BMI. Due to underreporting of energy intake by increasing level of overweight the absolute energy intake and energy expenditure could not be measured adequately in this study. The percentage of energy intake derived from fat was not related to heavy smoking. In spite of the fact that lifestyle factors did not explain the modifying effect of education on the association between smoking and BMI, it is likely that, among men, the observed abundant use of alcohol among heavy smokers at high educational level has contributed to their higher BMI when compared to never smokers. Among women, the more frequent alcohol use of heavy smokers at high educational level must have resulted in a lower average BMI than would have been observed with less use of alcohol since alcohol use was inversely associated with BMI among women. Alcohol use may thus be one of the reasons why the effect modification by education was more pronounced among men than women.

It has been suggested that the inverse association between smoking and relative body weight might no longer hold in populations with previously high but currently low prevalence of smoking [17]. In our study population smoking was still relatively common compared to other Western European countries, but smoking prevalence differed remarkably by level of education. Even though light smokers were leaner than never smokers at all educational levels, male heavy smokers weighed more than never smokers at high educational level where also the prevalence of smoking was lower than at low educational level. This finding suggests that the association between smoking and relative body weight may also differ in different subgroups within one population. If this is the case, it has both statistical and public health implications. From statistical point of view, if there are subgroups where the association between smoking and relative body weight differs, the apparent overall association depends on the relative proportions of these subgroups in the population. Also, adjustment for SES, which is frequently used in studies on the association between smoking and body weight, may be inappropriate and might in fact hide the existing differences between socioeconomic levels in the BMI-smoking relationship. From the public health point of view, if, for example, the weight of ex-smokers compared to never smokers differs between subgroups, stopping smoking may have different consequences with respect to body weight in these subgroups. There is of course no doubt that stopping smoking is to be recommended in all subgroups of a population. However, in some subgroups there may be less need to be concerned about the possible weight gain after smoking cessation. Therefore it might be possible and more effective to target the efforts to prevent weight gain after smoking cessation to the subgroups which need and profit most from such efforts.

Although the number of subjects in this study was large, the response rate was relatively low. On the basis of the results of the non-response study, non-respondents (in men) smoked somewhat more than respondents but there was no difference in education. Thus, among men, the proportion of smokers must have been slightly underestimated at all levels of education. We did not have information about the relative weight of the non-respondents. Even if such information would have been available, it would not have been comparable with the relative weight of respondents, since the weight of non-respondents cannot be measured objectively and self-reported weights are known to be biased. If the response rate would have been higher, the actual regression coefficients might have been different. But if the results obtained in this study were to be explained completely by differential non-response, it would have required substantial non-response of lean heavy smokers at high educational level and/or overweight heavy smokers at low educational level. We consider such a possibility relatively unlikely.

We did not find any obvious explanation to the effect modification of education in the smoking-BMI relationship. There are two possible explanations to these 'negative' findings. Either factors related to lifestyle and smoking habits do explain the effect modification but we did not measure these factors with required degree of precision. Unprecise measurements can result from limited reporting of the subjects or e.g. partly from the fact that some of the key variables were dichotomous. The observed clustering of unhealthy habits in heavy smokers at all levels of education (although more prononced at high educational level) supports, however, the finding that these factors cannot fully explain the effect modification. Another possible explanation is that some other factors which we did not measure in this study, such as slimming behavior, other measures of conscious and unconscious weight control, personality types or other psychosocial factors, are at play. It has been suggested that some people may adopt the habit of smoking in order to control body weight [4] and it is a general notion that many people sustain to smoke because they are afraid of weight gain [12]. Tendency to this type of behavior may differ between levels of education. For example, heavy smoking among people with high education might be more related to stress than among those with low education. Our observations are, however, based on cross-sectional data and cannot thus provide any evidence for temporal mechanisms in the relationship between smoking and relative body weight at different levels of education. Similarly, questions about reasons for smoking were not asked in this study.

In conclusion, we observed that the association between smoking and body mass index differed by level of education in our study population. These different associations could not be explained by differences in other aspects of lifestyle such as dietary fat intake, physical activity and alcohol consumption nor by differences in smoking behavior. It is unlikely that there are major genetic determinants that may explain these observations. Further research on the reasons why men and women with low education weigh relatively more than men and women with high education, why the effect of smoking differs by educational level other than fat intake, physical activity and alcohol consumption and whether these differences exist also in other populations is needed, because it may contribute to the understanding of the etiology of obesity in smokers, ex-smokers and never smokers.

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4.3 Educational level and relative body weight, and changes in their association over 10 years - an international perspective from the WHO MONICA Project

Abstract

Objective: To assess the consistency and magnitude of the association between educational level and relative body weight in populations with widely different prevalences of overweight, and to investigate possible changes in the association in these populations over 10 years.

Methods: Differences in age-adjusted mean body mass index (BMI) between the highest and the lowest tertile of years of schooling were calculated in 26 populations in the initial and final surveys of the WHO MONICA Project. The data are derived from random population samples including over 42,000 men and women aged 35-64 years in the initial survey (carried out in 1979-89) and almost 35,000 in the final survey (1989-96).

Results: In women, almost all populations showed a statistically significant inverse association between educational level and BMI: the difference between the highest and the lowest educational tertile ranged from -3.1 to 0.4 kg/m^2 in the initial survey, and from -3.3 to -0.3 kg/m^2 in the final survey. In men, the difference in BMI between the educational tertiles ranged from -1.2 to 2.2 kg/m^2 and from -1.5 to 1.2 kg/m^2 in the two surveys, respectively. About one fourth of the male populations in the initial survey and about a half in the final survey showed a statistically significant inverse association. About a half showed no significant association, and two and one populations in the two surveys, respectively, showed a statistically significant positive association. Smoking behaviour did not explain the observed associations. In about two thirds of the populations the differences in BMI between the educational levels increased over the 10-year period.

Conclusion: A lower education was associated with a higher BMI in about half of the male and in almost all female populations. In general, there was a small shift towards stronger inverse association and the differences in relative body weight between educational levels increased over the study period. Thus, socio-economic inequality in health consequences associated with obesity may widen in many countries. This has important implications for health promotion.

Introduction

Numerous studies have investigated the relationship between socio-economic status and relative body weight. In general, an inverse association has been observed in women in affluent societies, whereas the association in men is less consistent [1-6]. In less affluent societies a positive association between obesity and socio-economic status has been found both in men and women [1,7-9]. The WHO MONICA Project includes populations with a wide range of per capita income and other socio-economic indicators, and the prevalence of overweight also varies considerably among the populations [10-12]. Using this unique data set we explored the extent to which the association between socio-economic status and relative body weight differ among the MONICA populations. Educational level was used as an indicator for socio-economic status. We also investigated whether the differences observed among the populations in the association between educational level and relative body weight were related to the prevalence of obesity or to the distribution of education in the population, and whether smoking explained the association between educational level and relative body weight.

Remarkable socio-economic inequalities in self-perceived health, morbidity and mortality exist in many countries [13-17]. Because excess relative weight is related to the incidence of several chronic diseases and mortality [18,19], socio-economic differences in the prevalence of overweight and obesity may act as one factor through which these inequalities in health emerge. Therefore it is important to know if the association between socio-economic status and relative body weight has changed among the MONICA populations over the 10-year study period. Hence, we studied the association between educational level and relative body weight and the changes in this association in 26 populations which had collected data on years of schooling and weight and height in the initial and final MONICA surveys.

Methods

The WHO MONICA Project was designed to measure trends in incidence and mortality from cardiovascular disease, and to assess the extent to which these trends are related to changes in known risk factors. The project is carried out in 39 Collaborating Centres in 26 countries with several centres monitoring more than one geographically defined study population. Risk factors in the WHO MONICA Project are monitored through independent cross-sectional population surveys over a 10-year period [10,20]. The surveys included random samples of at least 200 people in each gender and ten-year age group, for the age range 35-64 years, and optionally 25-34 years. This study presents the data from the initial and final surveys. The survey periods ranged from May 1979 to February 1989 for the initial survey and from June 1989 to November 1996 for the final survey. In this paper, the age range from 35 to 64 years is considered. The overall participation rates for the populations included in the present study varied from 51% to 89% in the initial survey and from 48% to 90% in the final survey. The population sizes, participation rates and the survey periods have been described in more detail elsewhere [11,21].

Standard recommendations for the basic anthropometric measurements in MONICA were the following. Height and body weight were measured with participants standing without shoes and heavy outer garments. Height was recorded to the nearest 1 cm and weight to the nearest 200 g. Body mass index (BMI), used as a measure for relative weight, was calculated as weight divided by height squared (kg/m^2).

Educational level was measured in years of schooling. Years of schooling were obtained by asking: "How many years did you spend at school or in full-time study?" Because there were large differences in the disributions of years of schooling between populations and also between sexes and age groups within populations, years of schooling were divided into tertiles which were calculated separately for each sex and 10-year age group in each population and for each survey. Cut-points for the tertiles were selected between whole years of schooling in such a way that each tertile would contain as close as possible one third of the subjects. Due to clumping of the distributions, however, this was not always possible but the cut-points were chosen to ensure that the highest and lowest groups comprised at least 15% of the subjects in the sample. Because older age groups often had less education, the cut-points were usually lower in the older than the younger age groups.

Data on smoking were obtained using a standard questionnaire [22]. In the present analyses the respondents were classified as: 1) heavy smokers (those smoking 20 or more cigarettes per day), 2) light smokers (those smoking 1-19 cigarettes per day), 3) other current smokers (those reporting cigarettes occasionally, at least 1g of pipe tobacco per week or at least one cigar per week) 4) ex-smokers (those reporting having smoked cigarettes daily in the past but not currently) and 5) never smokers (those who were not current smokers and had never smoked cigarettes daily).

The data on weight and height measurements, years of schooling and smoking have been centrally assessed in the WHO MONICA Project, and any population with unsatisfactory quality of data has been excluded from this study.

Statistical methods

To describe the distributions of BMI and years of schooling in each population, the age standardized prevalence of obesity (BMI $\geq$ 30 kg/m^2) and the median years of schooling are given for men and women in each survey. Age standardized prevalences were calculated using the world standard population [23] as the reference population with weights 12, 11 and 8 for the 10-year age groups 35-44, 45-54 and 55-64 years respectively. Because the difference between the two cut-points for tertiles of years of schooling was narrow in some populations while wide in others due to the differences in school systems, we calculated the mean of the three age specific differences and used it as an indicator of the variation in levels of education.

To assess the differences in relative body weight by education, we calculated the mean BMI in the highest tertile of years of schooling and the differences between it and the other tertiles in each population in each survey with adjusting for 10-year age group. These were calculated using the general linear model (GLM) procedure of the SAS statistical software [24]. Confidence intervals for the differences in mean BMI were obtained from the standard errors of the regression coefficients assuming that the sampling distributions of the coefficients were normal. To assess the extent to which the differences in BMI by educational level were explained by smoking, the same analysis was also done with adjustment for smoking category. The statistical significance of the change in the association between BMI and educational level between the two surveys within a population was derived by testing the significance of the interaction term between survey and educational tertile in an analysis which included only the highest and lowest tertiles in the model.

Correlation coefficients between the prevalence of obesity and the difference in mean BMI between the highest and the lowest educational tertile were calculated in each survey to assess whether the association between educational level and BMI was related to the prevalence of obesity in the population. These correlations were ecological where each population presented one observation. To assess whether the differences in the BMI-education relationship between populations could be explained by the extent of the educational gap between the lower and higher educational tertiles, we calculated the correlation between the difference in mean BMI between the highest and lowest educational tertile and the mean difference of the upper and lower cut-off point of years of schooling in each survey. Because some of the observations were outliers, we used Spearman rank correlations instead of parametric correlations. All the analyses were carried out separately for men and women.

Table 1a. Age-standardized prevalence of obesity (BMI ≥ 30kg/m²), median years of schooling, mean of differences in age-specific tertile cut-off points of years of schooling (diff.) and number of observations in the initial and final MONICA survey in populations included in this study. Men aged 35-64 years, listed by prevalence of obesity in the initial survey.

Population	Initial survey				Final survey			
	% obese	years of schooling median	years of schooling diff.	N	% obese	years of schooling median	years of schooling diff.	N
CHN-BEI	3	9	4.3	612	4	9	3.0	480
BEL-GHE	9	11	4.0	533	10	12	4.3	487
FRA-TOU	9	10	3.7	678	13	12	3.0	609
SPA-CAT	10	7	3.7	987	16	8	3.0	1398
USA-STA	10	14	2.3	435	20	14	3.0	450
DEN-GLO	11	10	2.0	1456	13	11	2.0	607
ITA-BRI	11	6	2.0	620	14	8	3.3	651
SWE-NSW	11	8	1.7	646	14	10	2.3	568
UNK-BEL	11	10	0.7	929	13	11	2.0	812
UNK-GLA	11	10	0.3	504	23	10	0.7	678
ICE-ICE	12	10	3.3	648	17	12	4.3	693
SWI-VAF	12	13	2.3	627	16	13	2.0	570
FRA-LIL	13	9.5	2.7	646	17	11	3.0	571
POL-TAR	13	7	2.0	1237	15	9	2.0	621
RUS-NOI	13	9.5	3.7	608	15	11	5.0	623
RUS-MOC	14	15	4.3	774	8	15	1.7	557
ITA-FRI	15	8	2.7	722	17	9	3.3	685
FIN-NKA	17	7	1.7	1146	22	8	2.3	508
FIN-KUO	18	8	2.0	977	24	9	2.7	568
GER-AUU	18	11	1.3	711	18	12	2.0	658
POL-WAR	18	11	3.3	1297	22	12	3.0	751
YUG-NOS	18	11	3.3	606	17	12	2.0	566
FIN-TUL	19	8	1.7	1205	22	10	2.3	569
SWI-TIC	19	12	3.3	781	13	12	3.0	733
GER-AUR	20	11	1.3	850	24	12	1.7	819
CZE-CZE	22	11	2.7	948	22	11	1.7	894

Results

Tables 1a and 1b show the age standardized prevalence of obesity and the median years of schooling by the population and survey in men and women, listed by the prevalence of obesity in the initial survey. There were wide differences in the prevalence of obesity between the study populations ranging from 3% in Beijing to 22% in Czech Republic in men and from

10% in Beijing to 43% in Novosibirsk (intervention) in women in the initial survey, and from 4% in Beijing to 24% in Augsburg (rural) and Kuopio Province in men and from 8% in Beijing to 43% in Novosibirsk (intervention) in women in the final survey. In general, the prevalence of obesity increased in most populations between the two surveys. The largest increases, ten percentage points or more in men and seven percentage points or more in women, occurred in Glasgow and Stanford. Only a few populations showed a decline in the prevalence of obesity, Moscow (control) showing the largest decline in both men (six percentage points) and women (12 percentage points).

Table 1b. *Age-standardized prevalence of obesity (BMI ≥ 30kg/m²), median years of schooling, mean of differences in age-specific tertile cut-off points of years of schooling (diff.) and number of observations in the initial and final MONICA survey in populations included in this study. Women aged 35-64 years, listed by prevalence of obesity in the initial survey.*

Population	**Initial survey** % obese	years of schooling median	diff.	N	**Final survey** % obese	years of schooling median	diff.	N
CHN-BEI	10	6	3.3	635	8	9	3.7	643
DEN-GLO	10	9	2.7	1361	12	10	2.0	611
BEL-GHE	11	10	3.3	496	11	10	3.7	517
FRA-TOU	11	11	3.0	645	10	12	3.0	566
SWI-VAF	12	11	2.3	570	9	12	2.3	578
ICE-ICE	14	8	2.3	693	18	10	3.0	718
SWE-NSW	14	9	2.0	614	14	11	2.3	596
SWI-TIC	14	10	2.7	769	16	11	2.7	770
UNK-BEL	14	10	1.3	925	16	11	1.7	797
USA-STA	14	12	2.0	523	23	13	2.7	567
GER-AUU	15	11	1.7	677	21	11	2.0	669
ITA-BRI	15	5	1.3	649	18	5	2.3	666
UNK-GLA	16	10	0.3	480	23	10	0.7	727
FIN-TUL	17	8	2.0	1282	19	10	2.7	627
FRA-LIL	17	8	2.0	544	22	10	2.7	578
ITA-FRI	18	5	1.3	737	19	8	2.3	689
FIN-KUO	20	8	1.3	990	25	9	2.3	610
GER-AUR	22	11	1.7	854	23	11	1.7	872
FIN-NKA	23	8	1.7	1240	24	9	2.3	595
SPA-CAT	23	7	3.3	994	25	8	3.0	1211
POL-WAR	26	11	3.3	1327	28	12	2.0	763
YUG-NOS	30	8	3.3	576	27	11	3.7	601
CZE-CZE	32	10	2.7	990	29	11	2.3	946
POL-TAR	32	7	1.7	1441	37	8	2.0	696
RUS-MOC	33	14	3.3	642	21	15	2.7	527
RUS-NOI	43	10	3.0	659	43	12	3.3	656

The median years of schooling also varied considerably, ranging from 6 years (Area Brianza) to 15 years (Moscow control) in men and from 5 years (Area Brianza and Friuli) to 14 years (Moscow control) in women in the initial survey, and from 8 years (North Karelia and Catalonia) to 15 years (Moscow control) in men and from 5 years (Area Brianza) to 15 years (Moscow control) in women in the final survey. The mean of the differences in the age specific tertile cut-off points for years of schooling varied from 0.3 to 4.3 years in men and from 0.3 to 3.3 years in women in the initial survey, and from 0.7 to 5.0 years in men and from 0.7 to 4.0 years in women in final survey.

In men, the difference in mean BMI between the highest and the lowest tertile of years of schooling ranged from -1.2 to 2.2 kg/m^2 in the initial survey (Figure 1). In two populations, Moscow (control) and Tarnobrzeg Voivodship, educational level had a statistically significant positive association with BMI. In 18 populations no significant association was found, and in six populations there was a statistically significant inverse association.

In women, the difference in mean BMI between the highest and the lowest tertile of years of schooling ranged from -3.1 to 0.4 kg/m^2 in the initial survey (Figure 2). None of the populations showed a significant positive association, but 22 of the 26 populations had a statistically significant inverse association.

Figures 3 and 4 show the differences in mean BMI between the highest and lowest educational tertile in the final survey. The difference between the highest and the lowest tertile of years of schooling ranged from -1.5 to 1.2 kg/m^2 in men and from -3.3 to -0.6 kg/m^2 in women. For women, the results were similar to those in the initial survey. In men, the proportion of populations having a significant inverse association increased from six populations (23%) in the initial survey to 13 populations (50%) in the final survey.

Adjustment for smoking attenuated the difference in mean BMI between the highest and lowest educational tertile by an average of 0.2 kg/m^2 in those populations where the difference in BMI between the educational levels was positive (not shown). In those populations where the difference in BMI between educational levels was negative, i.e. in most populations, the difference in BMI between the tertiles increased on average by 0.1 kg/m^2 when adjusted for smoking.

Next we calculated the ecological correlation coefficients for the difference in mean BMI between the highest and lowest educational tertile and the age-standardized prevalence of obesity in men and women in each survey. The correlation coefficient was -0.19 (p=0.36) in men and -0.08 (p=0.70) in women in the initial survey, and –0.41 (p=0.04) in men and 0.01 (p=0.98) in women in the final survey. The negative association observed in men means that

Figure 1. Age adjusted difference (and 95% confidence interval) in mean BMI between the highest and lowest educational tertile (highest minus lowest tertile) in men aged 35-64 years in the initial MONICA survey.

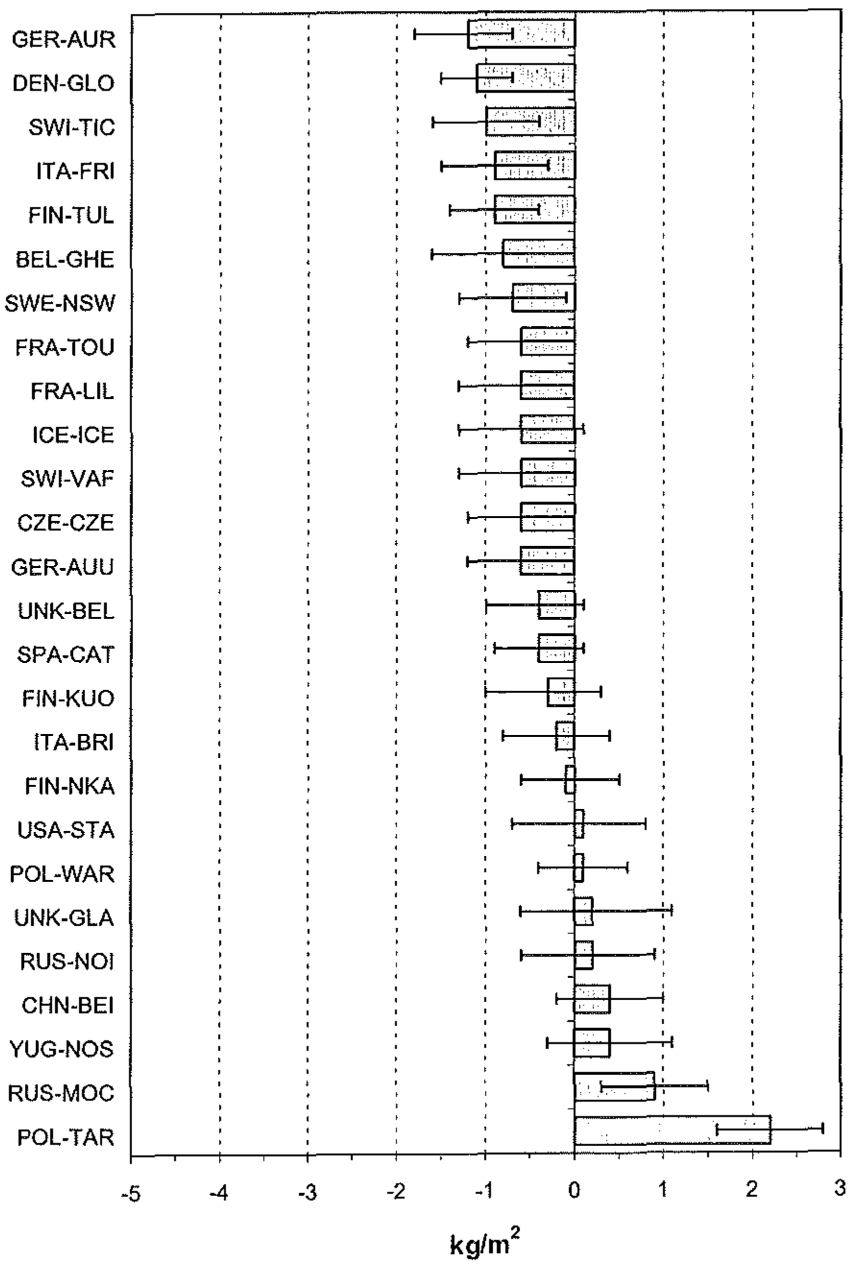


***Figure 2.** Age adjusted difference (and 95% confidence interval) in mean BMI between the highest and lowest educational tertile (highest minus lowest tertile) in women aged 35-64 years in the initial MONICA survey.*

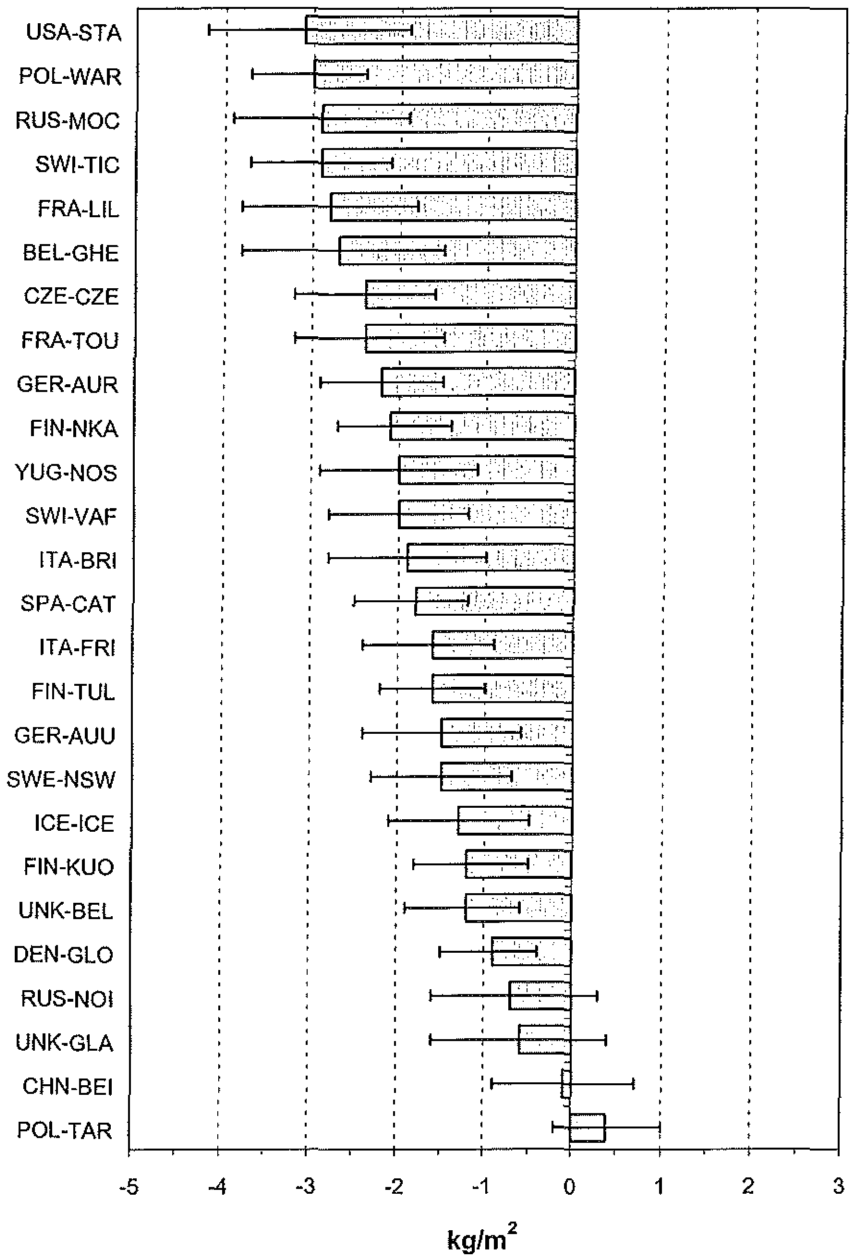


Figure 3. Age adjusted difference (and 95% confidence interval) in mean BMI between the highest and lowest educational tertile (highest minus lowest tertile) in men aged 35-64 years in the final MONICA survey.

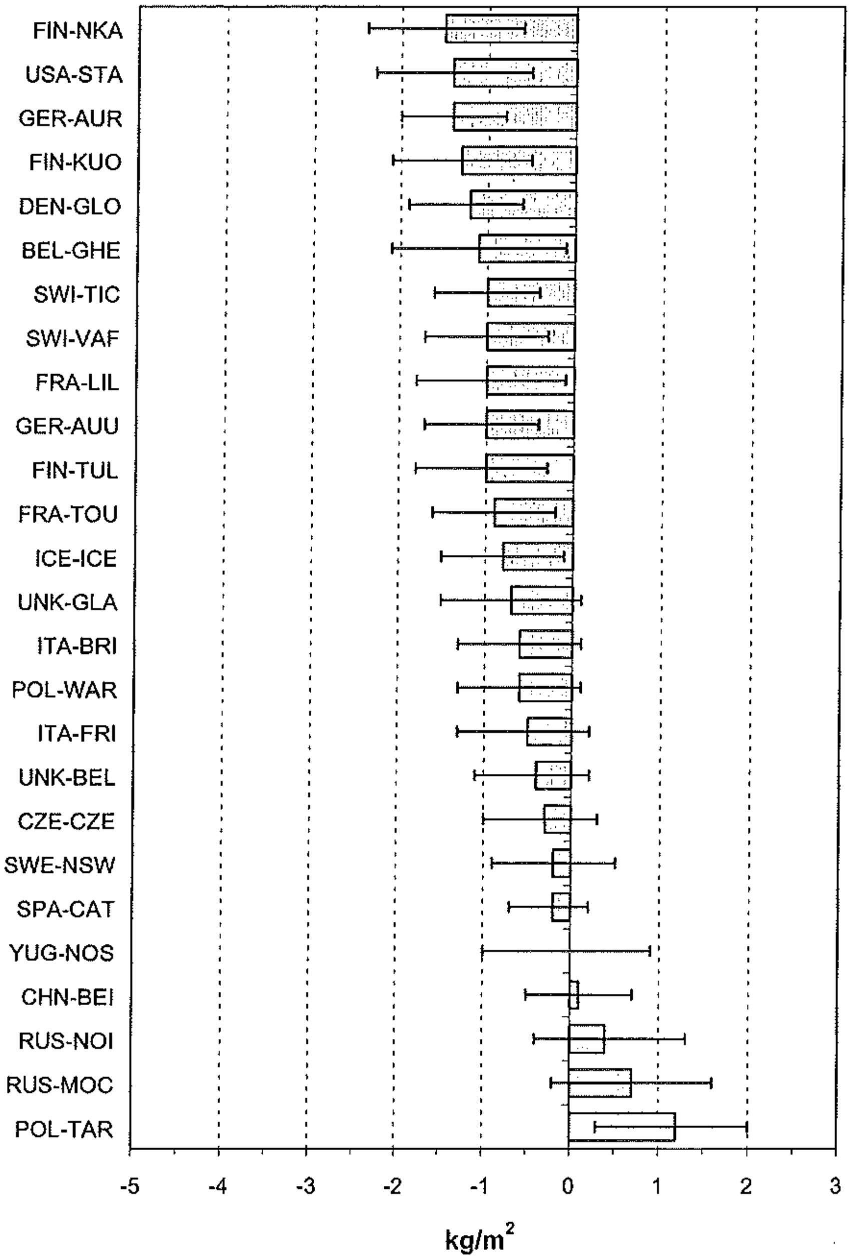
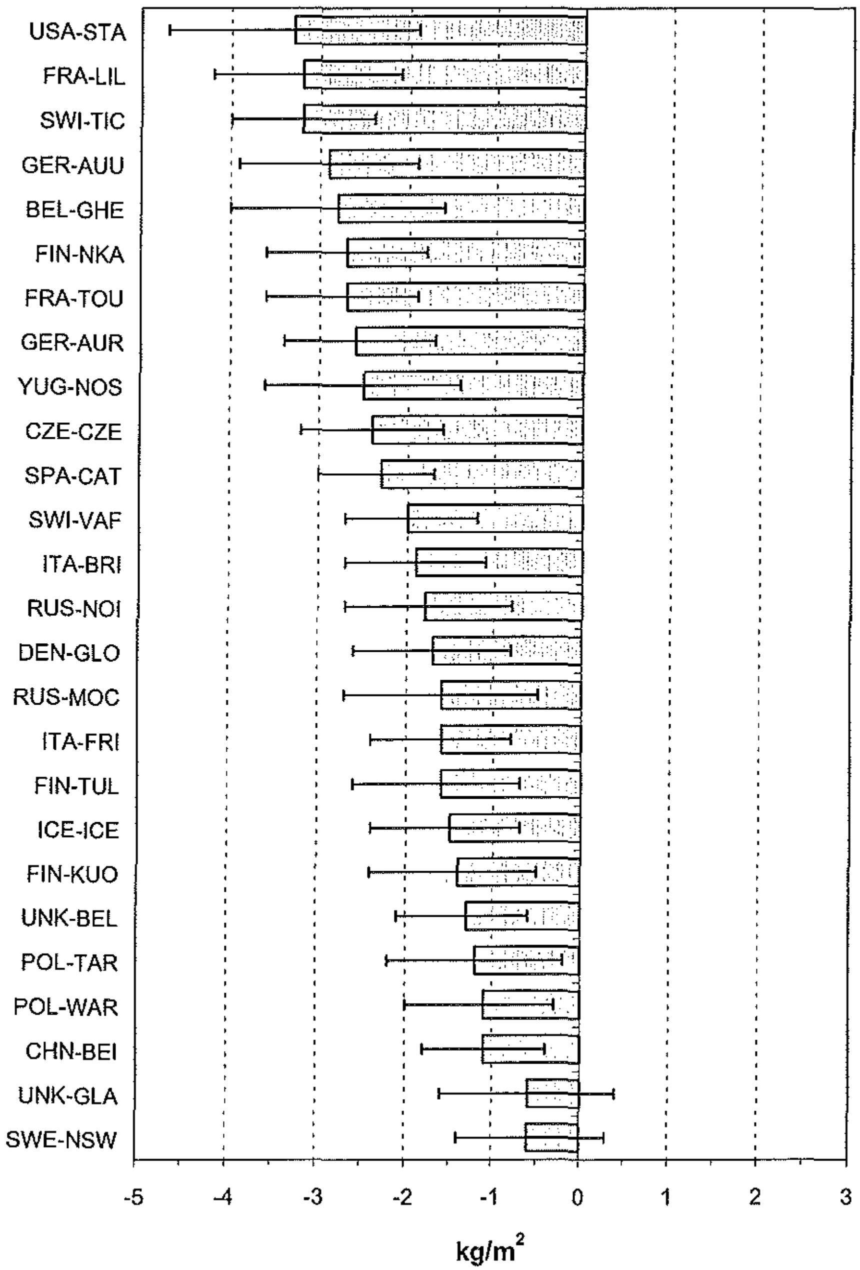


Figure 4. *Age adjusted difference (and 95% confidence interval) in mean BMI between the highest and lowest educational tertile (highest minus lowest tertile) in women aged 35-64 years in the final MONICA survey.*



in populations where the prevalence of obesity was relatively high, men with high education were leaner than men with low education, whereas in populations where obesity was rare, men with high education tended to be heavier than men with low education.

The correlation coefficient between the difference in mean BMI between the highest and lowest educational tertile and the mean difference between the upper and lower cut-off point of years of schooling was 0.21 (p=0.28) in men and –0.35 (p=0.08) in women in the initial survey, and –0.02 (p=0.92) in men and –0.30 (p=0.13) in women in the final survey. Although not statistically significant, the correlations were negative in women suggesting that in populations where the gap in education between the high and low educational levels was relatively wide, the negative association between educational level and BMI was strongest.

Table 2. Change between the initial and final MONICA survey in the difference in mean BMI (kg/m^2) between the highest and lowest educational tertile.

MEN		WOMEN	
Population	**Change [1]**	**Population**	**Change [1]**
POL-TAR	- 0.9	POL-WAR	- 1.9*
SWE-NSW	- 0.5	RUS-MOC	- 1.3
YUG-NOS	- 0.5	SWE-NSW	- 1.0
ITA-FRI	- 0.3	SWI-VAF	0.0
CHN-BEI	- 0.3	ITA-FRI	0.0
CZE-CZE	- 0.3	FIN-TUL	0.0
RUS-MOC	- 0.2	UNK-GLA	0.0
SPA-CAT	- 0.1	CZE-CZE	+ 0.1
SWI-TIC	- 0.1	ITA-BRI	+ 0.1
UNK-BEL	0.0	UNK-BEL	+ 0.1
DEN-GLO	+ 0.1	BEL-GHE	+ 0.1
FIN-TUL	+ 0.2	ICE-ICE	+ 0.2
GER-AUR	+ 0.2	USA-STA	+ 0.2
ICE-ICE	+ 0.2	FIN-KUO	+ 0.3
BEL-GHE	+ 0.2	SWI-TIC	+ 0.4
FRA-LIL	+ 0.3	GER-AUR	+ 0.4
RUS-NOI	+ 0.3	FRA-TOU	+ 0.4
SWI-VAF	+ 0.3	SPA-CAT	+ 0.5
FRA-TOU	+ 0.4	YUG-NOS	+ 0.5
ITA-BRI	+ 0.4	FRA-LIL	+ 0.5
GER-AUU	+ 0.4	FIN-NKA	+ 0.6
POL-WAR	+ 0.7	DEN-GLO	+ 0.7
UNK-GLA	+ 1.0	CHN-BEI	+ 0.9
FIN-KUO	+ 1.1*	RUS-NOI	+ 1.1
USA-STA	+ 1.4*	GER-AUU	+ 1.3
FIN-NKA	+ 1.5*	POL-TAR	+ 1.6*

[1] + denotes that the difference in BMI between educational levels increased and – denotes that the difference decreased from the initial to the final survey.
* p-value < 0.05.

In the majority of populations (62% for men and 73% for women) there was at least 0.1 kg/m^2 increase in the difference in mean BMI between the highest and the lowest educational tertile between the initial and final survey (Table 2), although the increase was statistically significant only in three populations (North Karelia, Kuopio Province and Stanford) in men and in one population (Tarnobrzeg Voivodship) in women. An increase (or decrease) of more than about 1.0 kg/m^2 in men and 1.4 kg/m^2 in women was statistically significant. This corresponds to a mean change of about 3.0 kg in a man with an average height of 1.72 m, and 3.6 kg in a woman with an average height of 1.60 m.

Discussion

Among the populations participating in the WHO MONICA Project we found a statistically significant inverse association between educational level and BMI in women in almost all populations. Women with higher education were leaner than those with lower education. In men, about one fourth of the study populations in the initial survey and about half in the final survey also showed such a statistically significant inverse association. Only two and one populations in the two surveys, respectively had a statistically significant positive association. In men, the association between BMI and educational level was positive, although not necessarily significantly so, in some Eastern and Central European populations and in Beijing. In women, no clear geographical pattern emerged. The difference in BMI between the educational levels was bigger in women than in men. In addition, in about two thirds of the populations the difference in mean BMI between the highest and the lowest educational level increased during the 10-year study period.

We investigated whether the association between educational level and BMI was related to the prevalence of obesity in the population. Because the range of educational levels was narrower in some populations than others, we also looked at whether the association between educational level and BMI was related to the variation in educational levels in the population. Furthermore, because smoking behaviour is known to be associated both with socio-economic status [25,26] and relative body weight [26,27], we assessed the effect of smoking on the association between educational level and BMI.

In men, the association between educational level and BMI seemed to be related to the prevalence of obesity in the population, although this was statistically significant in the final survey only. In populations where obesity was relatively common, subjects with higher education were leaner than those with lower education, whereas in populations with a low prevalence of obesity higher education was associated with high BMI. This is in agreement with the studies where an inverse association between the educational level and relative weight has been found in affluent societies with usually higher prevalences of overweight, whereas a positive association has been found in poorer societies [1-9]. Also, in men, the association between educational level and BMI was positive, although not necessarily statistically significantly so, in some Eastern and Central European populations and in Beijing which are less affluent than the other MONICA populations. In women, the association between educational level and BMI did not depend on the prevalence of obesity in the population but was related to the differential in years of schooling between the educational levels, although this correlation was rather weak. Only a small part of the variation in the BMI-education relationship among the populations was, however, explained by the prevalence of obesity in the populations or the differential in years of schooling between the educational levels. The prevalence of obesity explained 17% of the variation in the BMI-education relationship between populations in men in the final survey, and the mean difference in the cut-off points for educational tertiles explained 12% in women in the initial survey.

We also explored whether and to what extent the possible differences in relative weight by educational level could be explained by smoking. We found that the differences were not explained by smoking. On the contrary, adjustment for smoking increased the differences. This is to be expected because in low socio-economic groups smoking is more common and it is associated with lower relative weight [25-27]. But it also implies that if subjects with low education were not smoking more than subjects with high education, the socio-economic differences in BMI would be even bigger. This can be a matter of concern for health promotion, because the most urgent health goal is to encourage smokers to stop smoking. The increase in the differences in BMI between educational levels introduced by the adjustment for smoking were, however, relatively small (about 0.1 kg/m^2) suggesting that smoking has only small effect on the BMI-education relationship.

In a majority of populations there was an increase in the difference in mean BMI between the educational tertiles between the two surveys. Similarly diverging trends have been reported from eastern Finland over the period 1972-87 [28], and from the United States for the period 1960-80 [29,30]. These populations had also the largest increases in the difference in BMI between the educational tertiles among men in our data. In general, in men there was a trend towards inverse association and in women to a stronger inverse association. This has important public health implications. Because excess relative weight is associated with the incidence of many chronic diseases such as hypertension, cardiovascular diseases and diabetes mellitus, socio-economic differences in obesity are likely to contribute to these inequalities in health. The inequalities in health consequences of obesity are therefore likely to increase in many countries. Similar concerns have been raised also in studies [4,31,32]. The increasing inequalities in heath are discordant with the WHO health policy goal [33] to provide health for all.

There are several possible explanations for the increasing differences in BMI between the educational levels over the 10-year period observed in the study populations. Firstly, the age group 35-44 in the final survey can have stronger inverse association between education and BMI than the 55-64 age group in the initial survey which has moved out of the study range of the final survey. Secondly, differences in relative body weight between educational levels in the age groups remaining in the study (35-44 and 45-54 in the initial survey) might have increased with advancing age. The increase in weight with age may be more pronounced in those with low education than those with high education as suggested by some studies [31]. Finally, increasing differences in relative body weight between educational levels in all age groups can be due to secular trends. It is possible that all these factors operate at the same time.

We used years of schooling to measure educational level. Systematic measurement of educational level in different populations is complicated because the educational systems of the countries differ. The educational systems in some countries may have changed over time and thus the educational systems may differ even between birth cohorts within a country. The use of age-, sex- and survey-specific tertiles in this study ensured that the results were adjusted for educational differences between birth cohorts and changes in educational systems within the country. The relative differences in years of schooling between the highest and the lowest tertile can thus vary from one population to another. Therefore we investigated the association between the mean difference of the cut-off points of years of schooling and the difference in mean BMI between the highest and lowest educational tertile.

In this study, educational level was used as a proxy for the socio-economic status, but in some populations income or occupation may be better measures of an individual's social status [34]. Unfortunately, we did not have data available on the subjects' occupation or income. The level of urbanization of the population may modify the association between relative weight and socio-economic status. For example, it has been suggested that in China the relationship between obesity and income may be inverse in urban areas (as in other industrialized countries) but positive in rural areas [35]. In our study, Tarnobrzeg Voivodship in Poland, where the association between education and BMI in men was statistically significantly positive in both surveys, is a rural population.

We only compared the mean BMI in the highest and lowest educational tertile. This may be an oversimplification of the relationship. Some researchers have found an inverted U-shaped relation between educational level and BMI, especially in men [36]. In our study, there was an inverted U-shaped relationship between educational level and BMI in about one third of the male populations in the initial survey. In men in the final survey and in women in both surveys the number of populations showing such a pattern was smaller. The large number of study populations and the two surveys did not allow us to present all descriptive data for all subgroups.

The association between socio-economic status and relative weight is a complex one. The association is probably bidirectional, and confounded by other factors such as heredity [37]. The differences between socio-economic groups in relative weight may also reflect differences in other risk factors such as physical activity, dietary habits, smoking and alcohol consumption. Some studies have, however, suggested that differences in health behaviour explain only partly the association between socio-economic status and relative weight [38,39]. The differences between socio-economic groups in relative weight may also be affected by social and cultural norms, such as what is considered as "desirable weight", which vary by population, gender, age and the socio-economic status.

In summary, we found that low education was associated with a higher BMI in about half of the male and in almost all female populations of the WHO MONICA Project. In general, there was a shift towards a stronger inverse association and the differences in relative body weight by educational level increased during the 10-year study period. Thus, socio-economic inequality in health consequences associated with obesity may widen in many countries. Health promotion activities should be designed and directed to decrease such inequalities.

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5. Body fat distribution

5.1 Waist and hip circumferences, and waist-hip ratio in 19 populations of the WHO MONICA Project

Abstract

Objective: To assess differences in waist and hip circumferences and waist-hip ratio (WHR) measured using a standard protocol among populations with different prevalences of overweight. In addition, to quantify the associations of these anthropometric measures with age and degree of overweight.

Design: Cross-sectional study of random population samples.

Subjects: Over 32,000 men and women aged 25-64 years from 19 (18 in women) populations participating in the second MONICA survey from 1987-92.

Results: Age standardized mean waist circumference ranged from 83 to 98 cm between populations in men and from 78 to 91 cm in women. Mean hip circumference ranged from 94 to 105 cm and from 97 to 108 cm in men and women respectively, and mean WHR from 0.87 to 0.99 and from 0.76 to 0.84. Together, height, BMI, age group and population explained about 80% of the variance in waist circumference. BMI was the predominant determinant (77% in men, 75% women). Similar results were obtained for hip circumference. However, height, BMI, age group and population accounted only for 49% (men) and 30% (women) of the variation in WHR.

Conclusion: Considerable variation in waist and hip circumferences and WHR were observed among the study populations. Waist circumference and WHR, both of which are used as indicators of abdominal obesity, seem to measure different aspects of human body: waist circumference reflects mainly degree of overweight whereas WHR does not.

Introduction

It is generally accepted that not only obesity but also the distribution of body fat is associated with the development of several diseases. In particular abdominal obesity, indicated by a high waist-hip ratio (WHR), has been shown to predict diseases like hypertension, coronary heart disease, non-insulin dependent diabetes and stroke, to correlate with other cardiovascular risk factors and to increase mortality independent of body mass [1-3]. It has been suggested that this excess risk with central obesity is primarily due to metabolic alterations caused by intra-abdominal fat deposits [1].

Different studies have shown strikingly different values of WHR in different study populations [4]. These studies have usually investigated associations between WHR and other risk factors, diseases and mortality, or described these associations in different racial groups, such as Caucasians, Blacks [5], Mexican-Americans [6], Chinese [7], Micronesian Nauruans [8] etc. Many of these studies have not been population-based or have only investigated a very limited age range [9]. Also, different methods for measuring the circumferences have been applied. As a result, whereas the distribution of overall obesity in different populations is well documented in the literature [10,11], little is known about the distributions of waist and hip circumferences and WHR among populations in different countries and with varying degrees of overweight.

WHR is a ratio and as a result suffers from limitations in relation to its use in statistical analyses and in its interpretation [12,13]. Recently, some reports have suggested that waist circumference alone might be a better indicator of visceral fat accumulation and cardiovascular risk compared to WHR [14,15]. Waist and hip circumferences may reflect different aspects of body composition and distribution of fat and muscle. It is therefore relevant to obtain insight into population differences in these circumferences separately.

Abdominal obesity tends to increase with advancing age. Several studies have reported an increasing WHR with age [16-18], but few [19] have looked at the effect of age on waist and hip circumferences separately. The effect of age on abdominal obesity may, however, be confounded by the degree of overall obesity since relative weight also increases with age. This has to be taken into account when assessing the effect of age on waist and hip circumferences and WHR.

The main aim of this study was to describe the distributions of waist and hip circumferences and WHR in different populations and to investigate whether there were significant differences in relation to abdominal fat distribution among these populations. Secondly, we attempted to quantify the associations between waist, hip and WHR in relation to age and degree of overweight. We investigated these associations in 19 geographically well-defined populations of the WHO MONICA (MONItoring trends and determinants in CArdiovascular disease) Project which had measured waist and hip circumferences in their second cross-sectional survey from 1987-92.

Methods

The WHO MONICA Project was designed to measure trends in incidence and mortality from cardiovascular disease, and to assess the extent to which these trends are related to changes in known risk factors. The project is carried out in 39 Collaborating Centres in 26 countries with several centres monitoring more than one study population. Risk factors in the WHO MONICA Project are monitored through three independent cross-sectional population surveys [20,21]. The surveys included random samples of at least 200 people in each gender and ten-year age group, for the age range 35-64 years, and optionally 25-34 years. This study presents data from the second surveys. Since waist and hip circumference measurements were optional in the second MONICA survey, only about half of the centres measured these items. The survey periods ranged from January 1987 to September 1992. In this study, the age range from 25 to 64 years is considered. In Toulouse, only men were examined and it was also the only population which did not include age group 25-34 years in the survey. In Newcastle, the age group 25-34 was studied only in three of the five reporting units. The age group of an individual was obtained from the sampling frame at the time of sample selection. The overall participation rates for the populations included in the present study varied from 57% to 88%. The population sizes, participation rates and survey periods have been described in more detail elsewhere [22].

The recommended procedures for the measurement of the anthropometric variables were the following. Waist and hip circumferences were measured with participants standing without heavy outer garments and with empty pockets. Waist was measured at the level midway between the lower rib margin and the iliac crest with the participant breathing out gently. Hip was recorded as the maximum circumference over the buttocks. Both measurements were rounded to the nearest half cm, except in three populations (Newcastle, Gothenburg and Novi Sad) where they were recorded to the nearest full cm. All populations used the same standardized methods for these measures, except the Czech Republic which measured waist at the level of the umbilicus. Height and body weight were measured with participants standing without shoes and heavy outer garments. Body mass index (BMI), used for assessing the degree of overweight, was calculated as weight divided by height squared (kg/m^2). The quality of data on waist, hip, weight and height has been centrally evaluated in the WHO MONICA Project. Any population with unsatisfactory quality of data or response rate lower than 50% for any of the study items has been omitted from this analysis.

Statistical methods

Age standardized 10th, 50th and 90th percentiles, mean values and standard deviations of waist and hip circumferences and WHR are given for the common age range 35-64 years in each population. Age standardization was used to remove the distortion introduced by possible differences in age distributions between the study populations [23]. Age standardized mean values were calculated using the World Standard Population [24] as the reference population giving weights 12/31, 11/31 and 8/31 for the age group specific mean values in the 10-year age groups 35-44, 45-54 and 55-64, respectively. Identical age standardized mean values can be obtained by assigning appropriate weights for the individual data records. In this way, the standard deviation and the percentiles of the 'age standardized data' were also calculated. For comparison, the age standardized median BMI and height in the population are also given.

To assess the effect of age, unadjusted means of waist and hip circumferences and WHR were calculated in each 10-year age group for the age range 25-64 years (35-64 in the population which did not include the youngest age group) in each population. The difference in mean waist, hip and WHR between the oldest and the youngest age group is given to indicate the magnitude of the increase with age in each population. In addition, the effect of age was investigated by regression analysis using pooled data from all populations. This was done first by adjusting for the population only, that is assuming that the age effect was similar in all populations but allowing the mean level (intercept) differ between populations. Next, we added height and BMI into the model to investigate whether and to what extent the effect of age on waist, hip and WHR was explained by height and BMI.

Multiple regression analysis was also used for assessing the overall effect of height, degree of overweight, age group and population on waist, hip and WHR. We wanted to know the contribution of height and BMI, and how much of the remaining variance could be explained by age group and population. Regression models were constructed by adding these explanatory variables one by one into the model. Since BMI has been defined so that it is largely unrelated to height, the order in which BMI and height are added into the model should make little difference. Here, height was added into the model first because it is not a modifiable variable, and then BMI followed by age group and population. In our data, introducing BMI before height into the model would have decreased the proportion explained by BMI for waist circumference by 1% while increased the proportion explained by BMI for WHR by 1-3%. The change in the proportion explained by height would have been the opposite. Height was first introduced as a categorical variable (for each 10 cm) to check whether the association was linear. Based on visual inspection it was detected that the association was linear, and height was therefore treated as a continuous variable. Likewise, BMI was modelled only with a linear effect, because the second order term for BMI was negligible. 10-year age groups were used instead of age in years because the effect of age was not linear. Regression coefficients were calculated using the general linear model (GLM) procedure of SAS statistical software [25]. The proportions of variation in waist, hip and WHR explained by the independent variables were derived from the R-square statistics. Finally, to compare the results from the regression analysis based on individual data to those based on population level data, we calculated Pearson correlations between age standardized mean BMI and age standardized mean waist circumference in men and women. These correlations were ecological where each population presented one observation.

Results

Tables 1a and 1b give the age standardized percentiles, means and standard deviations for waist and hip circumferences and WHR, the median BMI and height, and the number of observations by population for the common age range 35-64 years in men and women respectively. Men had higher values of waist circumference than women did whereas there was little difference in hip circumference between men and women. Therefore, mean WHR was higher in men than in women. In men, age standardized mean waist circumference ranged from 83 (95% confidence interval (CI): 82.6, 84.3) cm in Beijing to 98 cm in the Czech Republic (95% CI: 97.9, 99.1) and Halle County (95% CI: 93.7, 95.0). Mean hip circumference ranged from 94 (95% CI: 93.7, 95.0) cm in Glostrup to 105 (95% CI: 103.6, 105.6) cm in Halle County, and mean WHR from 0.87 (95% CI: 0.866, 0.877) in Beijing to 0.99 (95% CI: 0.988, 0.996) in Glostrup. In women, age standardized mean waist circumference ranged from 78 cm in Perth (95% CI: 76.8, 78.6) and Gothenburg (95% CI: 77.4, 78.9) to 91 (95% CI: 89.8, 91.3) cm in the Czech Republic. Mean hip circumference ranged from 97 cm in Glostrup (95% CI: 95.7, 97.4) and Beijing (95% CI: 96.0, 97.1) to 108 (95% CI: 107.0, 108.3) cm in the Czech Republic, and mean WHR from 0.76 (95% CI: 0.756, 0.766) in Perth to 0.84 (95% CI: 0.835, 0.844) in the Czech Republic.

Table 1a. Percentiles (10th, 50th, 90th) and mean waist, hip and waist-hip ratio (WHR), and median body mass index (BMI, kg/m²) and height (cm) in 19 male populations in the second MONICA survey, age-standardized values for age group 35-64 years. Populations are listed in ascending order by mean WHR.

	WAIST (cm)					HIP (cm)					WHR					BMI	Height	
Population	10th	50th	90th	Mean	SD	10th	50th	90th	Mean	SD	10th	50th	90th	Mean	SD	50th	50th	N
CHN-BEI	70	84	97	83	10.1	88	95	104	95	6.3	.79	.87	.96	.87	.064	23.9	168	530
ITA-BRI	79	91	104	91	9.4	93	100	111	101	7.4	.82	.90	.98	.90	.065	26.0	170	582
FRA-TOU	81	93	106	93	10.4	95	103	111	103	7.3	.83	.91	.97	.90	.059	25.8	172	580
AUS-PER	81	92	105	92	9.6	95	102	109	102	6.1	.83	.91	.98	.91	.058	26.3	175	632
FIN-KUO	81	93	106	93	9.9	95	102	110	102	6.0	.83	.91	1.00	.91	.062	26.7	173	576
SWE-GOT	81	92	103	92	8.9	93	100	108	100	6.1	.85	.91	.99	.92	.054	25.3	178	620
FIN-TUL	82	94	107	94	10.0	95	103	111	103	6.5	.84	.91	1.00	.92	.060	26.9	175	551
ITA-FRI	81	92	105	93	9.8	92	100	109	100	7.0	.85	.92	.99	.92	.063	26.5	172	685
FIN-NKA	81	94	109	94	11.0	95	102	111	103	6.8	.84	.92	1.00	.92	.064	26.9	173	1099
GER-AUU	82	94	107	95	10.2	95	103	110	103	6.6	.84	.92	1.00	.92	.063	26.5	175	658
AUS-NEW	83	94	108	95	10.1	94	102	111	103	7.4	.86	.93	.99	.92	.054	26.8	173	676
GER-AUR	84	95	108	96	9.8	94	103	112	103	7.2	.85	.93	1.00	.93	.058	27.2	174	818
YUG-NOS	80	93	108	94	10.7	90	100	110	100	8.2	.86	.93	1.01	.93	.059	26.4	174	599
UNK-GLA	80	94	109	94	12.2	92	100	110	101	8.0	.85	.93	1.02	.94	.080	26.0	171	568
CZE-CZE*	85	98	112	98	10.7	96	104	114	104	7.8	.87	.94	1.02	.94	.062	27.6	174	1035
GER-HAC	85	97	112	98	11.0	96	104	113	105	8.2	.87	.94	1.00	.94	.053	27.1	173	292
SWE-NSW	81	92	104	92	8.8	91	98	106	98	5.7	.88	.94	1.01	.94	.054	25.8	175	600
SPA-CAT	85	96	108	96	9.4	91	99	107	99	6.7	.90	.97	1.03	.97	.050	26.8	168	1325
DEN-GLO	82	93	106	94	10.3	85	94	104	94	8.3	.92	.99	1.05	.99	.050	25.5	176	568

* waist circumference measured at the level of umbilicus

Table 1b. Percentiles (10th, 50th, 90th) and mean waist, hip and waist-hip ratio (WHR), and median body mass index (BMI, kg/m^2) and height (cm) in 18 female populations in the second MONICA survey, age-standardized values for age group 35-64 years. Populations are listed in ascending order by mean WHR.

	WAIST (cm)					HIP (cm)					WHR					BMI	Height	
Population	10th	50th	90th	Mean	SD	10th	50th	90th	Mean	SD	10th	50th	90th	Mean	SD	50th	50th	N
AUS-PER	67	76	92	78	10.6	92	100	114	102	9.4	.69	.76	.84	.76	.060	24.5	161	640
SWE-GOT	67	76	91	78	10.2	91	99	112	100	8.1	.71	.77	.86	.78	.061	23.9	165	622
FIN-TUL	68	79	96	81	11.3	93	101	115	103	8.9	.71	.78	.86	.78	.064	25.7	162	589
FIN-KUO	69	79	97	81	11.4	93	102	114	103	9.2	.71	.78	.86	.79	.059	25.9	160	626
FIN-NKA	69	80	97	81	11.3	93	102	116	103	9.4	.72	.79	.87	.79	.060	25.9	160	1199
UNK-GLA	68	80	99	82	13.0	90	101	117	102	11.7	.73	.79	.89	.80	.067	25.5	158	634
AUS-NEW	68	80	102	83	13.9	90	102	117	103	11.4	.72	.79	.91	.80	.075	25.5	160	673
GER-AUU	68	80	98	82	11.5	90	100	115	101	10.1	.73	.80	.89	.80	.061	24.9	162	685
GER-AUR	70	80	98	82	11.3	90	100	115	102	10.5	.74	.80	.88	.81	.059	25.9	161	831
ITA-BRI	67	78	97	80	11.7	88	98	112	99	9.6	.73	.80	.90	.81	.068	24.9	157	606
SWE-NSW	69	78	95	80	10.9	90	98	110	99	8.8	.75	.80	.89	.81	.056	24.4	163	610
DEN-GLO	68	77	92	79	10.4	85	95	109	97	10.3	.76	.82	.89	.82	.061	23.8	164	565
CHN-BEI	67	79	94	80	10.2	88	96	106	97	7.2	.74	.82	.91	.82	.068	24.2	156	680
GER-HAC	71	85	104	86	12.8	91	104	120	105	11.9	.75	.82	.90	.82	.069	26.6	160	365
ITA-FRI	69	81	99	83	12.3	90	100	113	101	9.9	.73	.82	.92	.82	.076	25.1	160	698
YUG-NOS	70	84	101	85	12.5	90	102	116	103	10.9	.75	.82	.89	.82	.059	27.5	160	598
SPA-CAT	74	86	101	87	10.4	94	104	116	104	8.7	.76	.83	.91	.83	.061	27.3	155	779
CZE-CZE*	74	89	110	91	13.7	94	106	124	108	11.4	.75	.83	.94	.84	.074	27.9	161	1068

* waist circumference measured at the level of umbilicus

WHR and especially waist circumference was higher in populations where the median BMI was relatively high compared to other populations, although this was more pronounced in women than in men. The mean values were similar to the medians (50th percentile), except for waist and hip circumferences in women where the distributions were slightly positively skewed.

Next, we calculated the mean values for waist and hip circumferences and WHR by 10-year age groups in each population. Tables 2a and 2b give the mean values in age group 25-34 and the difference in means between the oldest and the youngest age group. In general, all the measures increased with age. The measure which showed the smallest increase with age was hip circumference in men. In women, the effect of age on waist circumference was stronger in the Czech Republic, Friuli and Novi Sad than in the other populations. Figure 1 shows the population adjusted increase in waist circumference by age with and without adjustment for BMI and height. In women, the crude effect of age on waist was linear. The increase in waist circumference with age attenuated when adjusted for BMI and height. Because height contributed only a little to this attenuation compared with BMI, it can be concluded that a considerable proportion of the increase in waist by age is explained by increasing BMI, especially in women. Still, there remained a significant (p-value <0.001) increase in waist (over 4 cm in men and women) which was not due to height or BMI. Figure 2 gives the corresponding effect of age on WHR. The increase in WHR with age was more pronounced in the younger age groups in men whereas it was more pronounced in the older age groups in women. The difference in the effect of age on WHR between sexes was statistically significant (p-value for interaction term between sex and age group <0.001).

Both height and BMI were positively associated with waist circumference. The results of the regression analyses revealed that height accounted for very little (1% in men and less than 1% in women) of the variation in waist circumference whereas BMI accounted for about three quarters (Figure 3a). Age group and population explained an additional 5% or less. Jointly, height, BMI, age group and population explained 83% of the variation in waist circumference in men and 79% in women. Waist increased by 0.3 cm (s.e. 0.005 in men and 0.007 in women) for each cm of height in both sexes and by 2.4 cm (s.e. 0.01) in men and 2.1 cm (s.e. 0.01) in women for each kg/m^2 of BMI.

The results were fairly similar for hip as for waist circumference (Figure 3b). BMI accounted for 64% and 81% of the variance in men and women respectively. In men, height and population explained more than they did of waist circumference. Age had no independent effect on hip circumference. Height and BMI explained, however, considerably less of the variation in

Table 2a. Mean waist and hip circumference and waist hip ratio (WHR) in age group 25-34 and difference in means between age groups 55-64 and 25-34 (increase with age) in 19 male populations in second MONICA survey. Populations are listed in ascending order by mean WHR at age 25-34.

	Waist (cm)				Hip (cm)				WHR				
Population	At 25-34 years	s.e.	Increase with age	s.e.	At 25-34 years	s.e.	Increase with age	s.e.	At 25-34 years	s.e.	Increase with age	s.e.	Total N
CHN-BEI	79	0.8	7	1.1	93	0.5	3	0.7	.84	.005	.05	.007	699
GER-AUU	86	0.7	11	0.9	101	0.5	3	0.7	.86	.004	.08	.006	862
ITA-BRI	85	0.7	8	0.9	99	0.5	3	0.8	.86	.006	.05	.007	737
AUS-PER	86	0.7	8	1.2	99	0.6	3	0.8	.86	.004	.06	.007	815
UNK-GLA	86	0.9	10	1.2	99	0.5	2	0.8	.86	.005	.09	.007	707
FIN-TUL	87	0.7	11	1.0	100	0.6	5	0.7	.87	.004	.07	.006	720
GER-AUR	88	0.6	11	0.8	101	0.4	4	0.6	.87	.004	.07	.005	1070
FIN-KUO	87	0.8	8	1.1	100	0.5	2	0.7	.87	.004	.06	.006	741
FIN-NKA	87	0.5	9	0.8	100	0.4	4	0.5	.87	.003	.05	.005	1425
SWE-GOT	87	0.7	6	0.9	100	0.5	1	0.7	.88	.004	.05	.005	775
ITA-FRI	86	0.7	7	1.0	98	0.5	2	0.7	.88	.004	.06	.007	896
FRA-TOU**	90	0.7	7	1.0	102	0.5	3	0.7	.89	.004	.04	.006	580
AUS-NEW	89	1.4	8	1.5	100	0.9	4	1.0	.89	.008	.04	.008	747
YUG-NOS	86	0.7	9	1.0	97	0.6	4	0.8	.89	.005	.05	.006	778
GER-HAC	91	1.0	8	1.3	101	0.7	3	1.0	.90	.005	.04	.007	401
SWE-NSW	88	0.7	6	1.0	97	0.5	1	0.7	.90	.004	.05	.006	761
CZE-CZE*	92	0.5	11	0.8	101	0.4	5	0.6	.91	.003	.05	.004	1356
SPA-CAT	91	0.5	8	0.6	99	0.3	1	0.4	.92	.003	.07	.003	1719
DEN-GLO	87	0.7	8	1.0	90	0.6	7	0.9	.98	.003	.03	.003	740

* Waist circumference was measured at the level of umbilicus.
** Mean at 35-44 years and difference between age groups 55-64 and 35-44.

Table 2b. Mean waist and hip circumference and waist hip ratio (WHR) in age group 25-34 and difference in means between age groups 55-64 and 25-34 (increase with age) in 18 female populations in second MONICA survey. Populations are listed in ascending order by mean WHR at age 25-34.

	Waist (cm)				Hip (cm)				WHR				
Population	At 25-34 years	s.e.	Increase with age	s.e.	At 25-34 years	s.e.	Increase with age	s.e.	At 25-34 years	s.e.	Increase with age	s.e.	Total N
AUS-PER	73	0.8	7	1.3	99	0.7	3	1.1	.74	.005	.05	.007	822
SWE-GOT	73	0.7	8	1.0	97	0.6	5	0.8	.76	.005	.04	.007	772
FIN-KUO	76	0.7	10	1.0	99	0.6	6	0.9	.76	.004	.05	.005	803
FIN-NKA	74	0.5	12	0.8	97	0.4	9	0.6	.76	.003	.05	.004	1563
FIN-TUL	75	0.7	10	1.1	98	0.6	8	0.9	.76	.004	.04	.007	778
GER-AUU	73	0.7	13	1.0	96	0.7	9	0.9	.76	.004	.07	.006	861
ITA-FRI	73	0.6	15	1.1	95	0.5	8	0.9	.77	.005	.09	.007	894
CHN-BEI	72	0.7	12	0.9	94	0.5	3	0.7	.77	.005	.10	.006	859
GER-AUR	74	0.6	14	0.9	97	0.7	9	0.9	.77	.003	.06	.005	1082
UNK-GLA	76	0.9	9	1.2	99	0.8	5	1.1	.77	.005	.05	.007	781
ITA-BRI	74	0.8	13	1.2	95	0.7	8	1.0	.78	.005	.06	.007	753
SPA-CAT	77	0.5	15	0.8	99	0.4	8	0.7	.78	.003	.08	.005	1191
AUS-NEW	77	1.4	9	1.6	98	1.3	7	1.5	.79	.009	.04	.010	757
YUG-NOS	73	0.6	18	1.1	92	0.6	15	1.0	.79	.004	.06	.006	791
GER-HAC	79	1.2	12	1.7	99	1.1	10	1.6	.80	.005	.04	.008	480
SWE-NSW	76	0.8	7	1.1	95	0.6	6	0.9	.80	.004	.02	.006	791
CZE-CZE*	80	0.6	16	1.0	99	0.5	13	0.8	.81	.004	.05	.005	1410
DEN-GLO	76	0.7	6	1.1	92	0.8	8	1.1	.82	.004	.00	.006	735

* Waist circumference was measured at the level of umbilicus.

Figure 1. Effect of age on waist circumference. Unadjusted (adjusted only for population) and adjusted (for population, height and body mass index) increase in waist circumference compared with the age group 25-34 years in pooled data from 19 male and 18 female populations in the second MONICA survey.

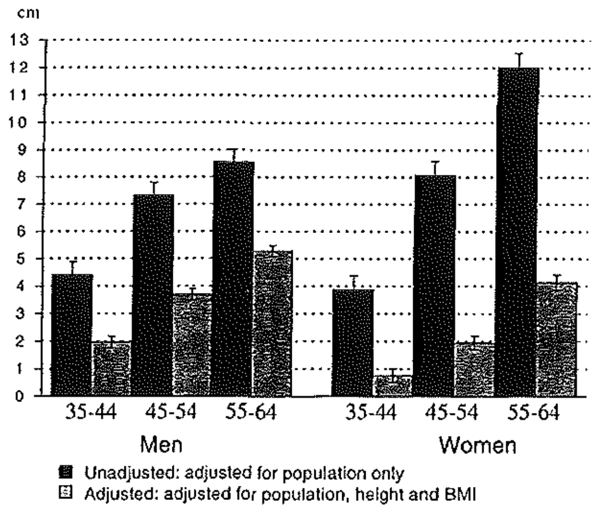
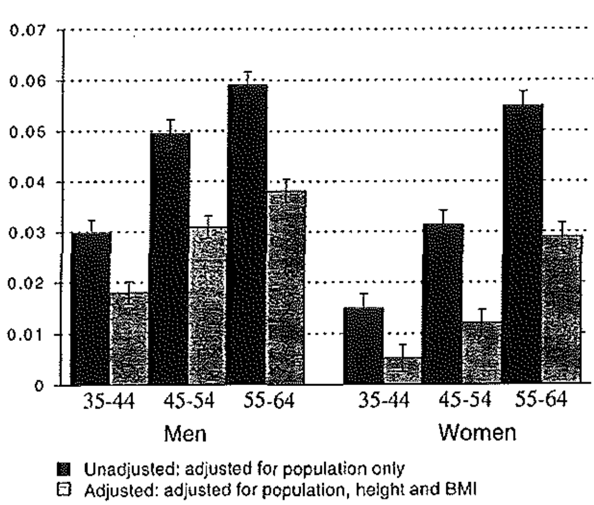


Figure 2. Effect of age on waist-hip ratio. Unadjusted (adjusted only for population) and adjusted (for population, height and body mass index) increase in waist-hip ratio compared with the age group 25-34 years in pooled data from 19 male and 18 female populations in the second MONICA survey.



WHR than in waist circumference, especially among women (Figure 3c). The variation explained by height and BMI together was 32% and 21% for men and women respectively. The proportion explained by population was higher for WHR (13% and 7%) than it was for waist and hip circumferences.

Because one study population (Glostrup) emerged as an outlier in analyses of hip circumference and consequently in analyses of WHR, we calculated the proportions of the variance explained of these measurements excluding this population. In men, the proportion of hip circumference explained by height (7%) and BMI (65%) increased slightly and the proportion explained by population (2%) decreased considerably when this population was excluded. The same concerns the proportions explained in WHR (height 2%, BMI 34%, age group 4% and population 7%). In women, the exclusion of this population had very little effect. Since one population (Czech Republic) measured waist at the level of umbilicus, we also carried out the analyses of waist and WHR excluding this population. This changed the proportions explained by height, BMI, population and age group at most by 1%.

The ecological correlations between the age standardized mean BMI and waist circumference was 0.88 for men and 0.85 for women. The variation explained by BMI in waist was thus about the same in the populations level analysis (77% in men, 73% in women) as in the individual level analysis (77% in men, 75% in women).

Discussion

Among 19 populations participating in the WHO MONICA Project considerable variation in the distributions of waist and hip circumferences and WHR was observed. The population-specific factors other than the included anthropometric parameters explained, however, only 13% or less of the variation in these measures. This small percentage includes both methodological variation and 'true' differences between populations. The major determinant of waist and hip circumferences is degree of overweight which alone explains about three quarters of the variation. The relation between age and waist circumference was not linear, neither before nor after adjusting for degree of overweight (except in women before adjustment). The age-relation also differed by gender: in men the increase in waist circumference was more pronounced in the younger age groups whereas in women it was more pronounced in the older age groups.

Figure 3a. Proportion of variance in waist circumference explained by height, body mass index, age group and population (in this order). Pooled data from 19 male and 18 female populations aged 25-64 years in the second MONICA survey.

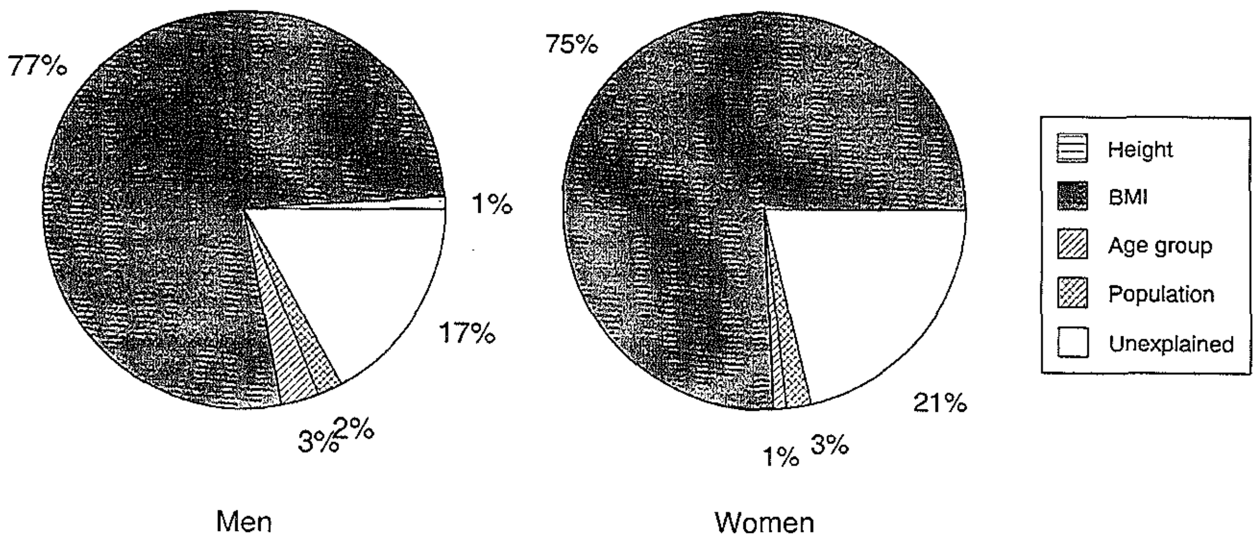


Figure 3b. Proportion of variance in hip circumference explained by height, body mass index, age group and population (in this order). Pooled data from 19 male and 18 female populations aged 25-64 years in the second MONICA survey.

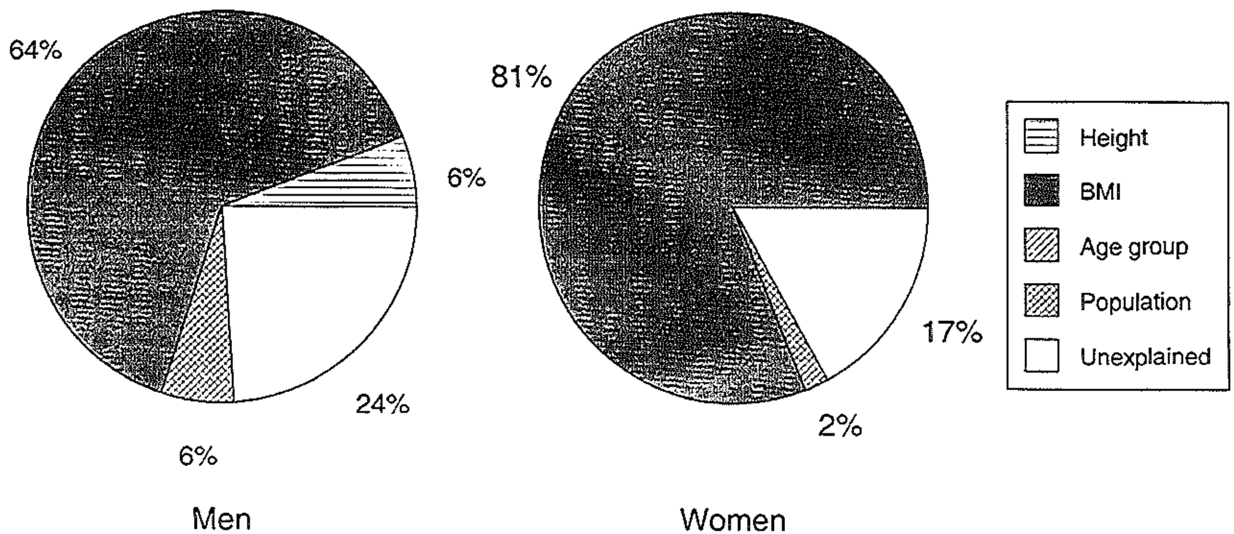
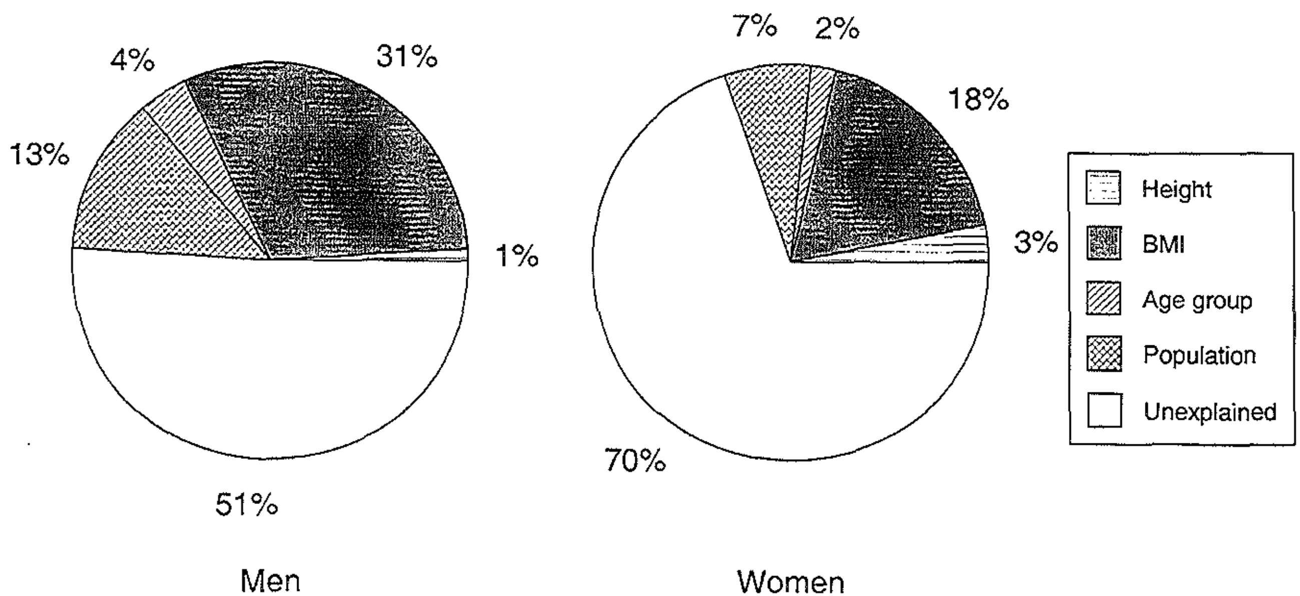


Figure 3c. Proportion of variance in waist-hip ratio explained by height, body mass index, age group and population (in this order). Pooled data from 19 male and 18 female populations aged 25-64 years in the second MONICA survey.



Because data on waist and hip circumferences and WHR representative of the general population and comparable between populations with varying prevalences of overweight are not available in the literature, the first aim of this study was to describe the distributions of these measurements among the 19 study populations and to investigate whether there are significant differences in abdominal fat distribution between the populations. Some of the populations did indeed show striking differences in fat distribution measured by waist and hip circumferences, and WHR. Men in Beijing had low mean waist and hip circumferences and also WHR when compared with other male populations, whereas men in Catalonia had relatively high mean WHR and waist circumference but relatively low hip circumference compared with the other populations. Men in Glostrup had the lowest mean hip circumference and the highest WHR. In women, the Czech Republic had the highest values for waist and hip circumferences, and for WHR. Women in Perth had lower mean WHR than the other female populations and also a relatively low waist circumference. The difference between populations with the highest and lowest age standardized mean value was 13-15 cm for waist and 11 cm for hip circumference.

In some populations men and women showed similar patterns in abdominal body shape whereas in others they did not. For example, in the Czech Republic, where both sexes have relatively high median BMI compared to other populations, both men and women had high mean waist and hip circumferences and WHR. In contrast, in Beijing, where both men and women are lean, men had low values of hip and even more pronouncedly low waist, and therefore a low WHR. Women had small hip circumference but waist was not smaller than elsewhere. Thus, the WHR of women in Beijing was relatively high and similar to that of the Southern European women.

For assessing the true differences between populations in body girth measurements, it is crucial that the methods are standardized across populations, since small differences in the anatomical measurement levels can result in very different results [26]. The measurement techniques and the anatomical levels where the actual measurements have been recorded have varied considerably in previously published studies, especially the way the waist circumference was defined. Thus, it has been difficult to judge to what extent these circumferences and WHR really differ between populations. In the WHO MONICA Project the measurements were based on standardized instructions and the quality of data of these measurements has been centrally assessed. In spite of this, there can still be some variation between the centres e.g. due to between-observer variation. Some studies [27] have reported very high between-observer correlations for waist and hip measurements. Unfortunately it is not possible to assess the magnitude of this effect in this study. One population (Glostrup) was an outlier concerning hip circumference and WHR values, especially among men, even though they applied the standard measurement technique. This may be one example of such between-observer variations. The fact that the Czech Republic measured waist circumference at the level of the umbilicus may have produced results at the higher end of the distribution and they are therefore not directly comparable to those of the other populations. But because it also had the highest values in hip circumference, for which the measurement level was standard, its relative position among the populations is probably justified and only the absolute values for mean waist and WHR may be somewhat overestimated.

The second aim of this study was to assess the effect of degree of overweight and age on waist and hip circumferences and WHR. Our findings confirm those of Shimokata et al. [19] that waist circumference and WHR increase with age independently of the increase in BMI. Hip circumference increased as well but to a lesser degree, especially in men. The increase in abdominal fat seems to take place earlier in life in men than in women. There were also differences between the populations with respect to the magnitude of the increase by age. In some study populations among women (the Czech Republic, Friuli and Novi Sad) the effect of age on waist was stronger than in other populations, but this could be explained by a bigger increase in weight with advancing age. In general, about half of the increase with age in waist circumference in men and in WHR in men and women, and as much as three quarters of the increase in waist with age in women, could be explained by increasing degree of overweight.

Many other factors, including behavioural, demographic and genetic factors, have been suggested as being linked with abdominal obesity. Behavioural factors such as cigarette smoking (positively) and physical exercise (inversely) have been found to be associated with central obesity [6,9,28]. Most of the studies which have assessed the effect of these factors have used WHR to measure abdominal obesity. For example, Marti et al. [18] found that jointly, physical exercise, resting heart rate, alcohol consumption, education and age explained 18% of the variation in WHR in Finnish men while age was the strongest determinant. Laws et al. [29] could explain 21% of the variation in WHR in men and 16% in women by age, BMI, alcohol consumption, cigarettes smoked per day and exercise (as dichotomous variable). Our findings are more in keeping with those of Haffner et al. [6] who could explain 27% and 13% of the variation in WHR by BMI in men and women respectively, and 10% by age, and those of Jones et al. [16] who could explain 47% of the variation in WHR by BMI and age in men. The lack of substantial behavioural effects have led some investigators to suggest that body fat distribution might primarily be under genetic control [6]. Genetic epidemiologists have, however, argued that biological inheritance accounts for only a small part of the variation in fat distribution [30,31].

The proportion of variation in WHR explained jointly by height, BMI, age group and population was 49% in men and 30% in women. This is in agreement with the findings of other studies [6,16] and reinforces the fact that WHR is difficult to interpret biologically. While waist circumference measures predominantly abdominal - both intra-abdominal and subcutaneous - fat, hip circumference can reflect many different aspects of body size, such as body frame, muscles and subcutaneous fat. When these two measures are combined as a ratio, any individual value of WHR can be heterogeneous regarding waist and hip circumference and also regarding the amount of intra-abdominal fat for which WHR is used as a proxy.

In this study, the proportion of variation explained by BMI was very high for waist circumference (77% in men, 75% in women) but only moderate for WHR (31% in men, 18% in women). The latter is natural because if two measures, which are both predominantly explained by BMI, are combined as a ratio, the proportion explained by BMI is far less for the ratio than for the individual variables. Although waist circumference and WHR are both used as indicators of abdominal obesity, they seem to measure different aspects of human body: waist circumference reflects mainly degree of overweight whereas WHR does not.

Even though the results for hip circumference were fairly similar to those for waist circumference, hip circumference seems to measure slightly different things in men and women. While in women it reflects mainly body fat (81% explained by BMI), in men it also seems to reflect body structure (6 % explained by height).

Some investigators have argued that waist/height ratio show stronger associations with intra-abdominal fat [32] and cardiovascular risk factors [33] than waist circumference. In the present study as well as in others [34] there was almost no association between height and waist circumference. The interpretation of the waist/height ratio is complex because it may reflect variation in waist and in stature. For these reasons we did not calculate waist/height ratios in this study.

In summary, we found considerable variation in waist and hip circumferences and WHR among the 19 MONICA populations. The predominant determinant of waist circumference was degree of overweight, while most of the variation in WHR remained unexplained by demographic and anthropometric variables.

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5.2 Varying sensitivity of waist action levels to identify subjects with overweight or obesity in 19 populations of the WHO MONICA Project

Abstract

Objective: It has been suggested in the literature that cut-off points based on waist circumference (waist action levels) should replace cut-off points based on body mass index (BMI) and waist-hip ratio in identifying subjects with overweight or obesity. In this paper we examined the sensitivity and specificity of the cut-off points when applied to 19 populations with widely different prevalences of overweight.

Design: Cross-sectional study based on random population samples.

Subjects: 32,978 subjects aged 25-64 years from 19 male and 18 female populations participating in the second MONICA survey from 1987-92.

Results: At waist action level 1 (waist circumference ≥94 cm in men and ≥80 cm in women), sensitivity varied between 40% and 80% in men and between 51% and 86% in women between populations when compared with the cut-off points based on BMI (≥25 kg/m^2) and waist-hip ratio (≥0.95 for men, ≥0.80 for women). Specificity was high (≥90%) in all populations. At waist action level 2 (waist circumference ≥102 cm and ≥88 cm in men and women respectively, BMI≥30 kg/m^2), sensitivity varied from 22% to 64% in men and from 26% to 67% in women, whereas specificity was >95% in all populations. Sensitivity was in general lowest in populations where overweight was relatively uncommon, whereas it was highest in populations with relatively high prevalence of overweight.

Conclusion: We propose that cut-off points based on waist circumference as a replacement for cut-off points based on BMI and waist-hip ratio should be viewed with caution. On the basis of the proposed waist action levels very few people would unnecessarily be advised to have weight management, but a varying proportion of those who would need it might be missed. The optimal screening cut-off points for waist circumference may be population-specific.

Introduction

A central distribution of body fat, indicated by a high waist-hip ratio, has been shown to be associated with other risk factors, many chronic diseases (e.g. hypertension, cardiovascular disease, non-insulin-dependent diabetes, stroke) and mortality [1]. Other measures, such as waist-height ratio [2,3] have also been recommended for the measurement of fat distribution. These indices do, however, suffer from serious limitations in relation to their use in statistical analyses and to the interpretation of the results [4,5].

More recently it has been argued that waist circumference alone might convey equally valid information as waist-hip ratio and BMI in measuring abdominal fat [6,7] and be at least as strongly associated with other risk factors [8]. If this were the case, the use of this single measurement would simplify the interpretation of epidemiological data as well as the public health recommendations relating to weight management. Lean et al. [7] have suggested two action levels for waist circumference based on BMI and waist-hip ratio. According to their results, men with waist circumference ≥94 cm and women with waist circumference ≥80 cm should gain no further weight (waist action level 1), and men with waist circumference ≥102 cm and women with waist circumference ≥88 cm should reduce their weight (waist action level 2). These action levels have been tested in British [7] and Dutch [8] populations in which very high sensitivities and specificities, in relation to cut-off points based on BMI and waist-hip ratio, were observed. However, for example Ko et al. [9] observed a very low sensitivity of waist action level 1 in the lean population of Hong Kong Chinese. The applicability of the proposed action levels in other populations remains to be shown. We tested their performance in 19 WHO MONICA populations participating in the second MONICA survey from 1987-92, for which data on waist circumference were available.

Methods

The WHO MONICA Project was designed to measure trends in incidence and mortality from cardiovascular disease, and to assess the extent to which these trends are related to changes in known risk factors. The project is carried out in 39 Collaborating Centres in 26 countries with several centres monitoring more than one study population. Risk factors in the WHO MONICA Project are monitored through three independent cross-sectional population surveys

[10,11]. The surveys included random samples of at least 200 people in each gender and ten-year age group, for the age range 35-64 years, and optionally 25-34 years. In this study we present data from the second surveys for the entire age range (25-64 years). Since waist and hip circumference measurements were optional in the second MONICA survey, only about half of the centres measured these items. The survey periods ranged from January 1987 to September 1992. In Toulouse, only men in the age range 35-64 years were examined. The overall participation rates for the populations included in the present study varied from 57% to 88%. The population sizes, participation rates and survey periods have been described in more detail elsewhere [12].

Standard recommendations for the anthropometric measurements in MONICA were as follows. Waist circumference was measured with participants standing without heavy outer garments and with emptied pockets. Waist was measured at the level midway between the lower rib margin and the iliac crest with the participant breathing out gently. The measurement was rounded to the nearest half cm, except in three populations (Newcastle, Gothenburg and Novi Sad) where it was recorded to the nearest full cm. All populations used the same standardized methods, except the Czech Republic where the waist circumference was measured at the level of umbilicus. The quality of data on waist has been centrally assessed in the WHO MONICA Project. Any population with unsatisfactory data quality or a response rate lower than 50% has been omitted from this study. Height and body weight were measured with participants standing without shoes and heavy outer garments. Body mass index (BMI) was calculated as weight divided by height squared (kg/m^2). Hip was recorded as the maximum circumference over the buttocks.

To assess the applicability of the waist action levels in MONICA populations, we calculated the sensitivity and specificity of these levels in each population using the same cut-off points for BMI and waist-hip ratio as Lean et al. [7] Sensitivity was calculated as true positives over the sum of true positives and false negatives. Specificity was calculated as true negatives over the sum of true negatives and false positives. "True positive" subjects were those with waist above the specified waist action level and either high BMI or low BMI with high waist-hip ratio. High BMI was defined as $BMI \geq 25$ kg/m^2 (at action level 1) and $BMI \geq 30$ kg/m^2 (at action level 2). High waist-hip ratio was defined as 0.95 for men and 0.80 for women at both action levels. "True negative" subjects were those with waist circumference below the action level and low BMI and low waist-hip ratio. "False negatives" were those with waist circumference below the action level but high BMI or high waist-hip ratio. Our definition of true and false negatives is therefore different from that used by Lean et al. The main difference was that Lean et al. considered subjects with only high BMI or only high waist-hip ratio as "true negatives" if they had waist *below* the action level, whereas they considered them as "true positives" if they had waist *above* the action level (see Table 1). This means, however, that they used different criteria of disease (need of weight management) for those with waist above the action level (high BMI *or* high waist-hip ratio) than for those with waist below the action level (high BMI *and* high waist-hip ratio). We considered subjects with only high BMI or only high waist-hip ratio as "false negatives" if they had waist below the action level and as "true positives" if they had waist above the action level. Our definition is therefore in accordance with the generally acknowledged definition of sensitivity and specificity in which all those with a marker of abnormality (high BMI or high waist-hip ratio or both) are regarded as true cases (in need of weight management) irrespective of their response to the test (waist circumference). "False positives" were those with waist circumference above the action level but low BMI and low waist-hip ratio.

Table 1. *Definitions of true positives (TP), false positives (FP), true negatives (TN) and false negatives (FN) used by Lean et al. (a) and in this study (b) to identify subjects with overweight or obesity using waist circumference in comparison with body mass index (BMI) and waist-hip ratio (WHR).*

a. Lean et al. [7]	Low BMI		High BMI	
	Low WHR	High WHR	Low WHR	High WHR
Low waist	TN	TN*	TN*	FN
High waist	FP	TP	TP	TP

b. This study	Low BMI		High BMI	
	Low WHR	High WHR	Low WHR	High WHR
Low waist	TN	FN*	FN*	FN
High waist	FP	TP	TP	TP

* Difference in definitions.

The significance of the differences in sensitivity among the populations was tested by chi square. This was based on the linear hypothesis of the equality of the sensitivities under the assumption that the estimates of sensitivity are approximately normally distributed with known variances. The squares of the standard errors of the estimates of sensitivity were used as the variances. In addition, because sensitivity appeared to be higher in populations with higher prevalences of overweight, we calculated Pearson correlation coefficients between sensitivity and prevalence of overweight (at action level 1) and obesity (at action level 2).

In addition to investigating sensitivity and specificity, we compared two definitions of overweight: one based on BMI (≥25 kg/m^2) and another on waist circumference (≥94 cm in men, ≥80 cm in women). Similarly, obesity was defined both as BMI ≥30 kg/m^2 (in men and women) and waist circumference ≥102 cm in men, ≥88 cm in women. Unweighted prevalences of overweight and obesity were calculated using both definitions.

Results

Waist action level 1

Excluding Glostrup which had a very different pattern from all other study populations due to very narrow hip circumference and high waist-hip ratio, there were very few subjects with both high waist-hip ratio and high BMI (ranging from less than 1% to 9%) among those who had waist below the action level. Accordingly, there were very few subjects with both low waist-hip ratio and low BMI (range 1-5%) among those who had waist above the action level. In men, the proportion of subjects with waist below the action level and high BMI but low waist-hip ratio was considerable and varied from 21% in Catalonia to 41% in Newcastle and Augsburg (rural). In women, the pattern of the above-mentioned proportions was more variable and less consistent across the populations. (Tables and figures for waist action level 1 are not shown, a full set of tables and figures is available on request.)

The prevalence of overweight varied considerably among populations whether defined by waist circumference (≥94 cm for men, ≥80 cm for women) or by BMI (≥25 kg/m^2 for both men and women). In men especially, the difference between the prevalences using the two definitions in several populations was 20% or more with BMI giving higher prevalences of overweight than waist circumference. In women, the two definitions gave more consistent results with the maximum difference of 10% (Kuopio Province). Furthermore, in women there was no consistency regarding which of the two definitions gave a higher prevalence of overweight.

Specificity of waist action level 1 was very high in all populations, ranging from 90% to 100%. Sensitivity was low and ranged from 40% in Beijing to 80% in Halle County in men.

In women, sensitivity was somewhat higher than in men, ranging from 51% in Glostrup to 86% in Czech Republic. The differences in sensitivity among the study populations were statistically significant (p-value < 0.001) both in men and women.

Waist action level 2

Tables 2a and 2b show the proportions of different categories of waist-hip ratio and BMI by waist action level 2 in men and women, respectively. In all populations most of those who had waist circumference below the action level also had a low waist-hip ratio and BMI. The proportion of subjects with low waist circumference but both high waist-hip ratio and high BMI was very low (ranging from less than 1% to 3%). Subjects who had a high waist circumference were more evenly distributed among those who had either high waist-hip ratio, high BMI or both (men) or among those who had high waist-hip ratio (women). Again Glostrup had a different pattern from other study populations, although less strikingly so than at action level 1. Among those with low waist circumference the proportion of subjects with only high BMI was small (less than 5% in all populations), but the proportion of subjects with only high waist-hip ratio varied considerebly among populations (from 7% in Beijing to 74% in Glostrup in men, and from 12% in Perth to 58% in Glostrup in women).

The prevalence of obesity defined by waist circumference (≥102 cm for men, ≥88 cm for women) gave relatively similar results as those estimated with BMI (≥30 kg/m^2 for both men and women) in most male populations, and only four populations (Czech Republic, Glostrup, Catalonia and Glasgow) showed more than 5% difference between the two definitions. Most female populations, however, showed more than 5% differences and seven populations (Newcastle, Beijing, Czech Republic, Augsburg (urban), Halle County, Friuli and Catalonia) showed 10% difference or more in prevalence estimates of obesity between the two definitions. When the two estimates did not agree, the prevalence of obesity was higher when defined by waist than by BMI.

Figures 1a and 1b give the sensitivities and specificities at waist action level 2 to detect obesity measured by waist-hip ratio and BMI by population in men and women, respectively. Specificity was very high, over 95% in all populations, whereas sensitivity varied markedly across the populations. In men sensitivity ranged from 22% in Glostrup to 64% in Halle County, and in women from 26% in Glostrup to 67% in the Czech Republic. Also at waist action level 2, there were statistically significant differences (p-value < 0.001) in sensitivity among the study populations in both genders.

Table 2a. Proportions of different categories of waist-hip ratio and body mass index by waist action level and unadjusted prevalence of obesity measured by waist circumference and BMI. Second MONICA survey, men aged 25-64 years.

ACTION LEVEL 2

MEN		Low BMI		High BMI		Prevalence (%) of obesity defined		Total
		Low WHR (%) [1]	High WHR (%)	Low WHR (%)	High WHR (%)	as waist ≥102cm	as BMI ≥30kg/m^2	N
Population								
AUS-NEW	waist<102	81	14	4	1	24	20	744
	waist≥102	7	26	18	48			
AUS-PER	waist<102	86	10	3	1	15	14	815
	waist≥102	6	27	17	50			
CHN-BEI	waist<102	92	7	2	0.2	4	4	707
	waist≥102	0	47	10	43			
CZE-CZE	waist<102	71	23	3	2	32	25	1356
	waist≥102	8	27	15	51			
DEN-GLO	waist<102	25	74	0	1	18	11	740
	waist≥102	0	47	2	52			
FIN-KUO	waist<102	84	12	3	1	16	16	761
	waist≥102	7	20	18	55			
FIN-NKA	waist<102	84	11	4	1	19	19	1447
	waist≥102	4	20	13	63			
FIN-TUL	waist<102	84	12	3	2	18	16	731
	waist≥102	7	24	14	55			
FRA-TOU *	waist<102	87	10	2	0.4	19	12	580
	waist≥102	15	31	18	37			
GER-AUR	waist<102	79	16	4	2	21	18	1078
	waist≥102	8	26	14	52			
GER-AUU	waist<102	84	13	3	0.1	19	15	864
	waist≥102	8	30	12	50			
GER-HAC	waist<102	81	17	2	1	29	18	401
	waist≥102	14	30	10	45			
ITA-BRI	waist<102	85	10	2	2	11	12	760
	waist≥102	6	28	20	46			
ITA-FRI	waist<102	78	17	3	1	15	15	910
	waist≥102	5	22	15	58			
SPA-CAT	waist<102	51	47	1	2	23	17	1731
	waist≥102	1	36	3	59			
SWE-GOT	waist<102	85	13	1	1	12	9	785
	waist≥102	6	31	17	45			
SWE-NSW	waist<102	69	27	2	1	13	11	773
	waist≥102	3	36	5	56			
UNK-GLA	waist<102	77	21	1	1	22	14	717
	waist≥102	5	37	8	51			
YUG-NOS	waist<102	73	24	2	1	17	15	780
	waist≥102	6	23	12	59			

* Age group 35-64 years.

[1] Key: Low WHR= waist-hip ratio < 0.95
Low BMI = body mass index < 30 kg/m^2
High WHR = waist-hip ratio ≥ 0.95
High BMI = body mass index ≥ 30 kg/m^2

Table 2b. Proportions of different categories of waist-hip ratio and body mass index by waist action level and unadjusted prevalence of obesity measured by waist circumference and BMI. Second MONICA survey, women aged 25-64 years.

ACTION LEVEL 2

WOMEN Population		Low BMI Low WHR (%) [1]	Low BMI High WHR (%)	High BMI Low WHR (%)	High BMI High WHR (%)	Prevalence (%) of obesity defined as waist ≥88cm	Prevalence (%) of obesity defined as BMI ≥30kg/m²	Total N
AUS-NEW	waist<88	71	26	2	1	31	19	755
	waist≥88	2	44	6	48			
AUS-PER	waist<88	85	12	2	0.3	17	14	826
	waist≥88	4	26	22	48			
CHN-BEI	waist<88	53	46	0.3	0.3	21	8	869
	waist≥88	0	62	2	36			
CZE-CZE	waist<88	55	42	2	0.4	48	30	1410
	waist≥88	2	40	6	53			
DEN-GLO	waist<88	40	58	1	0.5	17	8	735
	waist≥88	2	59	3	36			
FIN-KUO	waist<88	77	19	3	1	23	20	826
	waist≥88	1	25	9	64			
FIN-NKA	waist<88	74	21	3	1	23	21	1595
	waist≥88	1	26	12	62			
FIN-TUL	waist<88	76	19	4	1	21	19	795
	waist≥88	5	20	13	63			
GER-AUR	waist<88	62	34	3	1	26	21	1087
	waist≥88	3	30	10	57			
GER-AUU	waist<88	68	30	1	1	25	15	863
	waist≥88	2	41	9	47			
GER-HAC	waist<88	61	37	1	1	40	26	480
	waist≥88	1	37	9	53			
ITA-BRI	waist<88	64	33	2	2	23	17	775
	waist≥88	2	38	3	57			
ITA-FRI	waist<88	59	39	1	0.3	26	15	909
	waist≥88	1	46	5	49			
SPA-CAT	waist<88	60	36	2	1	33	22	1199
	waist≥88	1	38	5	56			
SWE-GOT	waist<88	79	20	1	0.5	14	10	782
	waist≥88	1	41	12	46			
SWE-NSW	waist<88	58	40	1	1	18	11	804
	waist≥88	0	45	1	54			
UNK-GLA	waist<88	70	27	2	0.2	27	19	797
	waist≥88	1	36	12	50			
YUG-NOS	waist<88	52	42	3	3	32	26	791
	waist≥88	0.4	30	4	65			

[1] Key: Low WHR= waist-hip ratio < 0.80
Low BMI = body mass index < 30 kg/m²
High WHR = waist-hip ratio ≥ 0.80
High BMI = body mass index ≥ 30 kg/m²

Figure 1a. *Sensitivity and specificity of waist action level 2 (≥102 cm) in respect with BMI (≥30 kg/m²) and waist-hip ratio (≥0.95). Men aged 25-64 years.*

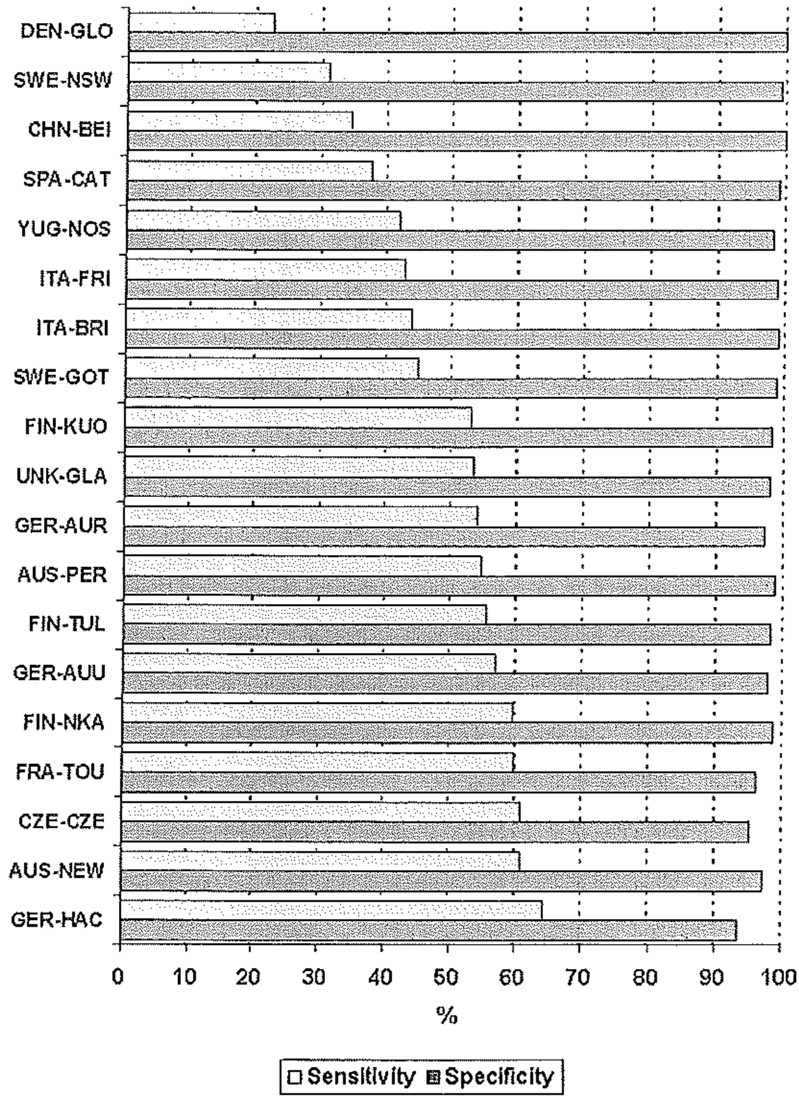
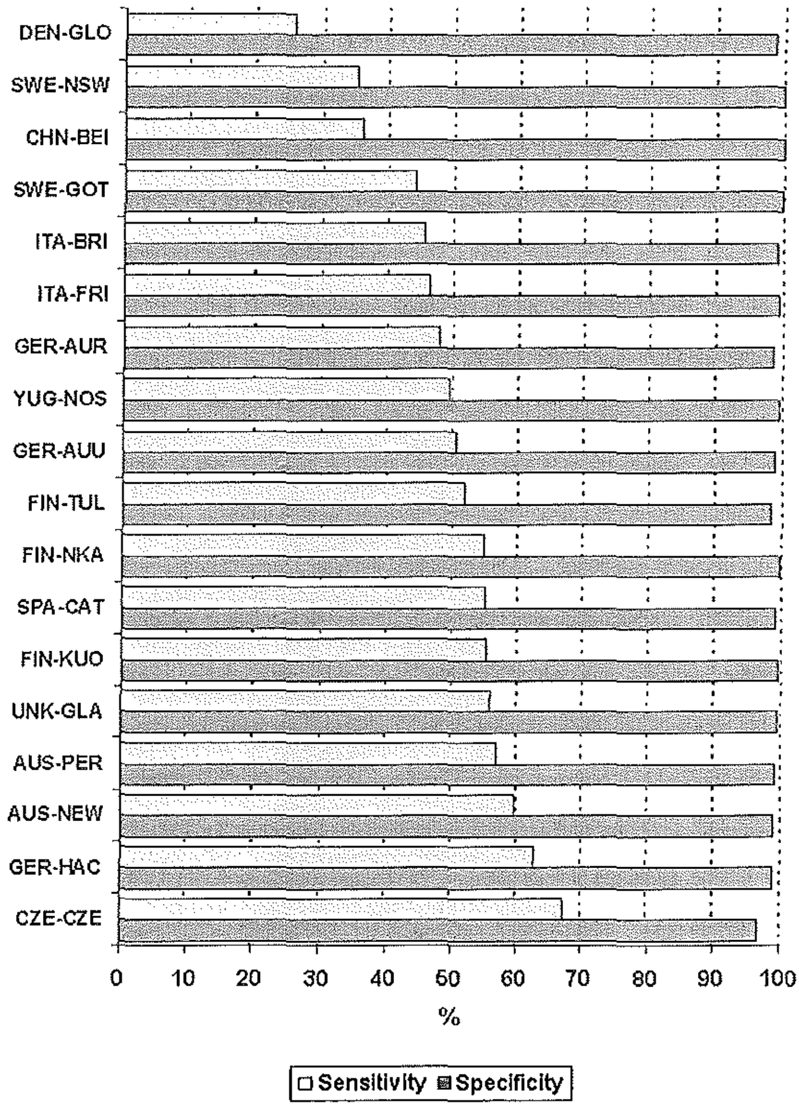


Figure 1b. *Sensitivity and specificity of waist action level 2 (≥88 cm) in respect with BMI (≥30 kg/m²) and waist-hip ratio (≥0.80). Women aged 25-64 years.*



Association between prevalence of overweight and sensitivity

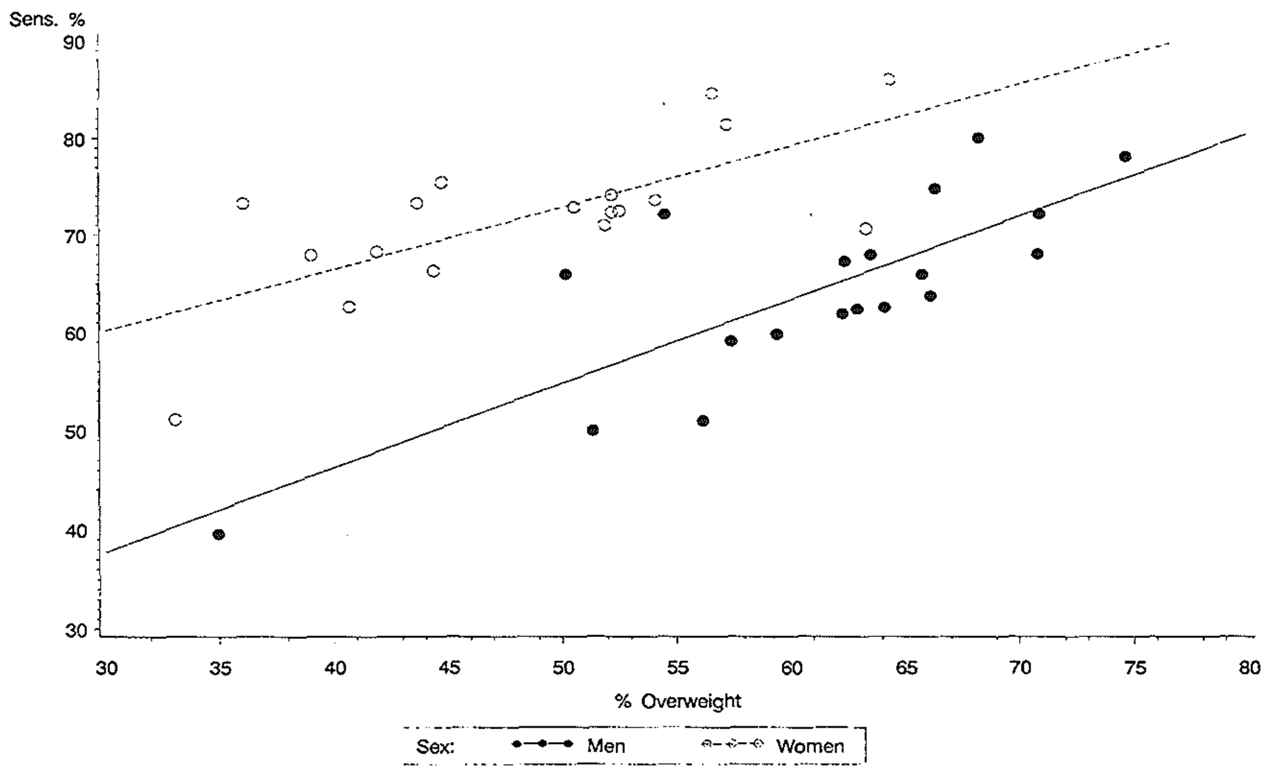
Because we discovered that the sensitivities of the waist action levels were lower in populations where the prevalence of overweight was lower, we decided to test the association between these two factors in the study populations. A strong positive correlation was found between sensitivity at waist action level 1 and prevalence of overweight (BMI ≥25 kg/m^2, correlation coefficient 0.79 in men and 0.72 in women, Figure 2a) and sensitivity at waist action level 2 and prevalence of obesity (BMI ≥30 kg/m^2, correlation coefficient 0.66 in men and 0.81 in women, Figure 2b). However, sensitivity was uncorrelated with the proportion of subjects with high BMI or waist-hip ratio, except in men at waist action level 1 (correlation coefficient 0.55).

Discussion

Our results show considerable differences in the sensitivity of the recommended waist action levels to detect overweight or obesity measured using "traditional" indicators across the 19 populations studied. At waist action level 1, sensitivity varied between 40% and 80% in men and between 51% and 86% in women. At action level 2, sensitivity was usually lower than that at action level 1 ranging from 22% to 64% in men and from 26% to 67% in women. Specificity was very high (≥90%) in all populations, for both men and women and for both action levels. This indicates that there would be very few false positives, i.e. subjects who would be recommended weight management unnecessarily, if the two waist action levels were applied in these study populations.

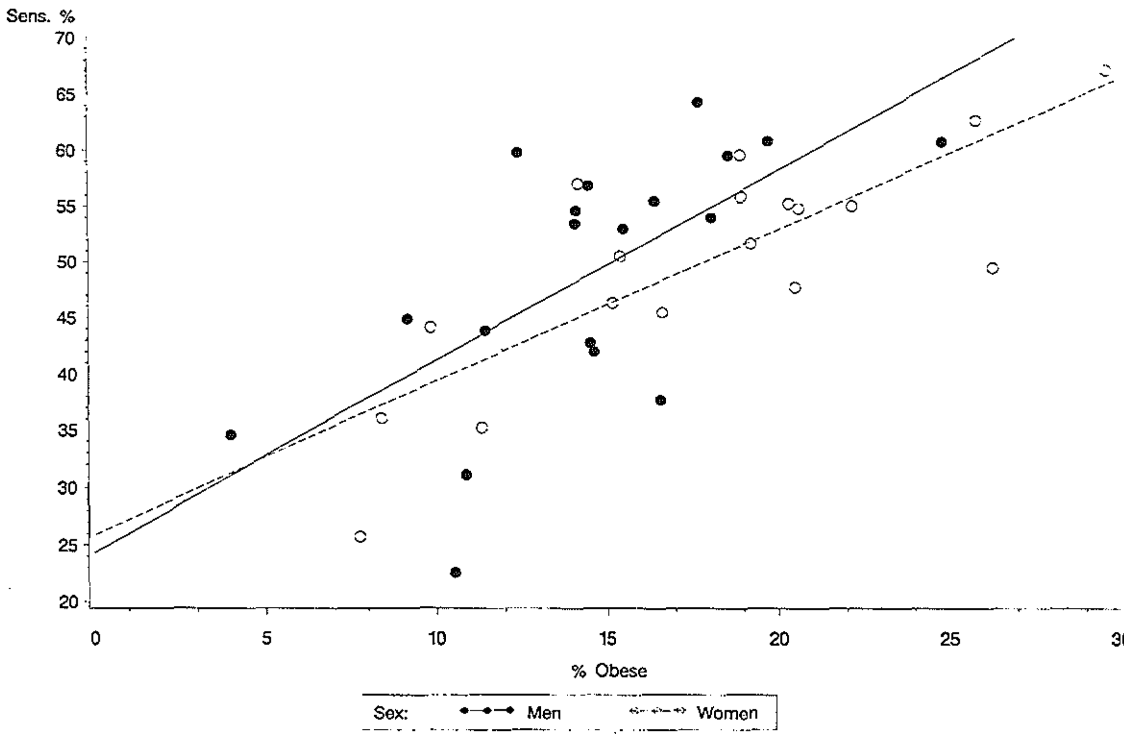
The low sensitivities observed in this study reflect the relatively large proportions of subjects with waist circumference below the action level but either high waist-hip ratio or high BMI. Thus, there is a relatively large group of people in need of waist management who would be missed if these waist action levels alone were adopted as screening tests for weight management. At waist action level 1, false negatives were mainly those with high BMI (≥25 kg/m^2) but low waist-hip ratio. The proportion of such men among those with waist below the action level ranged from 21% to 41%. At waist action level 2, false negatives were mainly those with low BMI (<30 kg/m^2) but high waist-hip ratio. The proportion of these subjects among those with waist below the action level varied between 7% and 74% in men and between 12% and 58% in women.

Figure 2a. Prevalence of overweight (BMI ≥25 kg/m²) vs. sensitivity at waist action level 1, 19 male and 18 female populations aged 25-64 years.



Men: Sensitivity = 12.1 + 0.86 * %overweight, R−square=0.62
Women: Sensitivity = 41.1 + 0.63 * %overweight, R−square=0.51

Figure 2b. *Prevalence of obesity (BMI ≥30 kg/m²) vs. sensitivity at waist action level 2, 19 male and 18 female populations aged 25-64 years.*



Men: Sensitivity = 24.3 + 1.7 * %obese, R-square = 0.43
Women: Sensitivity = 25.8 + 1.4 * %obese, R-square = 0.66

These are the subjects who would be missed if the weight management programme were solely based on the waist action levels introduced by Lean et al. [7] It is, however, debatable whether subjects with only high waist-hip ratio or only high BMI would really need weight reduction or surveillance and benefit from it. Lean et al. implicitly concluded that they do not need weight management and considered them as true negatives if their waist circumference was below the action level. This is, however, deciding the need of weight management on the basis of the test result (waist circumference) and not on the basis of the BMI and waist-hip ratio, and such a post-hoc decision is inappropriate in defining true and false negatives. We considered all subjects with either high waist-hip ratio or high BMI, or both, as cases (that is, in need of weight management), and therefore our estimates for sensitivity in Glasgow (72% in men and 73% in women at waist action level 1) were considerably lower than those of Lean et al. (97% in both men and women). Our definition of true and false negatives is in keeping with the one generally applied in assessment of tests in public health screening [13]. Further knowledge about the distribution of risk factors and health outcomes in subjects in the different categories of waist, waist-hip ratio and BMI - especially in those subjects with only high waist-hip ratio or high BMI - is needed before definitive recommendations regarding these subjects can be given. Nevertheless, the advantage of these waist action levels is that people with both high waist-hip ratio and high BMI would very seldomly be missed in screening for waist in any of the study populations. Moreover, people with low waist-hip ratio and low BMI would very rarely be inappropriately recommended for weight management.

Calculation of sensitivity and specificity requires an assessment of the true disease status. Lean et al. [7] used cut-off points for BMI and waist-hip ratio in their assessment. The cut-off points for BMI are well established, and they have been incorporated in the WHO recommendation [14]. The use of cut-off points described by Lean et al. for waist-hip ratio [15] is, however, only one possibility. Several other cut-off points have been suggested in the literature [16,17], and there is no consensus about the optimal cut-off points for waist-hip ratio. A change in the cut-off points for waist-hip ratio would cause a change in the cut-off points for waist circumference. Therefore, the scientific justification for the waist action levels is highly dependent on the validity of the cut-off points for BMI and waist-hip ratio.

Sensitivity and specificity are unaffected by the prevalence of the underlying disease or condition [18] which makes them useful for comparing indicators across different populations. In this study, a statistically significant positive correlation between sensitivity and prevalence of overweight (defined by BMI) was observed. This suggests that the interrelations between various anthropometric measurements vary in different populations. Sensitivity was in general lowest in Beijing, Glostrup and Northern Sweden where also the prevalence of overweight was relatively low. This is in agreement with the findings of Ko et al. [9] who also reported very low sensitivities of waist action level 1 (15% in men, 31% in women) among the lean population of Hong Kong Chinese. In contrast, Catalonia, the Czech Republic and Halle County, where overweight was relatively common, showed higher values of sensitivity. Moreover, because there is always a trade-off between sensitivity and specificity, the large differences in sensitivity observed among the study populations suggest that the optimal cut-off points for waist circumference, when based on the cut-off points of BMI and waist-hip ratio used, would vary between the study populations and be lower in populations with relatively low prevalence of overweight than in populations with relatively high prevalence of overweight. This may also explain why the results in the British [7] and Dutch [8] studies were similar, because the prevalence of overweight in these two studies was roughly the same. Our results are in agreement with the concept that in practise sensitivity and specificity may be related to the characteristics of the population under study [19], and therefore the screening test should be evaluated in the population in which it is going to be used.

Although BMI and waist circumference are highly correlated, there were large differences in the prevalence estimates of overweight and obesity defined by BMI in comparison with those defined by waist action levels. The differences in the prevalence estimates produced by the two definitions were smallest for obesity in men. This may be affected by the fact that waist action levels are defined separately for men and women but the recommendation based on BMI is the same for men and women. At waist action level 1, BMI tended to produce higher prevalence of overweight whereas, at waist action level 2, waist tended to produce higher prevalence of obesity, especially in men. This inconsistency is a further reason why the use of waist circumference cut-off points instead of BMI cut-off points should be done with caution.

For assessing the true differences in body girth measurements among populations, it is crucial that the methods are standardized across populations, since small differences in the anatomical measurement levels can produce very different results [20]. The fact that waist circumference was measured at the level of umbilicus in the Czech Republic did not seem to have any obvious impact on performance of the waist action levels. The prevalence of overweight and obesity was the highest in the Czech Republic irrespective of whether it was measured by waist circumference or by BMI. The distribution of proportions of the different categories of BMI and waist-hip ratio in Glostrup was, however, different from all the other study populations due to low mean BMI but very high waist-hip ratio. Although some investigators have reported high reliabilities for waist and hip circumference measurements [21], there can always be inter-observer variation in these measurements. The differences in Glostrup are most likely due to such inter-observer variation, because the centre has reported that the standard measurement techniques were applied and no particular quality problems were observed in the data.

To determine the applicability of the waist action levels in identifying subjects with overweight or obesity, even other criteria than sensitivity and specificity in relation to BMI and waist-hip ratio can be applied [22]. One such criteria is the relation of the waist action levels to morbidity and mortality. Currently no prospective studies using these specific cut-off points for waist circumference have been published in the literature. Moreover, the relationship between obesity and health outcomes can be modified by other factors such as lifestyle, genetic predisposition and comorbidity in the population. Therefore the interpretation of waist circumference in different populations may be different. Further data in each population on the effects of fat storage in specific regions of the body on health is needed before the applicability of a single measure can be evaluated.

In conclusion, we observed that the proposed action levels [7] based on the waist circumference alone are unsatisfactory in detecting people in need of weight management on the basis of either a high BMI and/or high waist-hip ratio. Moreover, a consirable variation in sensitivity was found among the study populations. Sensitivity was also lower in men than in women. We propose that caution should guide any decision to replace cut-off points based on BMI and waist-hip ratio with cut-off points based on waist circumference, although the specificity of these waist action levels seems to be high. Further insight into the health risks in 'false negative' subjects compared with 'true negative' subjects is needed for further evaluation. The findings of this study also suggest that optimal screening cut-off points may be population-specific. Thus, universal values applicable in different populations – as is possible for BMI – may not be possible for waist circumference.

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5.3 Misclassification of high risk elderly subjects by using waist action levels established for young and middle aged adults: results from the Rotterdam Study

Abstract

In the literature, cut-off points based on waist circumference (waist action levels) have been suggested to replace cut-off points based on body mass index (BMI) and waist-hip ratio (WHR) in identifying subjects with overweight or obesity and/or central fat distribution. These cut-off points have been based on analysis in mainly middle-aged and younger adults. In this paper we examined the applicability of the suggested waist action levels in an elderly population. The subjects comprised 6423 men and women aged 55 or over participating in the Rotterdam Study. Sensitivities and specificities of the proposed waist action levels in relation to the cut-off points for BMI and WHR were calculated. Also, cardiovascular risk factor levels at baseline and risk of death during a 5.5 year follow-up in the different categories defined by high/low waist circumference, BMI and WHR were investigated. At waist action level 1 (waist circumference $\geq$ 94 cm in men, $\geq$ 80 cm in women) sensitivity was 71% in men and 86% in women when compared to the cut-off points based on BMI ($\geq$ 25 kg/m^2) and WHR ($\geq$ 0.95 in men, $\geq$ 0.80 in women). At waist action level 2 (waist circumference $\geq$ 102 cm in men, $\geq$ 88 cm in women, BMI $\geq$ 30 kg/m^2, WHR $\geq$ 0.95 in men, $\geq$ 0.80 in women), sensitivity was considerably lower: 35% in men and 59% in women. This was mainly due to a large proportion of subjects with high WHR but low waist and BMI. Specificity was high (>90%) at both action levels. Cardiovascular disease risk factors, except smoking, tended to increase with increasing waist circumference, WHR and BMI. The risk of mortality was not increased in those with high waist circumference, BMI and/or WHR after adjustment for age and smoking. We conclude that the suggested cut-off points for waist circumference are only to a limited degree useful in identifying subjects with overweight and obesity and/or central fat distribution in an elderly population. This concerns especially the upper cut-off point (waist action level 2) and is mainly due to the increased central distribution of fat with advancing age. In the elderly with a relatively short follow-up period, waist action levels seem not to be useful in identifying groups at increased risk of death.

Introduction

Overweight and especially abdominal obesity are independently related to the incidence of several chronic diseases, such as coronary heart disease, non-insulin-dependent diabetes (NIDDM) and stroke as well as to overall mortality [1-7]. Aging is accompanied with changes in relative weight, body composition and fat distribution. While relative weight seems to increase at least until the age 50-60 years in men and women, it decreases in older age groups [8,9]. The reasons for these changes are unclear and may even be confounded by such factors as cohort effects and selective mortality of obese subjects during middle age. Relating to body composition, clinically important losses of fat-free mass with age both in men and women have been observed [9]. Furthermore, aging is associated with increasingly more central distribution of adiposity [10,11]. At any given level of overweight, more fat will be centrally distributed in older individuals. While this is a slowly progressive change in men, in women the accumulation of abdominal fat may begin to increase only after menopause [12,13].

The degree of overweight is usually measured using body mass index (BMI, weight (kg) divided by height squared (m^2)). Abdominal obesity has most often been measured using the ratio of waist to hip circumference (WHR), although also other indicators have been used in the literature. More recently it has been suggested that waist circumference would be a simple indicator of both degree of overweight and abdominal obesity [14,15] and to be more strongly correlated with cardiovascular risk factors [16] than BMI and WHR. Lean et al. [15] have suggested two action levels for waist circumference based on cut-off points for BMI and WHR. According to their results, men with waist circumference ≥94 cm and women with waist circumference ≥80 cm should gain no further weight (waist action level 1), and men with waist circumference ≥102 cm and women with waist circumference ≥88 cm should reduce their weight (waist action level 2). The action levels have also been shown to be associated with a higher prevalence of NIDDM, low back pain and respiratory insufficiency [17]. Some studies have, however, suggested that the waist circumference cut-off points of Lean et al. may not be useful in all populations, especially in populations where obesity is relatively uncommon [18,19]. Moreover, the waist action levels were based on population survey data from predominantly middle-aged subjects and their applicability in the elderly has not been investigated.

Given the changes in relative weight and fat distribution associated with aging we considered it important to explore the applicability of the suggested cut-off points for abdominal obesity in an elderly population. The study population comprised the subjects of the Rotterdam Elderly Study, a large population-based prospective cohort of over 7,000 men and women aged 55 years or over. The aim of the study was to investigate the applicability of the proposed cut-off points for waist circumference in relation to the cut-off points for BMI and WHR in the elderly by means of

1) sensitivity and specificity,
2) level of cardiovascular disease risk factors at baseline, and
3) risk of total mortality.

Methods

Study population

The Rotterdam Study is a prospective single centre population-based study, designed to investigate determinants of selected chronic diseases and disabilities in the elderly [20]. The conduct of the study was approved by the Medical Ethics Committee of Erasmus University and written consent was obtained from all participants. The cohort was defined as all inhabitants of Ommoord, a suburban district in Rotterdam, who were 55 years of age or older at 1 January 1990. All eligible participants were invited to participate, including those living in nursing homes. The baseline examinations started in May 1990 and continued until June 1993. Of the 10275 eligible subjects, 7983 (78%) agreed to participate. During a home visit, trained interviewers administered a questionnaire covering socioeconomic background, smoking habits, alcohol consumption, dietary habits, medical history and medication use. This was followed by two extensive clinical examinations, including anthropometric measurements, at the research centre. Those living in nursing homes or homes for the elderly, about 11% of the study population, were examined at their institutions.

Measurements

Standard recommendations for the anthropometric measurements were the following. Waist and hip circumferences were measured with participants in standing position without heavy outer garments and with emptied pockets. Waist circumference was measured at the level midway between the lower rib margin and the iliac crest with the participant breathing out gently. Hip circumference was recorded as the maximum circumference over the buttocks. Height and body weight were measured with participants standing without shoes and heavy outer garments. Body mass index (BMI) was calculated as weight divided by height squared (kg/m^2).

Cardiovascular disease risk factors investigated in this study were cigarette smoking, systolic and diastolic blood pressure, total and HDL-cholesterol and existing cardiovascular disease at baseline examination. Information on cigarette smoking was obtained by interview. Systolic and diastolic blood pressure were measured and total and HDL-cholesterol were examined from the plasma taken at the clinical examination. Existing cardiovascular disease was coded "yes" if the subject had suffered a diagnosed myocardial infarction or stroke, or undergone a coronary bypass surgery or percutane coronary angioplasty.

Information on vital status was acquired at regular intervals from the municipal authorities of Rotterdam. In addition, general practitioners working in the study district of Ommoord gave regularly computerized reports on the deaths of participants of the Rotterdam Study and general practitioners in Rotterdam but outside Ommoord district who had patients participating the Rotterdam Study were visited to obtain information on vital status. The end of the follow-up was set at 1 January 1998. The mean duration of follow-up was 5.5 years.

Statistical methods

7129 subjects visited the research centre. Only subjects with full data on weight, height and circumferences of waist and hip were included in the analyses of this study. This comprised altogether 6423 subjects.

To get insight into the distributions of measures of overweight and fat distribution in the elderly, we calculated the mean values for weight, height, BMI, waist and hip circumferences and WHR by 10-year age group. Because these measures may have different interrelationships in the elderly than in middle-aged subjects, we also looked at the correlations between these measures. Pearson correlation coefficients were calculated separately for two age categories: those 55-69 years and 70 years or older. The cut-off point 70 years was selected on the basis of the changes in body composition in the elderly and increasing uncertainty of the recommended measures such as BMI and WHR in the very old [21].

To assess the applicability of the waist action levels, we calculated the sensitivity and specificity of these levels using the same cut-off points for BMI and WHR as Lean et al. [15] Sensitivity was calculated as true positives over the sum of true positives and false negatives. Specificity was calculated as true negatives over the sum of true negatives and false positives. "True positive" subjects were those with waist circumference above waist action level and either high BMI or low BMI but high WHR. High BMI was defined as BMI ≥ 25 kg/m^2 (at action level 1) and BMI ≥ 30 kg/m^2 (at action level 2). High WHR was defined as ≥ 0.95 for men and ≥ 0.80 for women at both action levels. "True negative" subjects were those with waist circumference below the action level and low BMI and low WHR. "False negatives" were those with waist circumference below the action level but high BMI or high WHR. "False positives" were those with waist circumference above the action level but low BMI and low WHR. The sensitivities and specificities were calculated for the whole age range in men and women, and by two age groups: 55-69 years and 70 years or older. Because sensitivity was low at waist action level 2, we plotted the sensitivity and specificity curves using different values for waist circumference in relation to the cut-off points for BMI and WHR.

The subjects were divided into eight groups according to their waist circumference (low/high), WHR (low/high) and BMI (low/high). We looked at the proportion of current smokers, mean systolic and diastolic blood pressure, mean total and HDL-cholesterol and prevalence of cardiovascular disease at the baseline examination in the different categories at both action levels. Differences in means between the categories were tested using one-way analysis of variance and differences in proportions using chi-square test. We also tested whether the differences in mean risk factors and prevalence of cardiovascular disease at baseline could be explained by age and smoking, and adjusted therefore for these factors in the analysis.

We used Cox's proportional hazards model to estimate risk ratios and their 95% confidence intervals for total mortality in the different categories. The category of subjects with low waist circumference, low WHR and low BMI ("true negatives") was used as the reference category. Subjects who died during the first year of follow-up were excluded from this analysis because of possible underlying disease affecting the anthropometric measures at baseline examination. The analysis of mortality included 6258 subjects. Because age and smoking are possible confounders in the association between overweight and mortality, we calculated the crude risk ratios as well as adjusted for age and smoking. Age was used as a continuous variable and smoking was divided into three categories (current, past and non-smoker) in this analysis. All analyses were performed separately for men and women.

Results

Table 1 gives the mean values for BMI, weight, height, waist and hip circumferences and WHR in the Rotterdam Study men and women by 10-year age group. In both men and women, mean height decreased across all age groups. Weight declined over all age groups in men, whereas it started to decline after the age 65-74 years in women. In men mean BMI decreased after the age 65-74 years, whereas in women mean BMI decreased only after the age 75-84 years. In men, waist and hip circumferences and, consequently, WHR were relatively stable across all age groups, whereas in women mean waist circumference and WHR increased gradually across all age groups. There were fewer subjects in the oldest age groups, 75-84 and ≥85 years, than in the younger age groups, especially among men.

Very high correlations (r≥0.70) were found between BMI and waist, BMI and hip (in women), and waist and WHR. Correlation between waist and hip circumferences was over 0.60. Waist was positively correlated with height in men (r=0.20, r=0.13 in the two age groups 55-69 and ≥70 years respectively) and less strongly in women (r<0.10). There were only small differences in the correlation coefficients between the two age groups, usually with slightly stronger correlations in the younger age group. The correlation between WHR and BMI was, however, stronger in the older age group in men, whereas the opposite was true in women.

The number of subjects in each category defined by high/low waist circumference, BMI and WHR at waist action levels 1 and 2 is given in Table 2. There are very few false positive subjects at both action levels and in both men and women. At waist action level 1, the false negatives are divided between the categories of "low BMI and high WHR" and "high BMI and low WHR". At waist action level 2, the false positives are mostly those with high WHR and low BMI. Very few of these elderly have BMI over 30 kg/m^2, especially in men, and as a result true positives are mainly those with high WHR and low BMI at waist action level 2.

Table 3 gives the sensitivities and specificities of the waist action levels when compared to the cut-off points of BMI and WHR in all men and women and in the two age groups (55-69 and ≥70 years) separately. The table also shows the prevalence of overweight (BMI ≥ 25 kg/m^2, waist action level 1) and obesity (BMI ≥ 30 kg/m^2, waist action level 2). Specificity was very high (>90%) at both waist action levels in both sexes. At waist action level 1, sensitivity was 71% in men and 86% in women and somewhat higher in the older age group

Table 1. *Mean (standard deviation in parenthesis) body mass index (BMI), weight, height, waist circumference, hip circumference, waist-hip ratio (WHR) and number of subjects (N) by 10-year age group in the Rotterdam Study.*

MEN	**55-64**	**65-74**	**75-84**	**85+**	**All**
BMI (kg/m^2)	25.8 (2.9)	25.8 (2.9)	25.2 (3.2)	24.6 (3.4)	25.7 (3.0)
weight (kg)	81 (11)	79 (10)	74 (10)	70 (10)	78 (11)
height (cm)	177 (7)	175 (6)	172 (7)	169 (7)	175 (7)
waist (cm)	93 (9)	95 (9)	95 (10)	95 (10)	94 (9)
hip (cm)	99 (6)	99 (6)	98 (7)	99 (7)	98 (6)
WHR	0.95 (0.07)	0.96 (0.07)	0.96 (0.07)	0.96 (0.07)	0.96 (0.07)
N	1050	1028	478	84	2640

WOMEN	**55-64**	**65-74**	**75-84**	**85+**	**All**
BMI (kg/m^2)	26.3 (4.0)	27.0 (4.0)	27.0 (4.2)	26.6 (4.1)	26.7 (4.1)
weight (kg)	70 (11)	71 (10)	67 (11)	64 (11)	69 (11)
height (cm)	164 (6)	162 (6)	158 (6)	156 (7)	161 (7)
waist (cm)	85 (11)	88 (11)	90 (12)	92 (12)	88 (11)
hip (cm)	100 (8)	101 (9)	101 (9)	102 (10)	101 (9)
WHR	0.85 (0.08)	0.87 (0.09)	0.89 (0.09)	0.90 (0.09)	0.87 (0.09)
N	1413	1301	821	248	3783

Table 2. Number of observations in different categories of waist circumference, body mass index (BMI) and waist-hip ratio (WHR).

a. Waist action level 1

MEN	BMI < 25 kg/m²		BMI ≥ 25 kg/m²		
	WHR< 0.95	WHR ≥ 0.95	WHR< 0.95	WHR ≥ 0.95	All
Waist < 94 cm	674[TN] (55%)	216[FN] (17%)	266[FN] (22%)	79[FN] (6%)	1235 (100%)
Waist ≥ 94 cm	46[FP] (3%)	183[TP] (14%)	208[TP] (15%)	968[TP] (69%)	1405 (100%)

WOMEN	BMI < 25 kg/m²		BMI ≥ 25 kg/m²		
	WHR< 0.80	WHR ≥ 0.80	WHR< 0.80	WHR ≥ 0.80	All
Waist < 80 cm	471 (51%)	268 (29%)	153 (16%)	40 (4%)	932 (100%)
Waist ≥ 80 cm	15 (1%)	626 (24%)	162 (6%)	2048 (72%)	2851 (100%)

b. Waist action level 2

MEN	BMI < 30 kg/m²		BMI ≥ 30 kg/m²		
	WHR< 0.95	WHR ≥ 0.95	WHR< 0.95	WHR ≥ 0.95	All
Waist < 102 cm	1137 (54%)	921 (44%)	11 (1%)	20 (1%)	2089 (100%)
Waist ≥ 102 cm	31 (5%)	363 (66%)	15 (3%)	142 (26%)	551 (100%)

WOMEN	BMI < 30 kg/m²		BMI ≥ 30 kg/m²		
	WHR< 0.80	WHR ≥ 0.80	WHR< 0.80	WHR ≥ 0.80	All
Waist < 88 cm	723 (37%)	1173 (60%)	34 (2%)	32 (2%)	1962 (100%)
Waist ≥ 88 cm	11 (1%)	1129 (62%)	33 (2%)	648 (36%)	1821 (100%)

TN = true negative
FN = false negative
FP = false positive
TP = true positive

Table 3. Sensitivity and specificity of waist action levels in respect to cut-off points of body mass index (BMI) and waist-hip ratio (WHR), and prevalence of overweight (BMI ≥ 25 kg/m²) and obesity (BMI ≥ 30 kg/m²) in the Rotterdam Study.

MEN	Waist action level 1 *			Waist action level 2 **			
	Sensitivity	Specificity	Prevalence of overweight (%)	Sensitivity	Specificity	Prevalence of obesity (%)	N
All	70.7	93.6	57.6	35.3	97.3	7.1	2640
55-69	67.3	94.1	58.5	33.4	97.6	7.5	1624
70+	75.3	92.8	56.2	37.9	96.9	6.5	1016

WOMEN	Waist action level 1 *			Waist action level 2 **			
	Sensitivity	Specificity	Prevalence of overweight (%)	Sensitivity	Specificity	Prevalence of obesity (%)	N
All	86.0	96.9	63.5	59.4	98.5	19.7	3783
55-69	83.3	97.2	61.7	55.3	98.0	17.9	2073
70+	89.1	96.3	65.7	63.7	99.6	22.0	1710

* Waist circumference ≥ 94 cm in men and ≥ 80 cm in women compared with BMI ≥ 25 kg/m² or WHR ≥ 0.95 in men and ≥ 0.80 in women.
** Waist circumference ≥ 102 cm in men and ≥ 88 cm in women compared with BMI ≥ 30 kg/m² or WHR ≥ 0.95 in men and ≥ 0.80 in women.

than in the younger age group. At waist action level 2, sensitivity was considerably lower: 35% in men and 59% in women. This was due to a large proportion of subjects with low waist circumference and low BMI but high WHR, especially in men, as seen in Table 2. More than half of the study population was overweight, whereas only 7% of men and 20% of women were obese. The prevalence of overweight and obesity was higher in the younger age group than in the older age group in men whereas the pattern with age was opposite in women.

Because sensitivity was low at waist action level 2, we plotted the sensitivity and specificity at different values of waist circumference when compared to the cut-off points for WHR (0.95 in men, 0.80 in women) and BMI (30 kg/m^2). Figures 1 and 2 show that shifting the cut-off points for waist circumference 1-8 cm to the left (towards lower values) would increase the sensitivity considerably while the specificity would still be high.

Figure 1. *Percentage plot of sensitivity and specificity at waist action level 2 using different cut-off points for waist circumference compared to the cut-off ponts of body mass index (30 kg/m^2) and waist-hip ratio (0.95), men.*

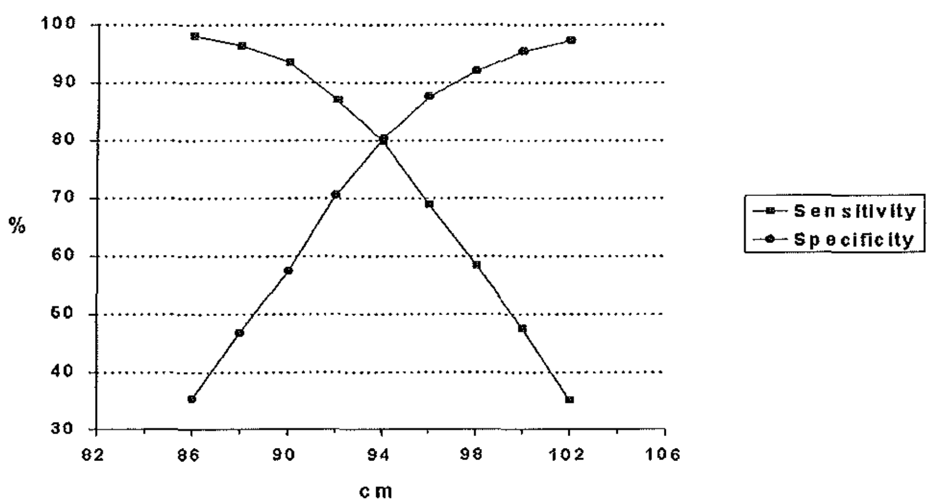
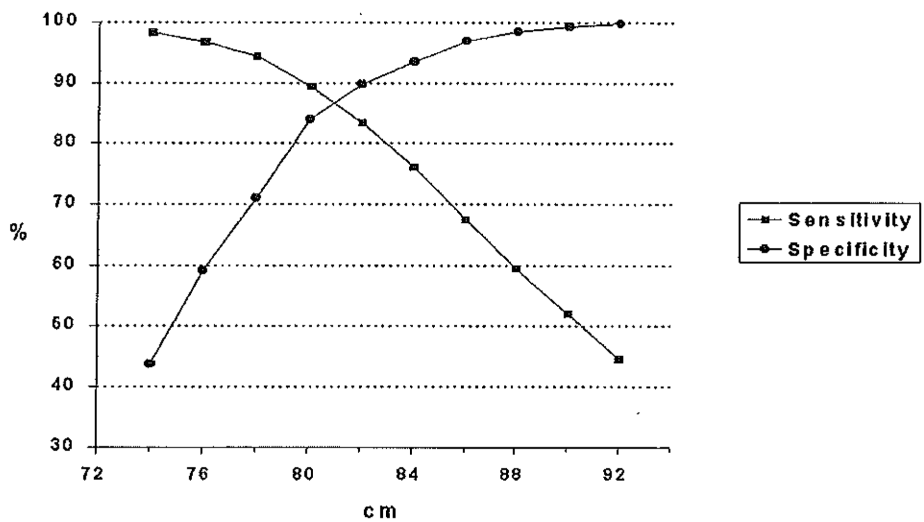


Figure 2. *Percentage plot of sensitivity and specificity at waist action level 2 using different cut-off points for waist circumference compared to the cut-off ponts of body mass index (30 kg/m²) and waist-hip ratio (0.80), women.*



Tables 4a and 4b give the mean age, the mean systolic and diastolic blood pressure, the mean total and HDL-cholesterol, the proportion of current smokers and the prevalence of cardiovascular disease at baseline in the different categories defined by waist circumference, BMI and WHR at the two waist action levels, respectively. Increased levels of blood pressure, total cholesterol and prevalence of existing cardiovascular disease were found especially in those with high waist circumference, high BMI and/or high WHR (true positives). Smoking, on the contrary, was most common in the categories with low waist circumference and low BMI, with or without high WHR (true negatives and part of false negatives). Age was in general higher in those with high BMI and/or WHR. Adjustment for age and smoking did not, however, explain the differences between the categories in blood pressure, cholesterol and prevalence of cardiovascular disease (not shown).

Table 5 shows the relative risks (risk ratios) for total mortality at waist action level 1 compared to the category of low waist (<94 cm in men, <80 cm in women), low WHR (<0.90 in men, <0.80 in women) and low BMI (<25 kg/m²) and at waist action level 2 compared to

Table 4a. Mean (standard deviation in parenthesis) age, systolic (SBP) and diastolic (DBP) blood pressure, total (TC) and HDL-cholestrol, proportion of current smokers and prevalence of cardiovascular disease (CVD) at baseline in different categories of waist circumference, body mass index (BMI) and waist-hip ratio (WHR) and p-value for difference between categories at waist action level 1.

MEN	BMI < 25 kg/m²		BMI ≥ 25 kg/m²		BMI < 25 kg/m²		BMI ≥ 25 kg/m²		p-value
	WHR< 0.95	WHR ≥ 0.95	WHR< 0.95	WHR ≥ 0.95	WHR< 0.95	WHR ≥ 0.95	WHR< 0.95	WHR ≥ 0.95	for diff.
	Waist < 94 cm				**Waist ≥ 94 cm**				
Age (years)	68.0 (8.5)	69.0 (7.8)	65.4 (7.0)	67.8 (7.2)	70.2 (9.2)	70.3 (8.5)	66.5 (7.4)	68.8 (8.2)	0.0001
SBP (mmHg)	135 (23)	137 (21)	138 (23)	143 (24)	139 (22)	137 (23)	141 (20)	142 (21)	0.0001
DBP (mmHg)	73 (12)	73 (11)	76 (12)	76 (13)	73 (12)	73 (12)	77 (11)	76 (11)	0.0001
TC (mmol/l)	6.1 (1.2)	6.2 (1.1)	6.2 (1.1)	6.2 (1.2)	6.0 (0.9)	6.3 (1.2)	6.4 (1.2)	6.5 (1.1)	0.0001
HDL (mmol/l)	1.3 (0.3)	1.3 (0.4)	1.2 (0.3)	1.2 (0.3)	1.1 (0.2)	1.2 (0.3)	1.2 (0.3)	1.2 (0.3)	0.0001
current smokers	29%	36%	16%	28%	33%	27%	15%	21%	0.001
CVD prevalence	17%	17%	18%	15%	15%	24%	22%	23%	0.043
N	674	216	266	79	46	183	208	968	

WOMEN	BMI < 25 kg/m²		BMI ≥ 25 kg/m²		BMI < 25 kg/m²		BMI ≥ 25 kg/m²		p-value
	WHR< 0.80	WHR ≥ 0.80	WHR< 0.80	WHR ≥ 0.80	WHR< 0.80	WHR ≥ 0.80	WHR< 0.80	WHR ≥ 0.80	for diff.
	Waist < 80 cm				**Waist ≥ 80 cm**				
Age (years)	66.7 (8.4)	68.3 (8.8)	65.2 (8.2)	69.6 (9.0)	68.9 (7.7)	71.0 (10.2)	67.8 (8.9)	70.4 (9.0)	0.0001
SBP (mmHg)	132 (23)	136 (23)	133 (22)	137 (22)	141 (21)	138 (24)	137 (21)	143 (22)	0.0001
DBP (mmHg)	70 (11)	72 (11)	73 (10)	71 (11)	72 (10)	72 (12)	74 (11)	75 (11)	0.0001
TC (mmol/l)	6.6 (1.2)	6.9 (1.2)	6.9 (1.1)	7.2 (1.0)	6.4 (0.6)	6.8 (1.2)	6.8 (1.1)	6.9 (1.2)	0.0001
HDL (mmol/l)	1.6 (0.4)	1.5 (0.4)	1.6 (0.4)	1.6 (0.4)	1.4 (0.3)	1.5 (0.4)	1.5 (0.4)	1.4 (0.3)	0.0001
current smokers	25%	27%	14%	18%	20%	21%	14%	16%	0.001
CVD prevalence	7%	7%	6%	5%	7%	9%	9%	11%	0.081
N	471	268	153	40	15	626	162	2048	

Table 4b. Mean (standard deviation in parenthesis) age, systolic (SBP) and diastolic (DBP) blood pressure, total (TC) and HDL-cholestrol, proportion of current smokers and prevalence of cardiovascular disease (CVD) at baseline in different categories of waist circumference, body mass index (BMI) and waist-hip ratio (WHR) and p-value for difference between categories at waist action level 2.

MEN	**BMI < 30 kg/m²**		**BMI ≥ 30 kg/m²**		**BMI < 30 kg/m²**		**BMI ≥ 30 kg/m²**		**p-value**
	WHR< 0.95	**WHR ≥ 0.95**	**WHR< 0.95**	**WHR ≥ 0.95**	**WHR< 0.95**	**WHR ≥ 0.95**	**WHR< 0.95**	**WHR ≥ 0.95**	**for diff.**
	Waist < 102 cm				**Waist ≥ 102 cm**				
Age (years)	67.2 (8.2)	68.9 (7.9)	65.9 (5.3)	65.7 (5.5)	67.0 (8.3)	69.9 (9.0)	67.6 (8.2)	67.9 (7.5)	0.0001
SBP (mmHg)	137 (23)	140 (22)	146 (26)	152 (22)	134 (20)	141 (21)	142 (14)	142 (20)	0.0004
DBP (mmHg)	74 (12)	74 (11)	77 (10)	83 (11)	74 (14)	76 (12)	77 (10)	78 (11)	0.0001
TC (mmol/l)	6.2 (1.1)	6.4 (1.2)	6.3 (1.6)	7.3 (1.6)	6.6 (1.4)	6.3 (1.1)	6.5 (1.1)	6.5 (1.1)	0.0001
HDL (mmol/l)	1.3 (0.3)	1.2 (0.3)	1.2 (0.3)	1.1 (0.3)	1.2 (0.3)	1.1 (0.3)	1.1 (0.2)	1.1 (0.3)	0.0001
current smokers	24%	26%	10%	25%	23%	21%	13%	22%	0.197
CVD prevalence	16%	17%	36%	5%	13%	20%	33%	26%	0.004
N	1137	921	11	20	31	363	15	142	

WOMEN	**BMI < 30 kg/m²**		**BMI ≥ 30 kg/m²**		**BMI < 30 kg/m²**		**BMI ≥ 30 kg/m²**		**p-value**
	WHR< 0.80	**WHR ≥ 0.80**	**WHR< 0.80**	**WHR ≥ 0.80**	**WHR< 0.80**	**WHR ≥ 0.80**	**WHR< 0.80**	**WHR ≥ 0.80**	**for diff.**
	Waist < 88 cm				**Waist ≥ 88 cm**				
Age (years)	66.5 (8.5)	69.0 (9.0)	68.7 (7.9)	67.6 (7.9)	66.2 (7.4)	71.4 (9.6)	68.8 (9.8)	71.1 (8.8)	0.0001
SBP (mmHg)	133 (23)	138 (23)	133 (20)	139 (20)	135 (27)	143 (23)	139 (17)	146 (21)	0.0001
DBP (mmHg)	71 (11)	72 (11)	72 (8)	72 (9)	73 (12)	74 (12)	75 (9)	76 (11)	0.0001
TC (mmol/l)	6.7 (1.2)	6.9 (1.2)	6.9 (1.3)	7.0 (1.0)	6.9 (0.6)	6.8 (1.3)	6.6 (1.1)	6.9 (1.3)	0.0128
HDL (mmol/l)	1.6 (0.4)	1.5 (0.4)	1.6 (0.4)	1.5 (0.4)	1.5 (0.3)	1.4 (0.4)	1.6 (0.4)	1.3 (0.3)	0.0001
current smokers	22%	21%	3%	10%	20%	16%	7%	15%	0.001
CVD prevalence	6%	8%	12%	3%	27%	7%	3%	12%	0.001
N	723	1173	34	32	11	1129	33	648	

Table 5. Risk ratios (95% confidence interval in parenthesis) for total mortality in different categories of waist circumference, body mass index (BMI) and waist-hip ratio (WHR) at waist action levels 1 and 2.

a. Waist action level 1

MEN	BMI < 25 kg/m²		BMI ≥ 25 kg/m²	
	WHR< 0.95	**WHR ≥ 0.95**	**WHR< 0.95**	**WHR ≥ 0.95**
Crude				
Waist < 94 cm	1.0	1.07 (0.74, 1.55)	0.50 (0.32, 0.78)	0.90 (0.50, 1.64)
Waist ≥ 94 cm	0.65 (0.24, 1.75)	1.80 (1.27, 2.55)	0.72 (0.46, 1.12)	0.97 (0.75,1.24)
Adjusted[1]				
Waist < 94 cm	1.0	0.80 (0.54, 1.16)	0.62 (0.39, 0.98)	0.95 (0.52, 1.73)
Waist ≥ 94 cm	0.50 (0.18, 1.35)	1.34 (0.94, 1.91)	0.83 (0.52, 1.30)	0.85 (0.66, 1.09)

WOMEN	BMI < 25 kg/m²		BMI ≥ 25 kg/m²	
	WHR< 0.80	**WHR ≥ 0.80**	**WHR< 0.80**	**WHR ≥ 0.80**
Crude				
Waist < 80 cm	1.0	1.59 (1.00, 2.53)	0.61 (0.28, 1.30)	0.85 (0.26, 2.76)
Waist ≥ 80 cm	0.76 (0.10, 5.52)	1.89 (1.30, 2.76)	1.17 (0.66, 2.10)	1.51 (1.08, 2.12)
Adjusted[1]				
Waist < 80 cm	1.0	1.35 (0.84, 2.17)	0.72 (0.34, 1.55)	0.73 (0.23, 2.37)
Waist ≥ 80 cm	0.53 (0.07, 3.86)	1.01 (0.68, 1.49)	0.88 (0.48, 1.62)	0.94 (0.67, 1.33)

b. Waist action level 2

MEN	BMI < 30 kg/m²		BMI ≥ 30 kg/m²	
	WHR< 0.95	**WHR ≥ 0.95**	**WHR< 0.95**	**WHR ≥ 0.95**
Crude				
Waist < 102 cm	1.0	1.32 (1.05, 1.65)	0.73 (0.10, 5.22)	1.10 (0.35, 3.46)
Waist ≥ 102 cm	0.54 (0.13, 2.19)	1.33 (0.97, 1.79)	2.08 (0.77, 5.62)	1.22 (0.79, 1.89)
Adjusted[1]				
Waist < 102 cm	1.0	1.05 (0.84, 1.33)	1.03 (0.14, 7.36)	1.33 (0.42, 4.18)
Waist ≥ 102 cm	0.52 (0.13, 2.10)	0.93 (0.68, 1.26)	1.80 (0.68, 4.87)	1.24 (0.79, 1.92)

WOMEN	BMI < 30 kg/m²		BMI ≥ 30 kg/m²	
	WHR< 0.80	**WHR ≥ 0.80**	**WHR< 0.80**	**WHR ≥ 0.80**
Crude				
Waist < 88 cm	1.0	1.49 (1.10, 2.02)	0.66 (0.16, 2.71)	npc
Waist ≥ 88 cm	2.71 (0.66, 11.10)	1.88 (1.39, 2.55)	0.35 (0.05, 2.53)	1.56 (1.11, 2.19)
Adjusted[1]				
Waist < 88 cm	1.0	1.07 (0.78, 1.46)	0.51 (0.13, 2.11)	npc
Waist ≥ 88 cm	2.66 (0.37, 19.28)	1.05 (0.77, 1.43)	0.29 (0.04, 2.12)	0.95 (0.67, 1.34)

[1] adjusted for age (in years) and smoking (current, former, never)
npc = not possible to calculate (no death cases in the category)

the category of low waist (<102 cm in men, <88 cm in women), low WHR (<0.90 in men, <0.80 in women) and low BMI (<30 kg/m^2). The table gives both the crude risk ratios and risk ratios adjusted for age and smoking. In men, those with high waist circumference, high WHR and low BMI (part of true positives) had a statistically significantly higher risk of death than the reference category at waist action level 1 in the crude analysis. After adjustment for age and smoking this difference was, however, not statistically significant. In the category of low waist, low WHR and high BMI (part of false negatives) the risk of death was lower than in the reference category, both before and after adjustment. In women, the risk of death was elevated in the category with low waist circumference, high WHR and low BMI (part of false negatives) and in the categories with high waist circumference, high WHR and low or high BMI (true positives), but after adjustment for age and smoking these differences were no longer statistically significant. At waist action level 2, the risk of death was increased in those with low waist, low BMI and high WHR (part of false negatives) in both men and women, and in women also in those with high waist circumference, high WHR and low or high BMI (true positives), but no statistically significant differences in the risk of death between the categories were observed after adjustment for age and smoking. Similar results were obtained when the three categories of false negatives as well as true positives were combined (not shown).

Discussion

This study shows that waist circumference cut-off points (waist action levels) established for young and middle-aged white adults may not be appropriate to identify elderly subjects at increased risk of cardiovascular disease or death because of their level of obesity or abdominal fat distribution. This concerns especially the upper cut-off point (waist action level 2) and is mainly due to increased central fat distribution with advancing age.

The specificity of the suggested waist action levels in relation to the cut-off points for BMI and WHR was high (>90%) indicating that there would be very few false positives i.e. subjects who would unnecessarily be advised weight management when they don't need it. The sensitivity was lower than specificity and it was lower at waist action level 2 (35% in men, 59% in women) than at waist action level 1 (71% in men, 86% in women). The sensitivity was also lower among men than among women and slightly lower in the younger age group than in the older age group. A low sensitivity indicates a large proportion of subjects who would be in need of weight management on the basis of their BMI or WHR but who would be missed if the suggested waist action levels were applied as screening tools for weight management in the study population. At waist action level 2, the low sensitivities result from a large proportion of subjects with low waist circumference and low BMI but a high WHR.

The low sensitivities at waist action level 2 in relation to the cut-off points based on BMI and WHR observed in this study are in agreement with other studies [18,19], where low sensitivities have been found in younger subjects in populations where obesity is relatively uncommon. In our study population of elderly subjects, the prevalence of obesity was low, especially in men, which may be one explanation for the low sensitivities observed. If the cut-off points for waist circumference were to be based on the used cut-off points for WHR and BMI, the optimal cut-off points for waist action level 2 could be considerably lower in the elderly. Lower cut-off points for waist circumference in older than in younger subjects were also suggested by Lemieux et al. [22] who proposed the cut-off point 100 cm for subjects under 40 years, and 90 cm for subjects over 40 years of age. Lemieux et al. based their cut-off points on the absolute amount of visceral fat and therefore, in constrast to Lean et al. [15], proposed identical cut-off points for men and women. We did not try to identify optimal cut-off points for waist circumference in the elderly on the basis of the cut-off points for BMI and WHR using, for example, ROC analysis, because the cut-off points especially for WHR are arbitrary and a more comprehensive evaluation is needed before recommendations can be given [23].

As said, the analysis on sensitivity and specificity shows that there would be a considerable misclassification of elderly subjects in categories based on waist circumference when compared to classification based on BMI and WHR, especially at waist action level 2. However, the misclassification is a problem only if those missed (false negatives) would be at increased risk compared to those classified as not at risk (true negatives). Also, even if the proportion of those misclassified is small, the waist cut-off points will be useful only if those classified as being at increased risk (true positives) are truly at increased risk compared to those classified as not at risk (true negatives). For these reasons, we compared the levels of cardiovascular risk factors at baseline and risk of total mortality during a 5.5 year follow-up in the different categories defined by low/high waist circumference, BMI and WHR.

The level of cardiovascular disease risk factors such as blood pressure and total cholesterol was in general increased in those with high waist circumference, high WHR and/or high BMI (true positives). The baseline prevalence of cardiovascular disease was also highest among those with high waist, WHR and BMI. Smoking, on the contrary, was most common in those with low waist and low BMI with or without high WHR (true negatives and part of false negatives). The effect of smoking on relative weight is different from the effect on fat distribution: smoking is associated inversely with BMI [24] but positively with WHR [25]. Even though the prevalence of smoking, and age, differed between the categories defined by waist circumference, WHR and BMI, adjustment for them did not change the results for the risk factors. We also adjusted for these factors in the analysis of risk of death.

In most studies, a U- or J-shaped association between BMI and mortality has been found whereas the association between WHR and mortality has been found to be monotonically positive. Larsson et al. [5] found the lowest risk of death in a 13 year long follow-up of 54 year-old men in those with the lowest WHR and the highest BMI. Folsom et al. [26], in turn, found the highest risk of total mortality in a 5-year follow-up of women aged 55 to 69 years in those with the highest WHR but lowest BMI. Baumgartner et al. [27] and Allison et al. [28] have highlighted the possible different roles of fat mass and lean (fat-free) mass on mortality. Decrease in BMI may reflect either a loss of fat mass or a loss of lean (fat-free) mass. Data from NHANES I and II studies have shown that BMI is more closely correlated to subcutaneous fat in younger than older men and women, and with muscle mass in older than younger adults [29]. Similarly, high WHR can indicate not only abdominal obesity but also loss of peripheral muscle. Lean body mass has been found to be the most important predictor of survival in critical illness [30].

In our study, the risk of death was increased in those with high waist and WHR and low BMI (action level 1) and in those with low or high waist, low BMI and high WHR (action level 2) in the crude analysis. In women it was also increased in those with high waist, WHR and BMI. The combination of low BMI and high WHR seems thus to be detrimental to health. This is in agreement with the findings of Larsson et al. [5] and Folsom et al. [26] Adjustment for age and smoking, however, removed these differences in mortality risks in our study. This indicates that the combination of high WHR and low BMI is at higher risk of death, at least partly, because it results from aging and smoking.

Except for the decreased risk of death among men with low waist, low WHR and high BMI at waist action level 1, we did not find any differences in risk of total mortality in men and women between true negatives and true positives after adjustment for age and smoking. This implies that, at least in an elderly population with a relatively short follow-up, waist action levels are not useful in identifying groups at increased risk of death when age and smoking are taken into account. Similar results were also obtained when the three categories of false negatives as well as true positives were combined, indicating that the lack of association was not just due to small numbers in some of the categories. In addition, similar results were obtained for the risk of cardiovascular disease, but the number of events was too small to find any statistically significant differences. We excluded from the analysis those who died during the first year of follow-up. These subjects may be loosing weight due to an existing illness and including subjects with existing illness may lead to an underestimation of the importance of overweight as risk factor in the elderly [31]. It is, however, possible that exclusion of those who died during the first year of follow-up is not sufficient to exlude all those with underlying illness. Some investigators have suggested that the risks of overweight and excess abdominal fat may be less pronounced in the elderly compared to younger adults [32,33]. It is also possible that the measures of overweight such as BMI, WHR and waist circumference have a different interpretation in terms of fat mass and fat-free mass in the elderly than in younger adults as discussed above.

The use of waist circumference cut-off points in identifying subjects with overweight and obesity and/or central fat distribution is based on the evidence that waist circumference reflects both the degree of overweight and central fat distribution. High correlations between waist circumference and both these measures have been observed in populations consisting of mainly middle-aged or younger adults [14-16]. Because of the changes in relative weight and body composition with advancing age, this might not be the same in the elderly. The high correlations between waist and BMI and waist and WHR observed in this study even in the older age group (70 years or older) support the view that the same relation between these measures hold in the elderly. Some investigators have argued that waist/height ratio show stronger associations with intra-abdominal fat [34] and cardiovascular risk factors [35] than waist circumference. In middle-aged and younger subjects it has been noted that height is not correlated with waist circumference and therefore there is no need to adjustment for height [36]. In our study, waist circumference was, however, positively correlated with height, especially in men, which suggests that it might necessary to adjust waist circumference for height among the elderly. The interpretation of the waist/height ratio is, however, complex because it may reflect variation in both waist and in stature.

In summary, we conclude that the suggested cut-off points for waist circumference are only to a limited degree useful in identifying subjects with overweight and obesity and/or central fat distribution in an elderly population. This concerns especially the upper cut-off point (waist action level 2) and is mainly due to the increased central distribution of fat with advancing age. If the waist action levels are based on cut-off points for BMI and WHR, the upper cut-off point for waist circumference should be considerably lower. Cardiovascular disease risk factors, except smoking, tend to increase with increasing waist circumference, WHR and/or BMI. In an elderly population with a relatively short follow-up, waist action levels seem not to be useful in identifying groups at increased risk of death.

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6. General discussion

In this thesis determinants of relative weight and body fat distribution were investigated paying special attention to the differences among populations in the associations between the determinant and the outcome. First, the main findings of the studies included in this thesis will be summarized. Second, some methodological issues relevant to the studies presented in this thesis will be discussed. The chapter will be closed by reflecting the impact of this study for future research and its implications for public health and clinical practice.

6.1 Main results

The thesis began with a review of the literature concerning anthropometric indicators of body fat distribution, especially of abdominal obesity, and cut-off points based on these indicators (chapter 2). It was found that numerous studies have been published suggesting different indicators using different and often unclear criteria of their selection. Many of the studies suffered from methodological limitations: they were based on a small number of subjects, often derived from cross-sectional data, based on indirect measurement of risk, or the indicators were complicated to interprete biologically or difficult to use in a public health context. Therefore there is no consensus in the research field about an optimal indicator of abdominal obesity and cut-off points based on it. A more comprehensive evaluation with a more systematic and solid scientific basis is needed before recommendations about an optimal indicator of abdominal obesity and cut-off points based on it can be given. The review also emphasized the need to distinguish the impact of visceral and subcutaneous fat and general adiposity in the development of different chronic diseases and mortality, and possible differences in this impact between sexes, age categories and ethnic groups.

Next, the methods used in this thesis were described (chapter 3). The study populations were introduced and the data quality assessment methods and results of this assessment of the measurements of weight, height, waist and hip circumference in the WHO MONICA Project were described. The latter was to emphasize that even in a multi-centre study with a common standardized protocol, the quality of the data cannot be taken for granted but should be evaluated before the data can be used in analyses for comparisons between centres or within centres over time.

Relative body weight

In chapter 4, some of the determinants of relative weight were investigated. Smoking is known to be associated with lower relative body weight [1-3]. It has, however, been suggested that this inverse relationship may be changing [4]. Considerable differences in the association between smoking and relative body weight were found among the 42 populations of the WHO MONICA Project (chapter 4.1). The inverse association was more pronounced in women than in men. In men, there were populations where no association between smoking and relative body weight was found. Moreover, in these populations there were fewer smokers and more ex-smokers than in populations with an inverse association between smoking and relative weight.

Educational level is often regarded as a confounding factor in studies of the smoking-BMI relationship, because subjects with low socio-economic status tend to smoke more and have a higher BMI than subjects with high socio-economic status [3,5]. In a study of the general population in the Netherlands, however, the association between smoking and relative body weight differed by educational level (chapter 4.2). In this population, the inverse association was more pronounced at the lower educational level. This finding has both statistical and public health implications. From statistical point of view, the adjustment for educational level in studies of the smoking-BMI relationship may be incorrect and in fact hide the differences by educational level in this association. From public health perspective, it may be important to know that there are subgroups in the population which would be in special need of weight management when advised to stop smoking and would benefit most from it. Similar findings as presented in our study have later been reported from a population-based study conducted in Finland [6].

In the analysis of educational level and relative weight (chapter 4.3), a statistically significant inverse association was found in almost all female populations and in a large number of male populations of the WHO MONICA Project. Subjects with lower education were in general heavier than subjects with higher education. Only 1-2 male populations showed a statistically significant positive association. In men, the association between educational level and BMI seemed to be related to the prevalence of obesity in the population: the higher the prevalence of obesity the more likely inverse the association. This is in concordance with previous research where an inverse association between socio-economic status and relative weight has been found in affluent populations, whereas in less affluent countries, with usually low prevalences of overweight, the association is positive [7]. In women the difference in BMI between educational levels was associated with the wideness of the educational gap between the educational levels: the wider the gap in education the wider the gap also in BMI, although this association was weak. In this study we also looked at the changes in the association between educational level and BMI during the 10-year study period of the WHO MONICA Project. In two thirds of the populations the differences in BMI between the educational levels increased. This has important public health implications because it suggests that inequalities related to overweight and its health consequences may widen in many countries.

Body fat distribution

In the analysis regarding body fat distribution, the distributions of related anthropometric measurements, waist and hip circumferences and waist-hip ratio (WHR), were described in the WHO MONICA populations (chapter 5.1), because data representing the general population and comparable between populations with varying degree of overweight are scarse in the literature. Considerable differences in body fat distribution among the 19 study populations were found. Also, the effect of age and degree of overweight on these measurements was analysed. Although waist circumference and WHR increased with age, a considerable proportion of this effect – but not all – was explained by increasing BMI with age. Waist circumference seemed to reflect predominantly the degree of overweight: about three quarters of the variance in waist circumference was explained by BMI. Hip circumference reflected the degree of overweight, but in men also body frame. Most of the variance in WHR remained, however, unexplained by the limited variables available. This implies that waist circumference and WHR, both used as indicators of abdominal obesity, measure different aspects of the human body.

In chapter 5.2 the applicability of the cut-off points for waist circumference suggested in the literature [8] to replace cut-off points for BMI and WHR in identifying subjects with overweight or obesity was investigated in the different populations of the WHO MONICA Project. It was found that the recommended cut-off points (waist action levels) were not always adequate in detecting individuals who would be in need of weight management on the basis of their BMI or WHR. Moreover, the sensitivity of the suggested cut-off points varied between populations and was higher in populations with relatively high prevalence of overweight (measured by BMI). Universal cut-off points – which are possible for BMI – may therefore not be possible for waist circumference.

In chapter 5.3 the applicability of the waist circumference cut-off points (waist action levels) to identify subjects with overweight or obesity and/or central fat distribution was investigated in the elderly population of men and women (55 years of age or older) participating in the Rotterdam Study. The applicability was evaluated both in relation to the cut-off points for BMI and WHR the waist action levels were originally based on and in relation to cardiovascular risk factors at baseline and risk of death during a 5.5-year follow-up. It was found that the suggested cut-off points for waist circumference were only to a limited degree useful in identifying subjects with overweight or obesity and/or central fat distribution in this elderly population. This concerned especially the upper cut-off point and was mainly due to the increased central distribution of fat with advancing age. Cardiovascular disease risk factors, except smoking, tended to increase with increasing waist circumference, BMI and WHR. The risk of mortality was, however, not increased in those with high waist circumference, BMI and/or WHR after adjustment for age and smoking. In the elderly with a relatively short follow-up period, the waist action levels seem not to be useful in identifying groups at increased risk of death.

6.2 Methodological considerations

Reliability and validity of measurements

Reliability, or precision, refers to the extent to which a measurement is free of random error [9]. Reliability is usually studied with repeating the measurement on different subjects, by different investigators or at different times. Validity refers to the extent to which a measurement is free of systematic error [9]. The best way to study the validity of a measurement is to compare it against a gold standard. Often such a gold standard is not available, and the predictive value of the measure (predictive validity) or the association with other relevant measurements (construct validity) can be assessed.

The measurements of relative weight (weight and height) and body fat distribution (waist and hip circumferences) used in this study are known to be generally very reliable [10,11]. The validity of these measurements can, however, be threatened if standard procedures for these measurements have not been followed. In chapter 3.2 the methods applied in the WHO MONICA Project to assess the adherence of the Collaborating Centres to the common study protocol and the results of this assessment were described. Any population with possible problems in the quality of data has been omitted from the studies in this thesis. Similar quality assessments have been carried out for the MONICA data on smoking behaviour and educational achievement [12,13]. Although the centrally assessed data quality cannot quarantee total freedom from between-observer variation, especially for the measurements of body fat distribution, it can facilitate to detect populations where quality problems, which could threaten the validity of the measurements, may have occurred.

Internal validity of results

Internal validity is the extent to which the results are valid for the the target population i.e. free of bias [9]. It is mainly influenced by selection bias, information bias and bias due to confounding. Selection bias and information bias can either lead to an under- or overestimation of the true association and one cannot adjust for their effect in the analysis.

Selection bias results from procedures used to select subjects that lead to an effect estimate among subjects included in the study which differs from the estimate obtainable for the whole population. This happens when the respondents differ systematically from the non-respondents and nonresponse is related to the exposure as well as to the outcome. When the response rate is low, the probability of selection bias increases. In the WHO MONICA Project, the response rates and possible selection bias, on the basis of information on non-respondents, have been assessed in a separate study [14]. On the basis of the results of this study it was decided that any population with response rate lower than 50% is excluded from the collaborative analyses of the MONICA Project. In the Project on Cardiovascular Disease Risk Factors in the Netherlands, a separate non-response study has been carried out and the characteristics of the non-respondents and respondents were compared [15]. In chapter 4.2 the possible effect of non-response on the results on the effect of smoking on relative weight at different levels of education has been discussed. In the Rotterdam Study the participation rate was rather high (>70%) giving confidence to the representativeness of the study population. The response rate, however, declined with advancing age [16]. It is therefore possible that among the very old, the study population is a selection of relatively healthy individuals who were able to answer the survey questions and who could attend the survey examination or, if living in nursing homes or in homes for the elderly, could be examined there.

Information bias occurs when there are errors in the classification of subjects in the measurements of the exposure which differ according to the outcome, or in the classification of subjects concerning outcome which differ by exposure [9]. Because relative weight and body fat distribution were measured, and not self-reported, and are continuous variables, the problem of differential misclassification is minimal. It is also unlikely that subjects would have reported their smoking habits or educational level differently depending on their relative weight.

Not adjusting adequately for confounding is a major threat to the validity of the results of epidemiologic studies. In our study the effect of confounding was most clearly illustrated in the association between age and waist circumference and WHR (chapter 5.1). The crude increase in waist circumference and WHR with age was first presented and then adjusted for height and BMI. The effect of age on waist circumference and WHR attenuated considerably when adjusted for height and especially BMI, indicating that a major proportion of the increase in these measurements with age could be explained by increasing BMI with age.

Regarding relative weight, the determinants studied, educational level and smoking, are both related to the outcome (relative weight) and to each other making the interrelationships very complicated. In most populations, higher educational level was associated with lower relative weight than lower educational level. Because at lower educational level smoking was more common than at higher educational level and smoking is related to lower relative weight, adjustment for smoking increased the differences in relative weight between the educational levels in most populations, instead of explaining them (chapter 4.3). This means that if subjects with lower education were not smoking more than subjects with higher education, the difference in relative weight between the educational levels would even be bigger. Adjustment for education did not, however, affect the estimates of the association between smoking and relative weight (chapter 4.1). Instead it was found that the association between smoking and relative weight differed by educational level so that the inverse effect of smoking on relative weight was more pronounced at lower educational level (chapter 4.2). This means that instead of being a confounder, educational level was found to be an effect modifier in the smoking-BMI relationship. Investigation of a statistical interaction may point out the existence of high risk groups for whom modification of risk factors may be especially beneficial. This was the case in our study: subjects with lower education would benefit most from weight management when recommended smoking cessation.

External validity of results

External validity refers to the generalizability of the results of an epidemiologic study [9]. .Although in this thesis most of the studies were conducted in the large number of populations of the WHO MONICA Project, one should be cautious against generalizing the results outside the range of these populations. First of all, the MONICA populations are not a representative sample of the world's populations. Most of the populations are concentrated in Europe with occasional populations in North America, Australia/New Zealand and Asia. Secondly, the MONICA populations are not necessarily representative of their countries, but a larger or smaller geographical area where the population is defined. Thirdly, as was observed in this thesis, many of the associations studied differed remarkably between populations and may even differ between areas within countries.

Nevertheless, the unique strength of the studies based on the data collected in the WHO MONICA Project stems from the fact that the same standard protocol has been used for such a wide variety of populations. Strengthened by a central assessment of the quality and analysis of data, this enables international comparisons which earlier would mostly have been impossible.

The age range studied has been 35-64 or 25-64 years in most of the studies included in this thesis. In chapter 5.3 we found that the applicability of the waist circumference cut-off points in identifying subjects with overweight or obesity and/or central fat distribution in the elderly (≥ 55 years) was different from that observed in the predominantly middle aged populations. This emphasizes the need for caution against generalizing the results of these studies outside the age range considered.

Cross-sectional studies

Most of the studies included in this thesis are based on a cross-sectional study design. This implies that the determinants and the outcomes are measured at the same point of time. Therefore it is not possible to know the temporal order of the events or to assess the effect of a change in the determinant on the outcome (relative weight, body fat distribution). In epidemiology this means that we are studying associations, not effects, and cannot always even be sure which one is the determinant and which outcome. Often the logical order can be based on other studies which have used a longitudinal design. But, for example, the direction of the association between socio-economic status and relative weight is not straightforward [17]. Although it is often assumed that a person's socio-economic status effects his or her dietary habits and patterns of physical exercise which then affect relative weight, it is also possible that a person's relative weight can effect his or her socio-economic status through e.g employment.

In the study on the association between educational level and relative weight (chapter 4.3), we used data from two independent cross-sectional surveys conducted approximately 10 years apart. This enables one to assess the changes in the association over time. The samples at the two points of time consist of different individuals which represent partly the same birth cohorts which age over the time period and partly different birth cohorts. The level of analysis is therefore not an individual but a population.

When assessing the applicability of the suggested waist circumference cut-off points in the elderly (chapter 5.3), we studied, in addition to the sensitivity and specificity against the cut-off points for BMI and WHR and the risk factor levels at baseline examination, the risk of all-cause death during a 5.5-year follow-up of the participants. This was the only part of this thesis where longitudinal analyses on individuals were carried out. Longitudinal analyses are generally considered more suitable than cross-sectional analyses to study changes in health and causal relationships, because the temporal order of events is then known and individual patterns of change can be observed. However, performing and interpreting longitudinal analyses is not as simple as it may seem. In our study, the problem of interpretation stems from the fact that we have the values for BMI, WHR and waist circumference available at the baseline examination only. We do not know, for example, whether and what proportion of the lean subjects may be loosing weight due to a pre-existing illness. We excluded those who died during the first year of follow-up, but it is possible that the exclusion was not sufficient to eliminate this effect completely. Also, the follow-up was relatively short and therefore the effect of loosing weight or muscle mass may have overweighed the effect of overweight on mortality. It would be important in future studies to be able to study separately the effects of muscle mass and fat mass on mortality.

6.3 Implications for future research

Existing data

There are many questions which could be further elucidated with the data used in this thesis. For example, it would be interesting to know how the association between smoking and relative body weight may have changed during the 10-year study period of the WHO MONICA Project and, as smoking has become less common [18], whether the inverse association has been attenuated or even turned into a positive association among these populations. This is important because the results effect people's attitudes towards smoking initiation and cessation in relation to weight and weight gain. It would also be relevant to know whether the association between smoking and relative body weight differs between educational levels in the MONICA populations as was observed in the general population in the Netherlands, i.e. whether this is a general or population-specific phenomenon. In addition, as stated in chapter 4.3, it would be interesting to explore more specifically where the increasing differences in BMI between educational levels in the populations of the WHO MONICA Project stem from, i.e. whether the increasing differences are produced by specific age groups or are a result of a secular trend going on in the society.

Regarding the determinants of body fat distribution, we have not investigated the effect of smoking. Although it is known that smokers generally have a higher WHR than non-smokers [19,20], it would be important to know whether there are differences in this association for example among the MONICA populations as was observed regarding the association between smoking and relative weight.

In chapter 5.3 we examined the applicability of waist circumference cut-off points in the elderly. It would also be interesting to know how much of the variation in waist and hip circumferences and WHR is explained by height, BMI and age in this study population, i.e. whether aging affects the estimates obtained from predominantly middle-aged populations.

Other data

This thesis has concentrated only at some of the determinants of relative weight and body fat distribution. The determinants of relative weight explored were smoking and educational level and the determinants of body fat distribution age and degree of overweight. Many of the factors related to relative weight and body fat distribution mentioned in chapter 1 such as physical activity, alcohol intake and dietary habits were not considered. This omittance is partly due to that these factors were not included in the core study of the WHO MONICA Project and data on them were therefore not available for the MONICA populations. But studies of these factors also require a different methodology. For example, the relation between relative weight and dietary habits cannot be studied accurately because of increased selective underreporting of energy intake with increasing degree of overweight [21,22]. Similar methodolocigal difficulties limit the interpretation of studies on physical activity and alcohol intake. This does not, however, mean that physical activity, alcohol intake or dietary patterns would not be important factors to study when differences in relative body weight and fat distribution between populations are investigated, but for them different study designs as those used in this thesis are required.

In chapter 2 the relevant literature on abdominal indicators was reviewed. The conclusion was that a more comprehensive evaluation with a more systematic and solid scientific basis is needed before a consensus about an optimal indicator for abdominal obesity can be reached and public health recommendations can be given. In addition, the roles of fat distribution and relative weight in the process of developing a disease and possible differences between age categories, gender and ethnic groups in these processes need further clarification. This requires, however, large scale follow-up studies. Furthermore, the knowledge of a factor being a determinant of a disease is not enough to make public health recommendations, there has to be scientific evidence that modification of the factor leads to improvement in health. This can be only assessed in intervention studies.

Regarding the elderly, the effect of overweight and body fat distribution on total mortality is unclear. Some studies have suggested that the ideal weight could be considerably higher in the elderly than in younger subjects [23,24], whereas others do not share this view [25,26]. It seems that in the elderly underweight and weight loss, maybe due to loss of muscle mass, seem to be more serious problems than moderate overweight. This needs, however, to be clarified in future research.

6.4 Public health implications

Overweight is an important public health problem because the increased morbidity and mortality associated with it. Obesity, in particular, also increases the probability of disability and have an adverse effect on the quality of life of the individual. The magnitude of the problem is emphasized by the high prevalence of obesity in most industrialized countries and increasing trends in both industrialized and developing countries. The costs are high both to the individual and the society. Conservative estimates of the economic costs of obesity are 3-8% of total health care expenditure in countries such as Finland, the Netherlands, France, the USA, Australia and Sweden [27].

In this thesis some of the determinants of relative weight and body fat distribution were discussed. The determinants of relative weight considered were smoking and educational level. The association between smoking and relative body weight is important from the public health point of view, because many people sustain to smoke because they are afraid of weight gain after stopping smoking [28]. Our results show that smoking is not necessarily associated with relative weight and that the association may even be different in different subgroups within a population. It would be important to emphasize that weight gain does not necessarily follow smoking cessation and try to reach the subgroups who would need and benefit most from weight management after smoking cessation.

An increasing difference in relative body weight between educational levels in a majority of the populations of the WHO MONICA Project was observed over the 10-year study period. The increasing socio-economic differences in relative body weight convey an important challenge to public health policies. In many countries, socio-economic inequalities in morbidity and mortality have been reported [29-32]. If the increasing differences in relative weight are not tacled, it is likely that in many countries the inequalities in health consequencies of overweight such as hypertension, cardiovascular diseases and non-insulin-dependent diabetes will increase. This is in disagreement with the WHO health policy goal to provide health for all [33].

From public health perspective it would be important to find optimal indicators for body fat distribution and reference cut-off points where an intervention would be desirable. Because there is no consencus in this field and, in the literature, different suggestions are often based on unclear criteria as indicated in the review included in this thesis, it would be advisable to abstain from giving public health recommendations in this respect before a more scientifically justified basis has been reached.

6.4 Implications for clinical practice

The implications of this study for the clinical practice can be summarized in the following three main points:

1) *Smoking and relative body weight.* Clinical studies have shown that smoking leads to weight loss and stopping smoking often leads to weight gain. The relation between smoking and relative body weight, however, differs greatly across populations and may point towards the importance of associated life-styles and socio-economic factors.

2) *Socio-economic status and relative body weight.* Obesity may increasingly become a problem of low socio-economic status. This has implications for strategies for weight management and prevention. For example, many less wealthy obese people may not be able to participate in physical activity programmes, buy the low caloric foods, or pay for anti-obesity medication or treatment. This emphasizes the importance of prevention as the strategy to reduce obesity in individuals as well as in populations.

3) *Body fat distribution.* Waist circumference may be a helpful complementary or alternative measure to BMI of the health risks associated with obesity. The classifications according to waist circumference, however, needs careful re-examination. The current rationale for cut-off points works with wide variety of sensitivity in different populations. Current classifications seem to work best in relatively overweight Caucasian middle-aged populations, but in other populations and age groups their validity is uncertain. Therefore, current classifications should be used with great caution in clinical practise.

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Summary

Overweight is a risk factor for several chronic diseases, such as coronary heart disease, non-insulin-dependent diabetes (NIDDM) and stroke, as well as for overall mortality. It is a common condition in most industrialized countries and growing problem also in many developing countries. For example, more than half of the population aged 35-64 in Europe seems to be overweight or obese. While public health efforts to reduce the level of such risk factors as smoking, blood pressure and serum cholesterol have been successful in many countries, overweight remains an increasing public health problem. The prevalence of overweight has increased during the past decade in most countries which have reliable data on trend estimates.

In addition to the degree of overweight, body fat distribution has been found to be related to health. Adbominal obesity has been found to be more closely linked to the development of cardiovascular disease, NIDDM, stroke and mortality than the degree of overweight. Knowledge on fat distribution and prevalence of abdominal obesity in general populations in the literature is scarse. Furthermore, the results are diffcult to compare between populations because different studies have used different methods. Even less is known about trends over time in body fat distribution measures within populations.

Overweight in individuals in any population is the result of a long-term positive energy balance, but very little is known about the factors that may explain the large differences in the prevalences of overweight between populations. The objective of this thesis was to elucidate some of the determinants of relative weight and body fat distribution. The perspective was international, comparing the determinants and their associations with relative weight and body fat distribution in populations with widely different prevalences of overweight.

Most of the studies included in this thesis are based on the data from the WHO MONICA Project. The MONICA Project was designed to monitor the incidence and mortality from cardiovascular disease, and to assess the extent to which these trends are related to known risk factors. The MONICA Project comprise 54 study populations in 26 countries. The populations are mainly concentrated in Europe but include some areas in the USA, Canada, China, Australia and New Zealand. Risk factors in the WHO MONICA Project are monitored through independent cross-sectional population surveys over a 10-year period ranging from the early 1980s to the 1990s. The surveys included random samples of at least

200 people in each gender and ten-year age group, for the age range 35-64 years, and optionally 25-34 years.

One of the studies included in this thesis is based on data from the Monitoring Project on Cardiovascular Disease Risk Factors in the Netherlands. The Project was carried out in 1987-91 in three towns (Amsterdam, Maastricht and Doetinchem) in the Netherlands. The age range for this study was 20-59 years. Each year new random samples were selected from the municipal registries of these towns, and during the four years altogether about 36,000 men and women participated in the project.

One of the studies included in this thesis is based on data from the Rotterdam Study. The Rotterdam Study is a prospective single centre population-based study, designed to investigate determinants of selected chronic diseases and disabilities in the elderly. The cohort was defined as all inhabitants of Ommoord, a suburban district in Rotterdam, who were 55 years of age or older at 1 January 1990. All eligible participants were invited to participate, including those living in nursing homes. The baseline examinations started in May 1990 and continued until June 1993. Of the 10275 eligible subjects, 7983 (78%) agreed to participate. During a home visit, trained interviewers administered a questionnaire, covering socioeconomic background, smoking habits, alcohol consumption, dietary habits, medical history and medication use. This was followed by two extensive clinical examinations at the research centre. Those living in nursing homes or homes for the elderly, about 11% of the study population, were examined at their institutions.

First, some of the determinants of relative weight were investigated. Smoking is known to be associated with lower relative body weight. We found, however, remarkable differences in this association among the 42 populations of the WHO MONICA Project (chapter 4.1). The inverse association was more pronounced in women than in men. In men, there were populations where no association between smoking and relative body weight was found. Moreover, in these populations there were fewer smokers and more ex-smokers than in populations with an inverse association between smoking and relative weight.

Educational level is often regarded as a confounding factor in studies of the smoking-BMI relationship, because subjects with low socio-economic status tend to smoke more and have a higher BMI than subjects with high socio-economic status. In a study of the general population in the Netherlands we found, however, that the association between smoking and relative body weight differed by educational level (chapter 4.2). In this population, the inverse association was more pronounced at the low educational level. This finding has both statistical and public health implications. From statistical point of view, the adjustment for educational level in studies of the smoking-BMI relationship may be incorrect and in fact hide the differences by educational level in this association. From public health perspective, it may be important to know that there are subgroups in the population which would be in special need of weight management when advised to stop smoking and would benefit most from it.

In the analysis of educational level and relative weight (chapter 4.3), a statistically significant inverse association was found in almost all female populations and in a large number of male populations of the WHO MONICA Project. Subjects with lower education were in general heavier than subjects with higher education. Only 1-2 male populations showed a statistically significant positive association. In men, the association between educational level and BMI seemed to be dependent on the prevalence of obesity in the population: the higher the prevalence of obesity the more likely inverse the association. In women, the difference in BMI between educational levels was associated with the wideness of the educational gap between the educational levels: the wider the gap in education the wider the gap also in BMI, although this association was relatively weak. In this study, we also looked at the changes in the association between educational level and BMI during the 10-year study period of the WHO MONICA Project. In two thirds of the populations the differences in BMI between the educational levels increased. This has important public health implications because it suggests that inequalities related to obesity and its health consequences may widen in many countries.

Regarding body fat distribution we first described the distributions of rélated anthropometric measurements, waist and hip circumferences and waist-hip ratio (WHR), in the WHO MONICA populations (chapter 5.1), because data representing the general population and comparable between populations with varying degree of overweight is not available in the literature. Remarkable differences in body fat distribution among the 19 study populations were found. We also looked at the effect of age and degree of overweight in these measurements. Although waist circumference and WHR increased with age, a considerable proportion of this effect – but not all – was explained by increasing BMI with age. Waist circumference seemed to reflect predominantly the degree of overweight. Hip circumference reflected likewise the degree of overweight, but in men also body frame. Most of the variance in WHR remained, however, unexplained. This implies that waist circumference and WHR, both used as indicators of abdominal obesity, measure, in fact, different aspects of human body.

In chapter 5.2 the applicability of the cut-off points for waist circumference suggested in the literature to replace cut-off points for BMI and WHR in identifying subjects with overweight or obesity was investigated in the different populations of the WHO MONICA Project. We found that the recommended cut-off points are not always successful in detecting individuals who would be in need of weight management on the basis of their BMI or WHR. Moreover, the sensitivity of the suggested cut-off points varied between populations and was higher in populations with relatively high prevalence of overweight (measured by BMI). Universal cut-off points – as possible for BMI – may therefore not be possible for waist circumference.

In chapter 5.3 the applicability of the waist circumference cut-off points to identify subjects with overweight or obesity and/or central fat distribution was investigated in the elderly population of men and women (55 years of age or older) participating in the Rotterdam Study. The applicability was evaluated both in relation to the cut-off points for BMI and WHR the waist circumference cut-off points were originally based on and in relation to cardiovascular risk factors at baseline and risk of death during a 5.5-year follow-up. We found that the suggested cut-off points for waist circumference were only to a limited degree useful in identifying subjects with overweight or obesity and/or central fat distribution in this elderly population. This concerned especially the upper cut-off point and was mainly due to the increased central distribution of fat with advancing age. Cardiovascular disease risk factors, except smoking, tended to increase with increasing waist circumference, BMI and/or WHR. The risk of mortality was, however, not increased in those with high waist circumference, BMI and/or WHR after adjustment for age and smoking. In the elderly with a relatively short follow-up period, waist action levels seem thus not to be useful in identifying groups at increased risk of death when age and smoking are taken into account.

In chapter 6, the main results of this thesis were summarized and some methodological aspects relevant for the studies presented in this thesis were discussed. Some ideas for future research, either using data from the studies included in this thesis or from other sources, were given and implications of the results for public health and clinical practice were highlighted.

Samenvatting

Overgewicht is een risicofactor voor verschillende chronische aandoeningen als coronaire hartziekten, type 2 diabetes mellitus and cerebrovasculaire accidenten (CVA's) en ook voor vroegtijdig overlijden. Overgewicht komt veel voor in veel geïndustrialiseerde landen maar ook een toenemend probleem in veel (voormalige) ontwikkelingslanden. Meer dan de helft van de Europese bevolking in de leeftijd van 35-64 jaar heeft ten minste overgewicht. Hoewel preventie programma's in veel landen met succes de niveaus van risicofactoren als roken, hoge bloeddruk en verhoogde cholesterol concentraties hebben beïnvloed lijken ze weinig effect gehad te hebben op de prevalentie van overgewicht. The prevalentie van overgewicht is toegenomen in de meeste landen die daarover betrouwbare informatie verzameld hebben.

Niet allen het lichaamsgewicht maar ook de lichaamsvetverdeling is gerelateerd aan gezondheid. Een abdominale vetverdeling is in veel onderzoeken een betere voorspeller van cardiovasculaire ziekten, type 2 diabetes mellitus en CVA's dan de mate van overgewicht. Informatie over het voorkomen van een abdominale vetverdeling in de algemene bevolking is schaars. De beschikbare informatie in de literatuur is daarnaast moeilijk te interpreteren vanwege methodologische verschillen.

Overgewicht is altijd het resultaat van een periode van positieve energie balans maar er is weinig bekend over de factoren die de grote variatie in het voorkomen van overgewicht tussen populaties kunnen verklaren. Het doel van dit proefschrift was om meer inzicht te krijgen in de determinanten van variatie in lichaamsgewicht en vetverdeling. Het internationale karakter van enkele onderzoeken maakt het mogelijk deze factoren te bestuderen in populaties met zeer verschillende prevalenties van overgewicht.

Het merendeel van deze onderzoeken is gebaseerd op de resultaten van het WHO MONICA Project. Het WHO MONICA Project is opgezet om de incidentie en sterfte aan cardiovasculaire ziekten te monitoren en om daarnaast trends daarvan in de tijd te relateren aan trend in risicofactoren. Het WHO MONICA Project omvatte 54 onderzoekspopulaties in 26 landen. De bestudeerde populaties kwamen vooral uit Europa maar er waren ook centra in the VS, Canada, China, Australië en Nieuw Zeeland. De trends van risicofactoren werden gevolgd gedurende tien jaren vanaf het begin van de jaren tachtig tot de jaren negentig. De populaties bestonden uit ten minste 200 personen voor iedere tien-jaar's leeftijdsgroep per geslacht. De leeftijd was 35-64 jaar in meeste landen maar in sommige landen werden ook 25-34 jarigen onderzocht.

Een ander onderzoek dat werd geanalyseerd betrof het Peilstations Project Hart en Vaatziekten dat in de periode 1987-1991 werd uitgevoerd in Amsterdam, Doetinchem en Maastricht. Ieder jaar werd een nieuwe steekproef van 20-59 jarigen uitgenodigd voor een lichamelijk onderzoek op Gemeentelijke Gezondheids Diensten en in totaal werden ruim 36,000 personen onderzocht.

Gegevens over oudere personen werden verkregen door analyse van de resultaten van de ERGO studie in Rotterdam. De ERGO studie is een prospectief onderzoek onder ouderen in Ommoord, een stadsdeel in Rotterdam en betrof personen van 55 jaar of ouder. Het onderzoek werd uitgevoerd tussen 1990 en 1993 en in totaal werden 7983 personen onderzocht (78% van de uitgenodigde steekproef). Gedurende een huisbezoek werden vragenlijsten afgenomen waarin vragen waren opgenomen over leefstijl en gezondheidsaspecten als medicijngebruik. Daarna werd een lichamelijk onderzoek uitgevoerd in een onderzoekscentrum. Bij personen die woonden in een bejaardentehuis of zorg instelling werd het onderzoek aldaar uitgevoerd.

In het eerste deel van dit proefschrift werden enkele determinanten van lichaamsgewicht onderzocht. Roken verlaagt meestal het gewicht en stoppen met roken leidt over het algemeen tot gewichtstoename. De relatie tussen rookgewoonten en lichaamsgewicht verschilde echter sterk tussen de 42 verschillende onderzoekspopulaties in het WHO MONICA Project (hoofdstuk 4.1.). De inverse relatie tussen roken en gewicht was sterker bij vrouwen dan bij mannen. Bij mannen werd in een aantal populaties helemaal geen relatie tussen roken en gewicht gevonden. Het betrof dan meestal populaties met een relatief laag percentage rokers en een hoog percentage ex rokers.

Een verklaring zou kunnen zijn dat in landen waar weinig (meer) gerookt wordt de rokers gekenmerkt worden door een 'clustering' van andere ongunstige leefgewoonten (bv. inactiviteit, hoge vet-inname) die het lichaamsgewicht laten toenemen. Binnen Nederland werden bij verschillende niveaus van opleiding verschillende associaties tussen roken en lichaamsgewicht gevonden (hoofdstuk 4.2.). Ook hier zou een 'clustering' van risico gedrag bij rokers met een relatief lage opleiding de verklaring kunnen zijn. De associaties tussen roken en lichaamsgewicht bleken echter sterker bij een laag opleidingsniveau en bovendien niet te verklaren door verschil in leefstijl factoren. Deze cijfers kunnen er op wijzen dat bij personen met een lage opleiding stoppen met roken tot een relatief grote gewichtstoename leidt.

De relatie tussen opleidingsniveau en lichaamsgewicht werd nader onderzocht in hoofdstuk 4.3. In vrijwel alle populaties in het WHO MONICA Project werd gevonden dat overgewicht vaker voorkwam bij personen met een relatief lage opleiding maar deze bevinding was meer consistent bij vrouwen dan bij mannen. Bij mannen bleek de sterkte van de associatie tussen opleidingsniveau afhankelijk van de prevalentie van overgewicht: bij vaker voorkomen van overgewicht hoe sterker de inverse relatie. Bij vrouwen hing het verband tussen opleidingsniveau en gewicht af van de grootte van spreiding in opleidingsniveau in de populatie: hoe groter de contrasten in opleiding hoe groter het verschil in lichaamsgewicht of body mass index (BMI). De verschillen in overgewicht tussen opleidingsniveaus bleken tevens toe te nemen in de tijd. In twee-derde van de populaties werd een toename gevonden in de verschillen tussen met een hoge versus een lage opleiding. Deze bevinding kan belangrijke volksgezondheids-implicaties hebben omdat het suggereert dat de sociale ongelijkheid in het voorkomen van overgewicht (en wsch. ook de gevolgen zoals type 2 diabetes, hypertensie etc) aan het toenemen is.

Wat betreft de lichaamsvetverdeling is eerst met behulp van de gegevens uit het WHO MONICA Project een beschrijvende studie uitgevoerd naar variatie in middel-omtrek, heup-omtrek en de verhouding daartussen (hoofdstuk 5.1.) Er werden grote verschillen in lichaamsmaten gevonden tussen de 19 populaties. Na correctie voor verschillen in BMI, lengte, en leeftijd verklaarde overige verschillen tussen de populaties slechts 2-3% in de variatie in middel-omtrek. De middel-omtrek nam toe met de leeftijd ook na correctie voor lengte en BMI. De bijdrage van determinanten van de middel-heup omtrek verhouding waren sterk verschillend van de bijdrage van determinanten aan de middel-omtrek. Deze twee maten weerspiegelen waarschijnlijk verschillende aspecten van vetverdeling.

In de literatuur worden afkappunten gesuggereerd voor de middel-omtrek om de classificatie van de BMI and middel-heup omtrek verhouding te vervangen. In hoofdstuk 5.2. werd onderzocht in hoeverre deze indeling naar middel-omtrek inderdaad dezelfde personen identificeert als de combinatie van BMI en middel-heup ratio. De sensitiviteit varieerde echter sterk tussen populaties en was zeer laag in populaties waar overgewicht (hoge BMI) weinig voorkwam. De simpele indeling naar middel-omvang is dus mogelijk niet van toepassing op alle populaties.

In hoofdstuk 5.3. werd de toepasbaarheid van de indeling naar middel-omvang tevens onderzocht bij ouderen in Rotterdam (ERGO onderzoek). Ook daarbij bleek dat de naar middel-omtrek niet adequaat de indeling naar BMI and middel-heup ratio kan vervangen. Hoewel ook bij ouderen de niveaus van cardiovasculaire risicofactoren (behalve roken) duidelijk toenamen met toenemende middel-omvang (en toenemende BMI en middel-heup ratio) werd niet gevonden dat personen met een grote middel-omvang een groter risico hadden op overlijden binnen een 5.5 jaar follow-up periode.

In hoofdstuk 6 worden de voornaamste resultaten samengevat en methodologische aspecten bediscussieerd. Implicaties van de bevindingen voor gezondheidsbeleid en de klinische praktijk werden tevens kort aangegeven.

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I want to thank my friends in Finland, Kirsti, Mari and Salla and their families for being always there when I needed temporary accommodation. And for being my friends, of course. I also want to thank my sisters Birgi and Sini and their families for their support. Likewise, I want to remember my nearly 92 year old grandmother, a personification of strong will.

Äiti ja isä, kun olin pieni tyttö, katselin usein tuvan ikkunasta Pyhäjärven selkää ja ihmettelin mitä sen takana mahtaa olla. Nyt olen nähnyt siitä pienen osan, mutta paljon on vielä näkemättä.

Christer, du har gett mig det viktigaste: mitt hem är hos dig.

To make a PhD in a 'foreign' country might seem glamorous to many, but it is not always sunshine. One has also to prepared to deal with prejudice, ignorance and even hostility. When I first started the work described in this thesis at the RIVM, I soon learned that Finland did not rank high on the Dutch agenda. More than one person asked me the following three questions: "Why did you come here?", "Could you not study in your own country?" and "When are you going back?". When I then returned to Finland after getting the MSc degree, some people there were wondering whether my Dutch degree was of any value.

It has not been easy with the financial part either. After the initial MSc year, I have had funding for altogether seven months, divided into three years, to prepare this thesis. This has meant not only a torture for the nerves, but also that, during the last five years, I have lived in 14 different addresses, in some of them several different times. And most of the time my bags have been heavy to carry.

The situation eased only in the end after I had gotten several of the papers published or accepted for publication, but at that stage it was too late in regard to this thesis.

But of course, the choice to go on has been my own. I guess the feeling when one sees the numbers turn into associations which are in keeping or contradict what others have found and one knows that one has found 'something' meaningful, regardless of whether it will ever get published or not, counts for more than all obstacles and difficulties together.

Last but not least, I want to thank dr. Barbro Renck for employing me to the Centre for Public Health Research at Karlstad University where new challenges are awaiting.

About the author

Anu Molarius was born on 12th October 1964 in Kesälahti, North Karelia, Finland. In 1988 she graduated from the University of Helsinki, where she studied administrative sciences and also computer science and some statistics. During 1986-1991 she worked in different positions, for instance, as a programmer at the National Public Health Institute (KTL), Helsinki and as a researcher at the Department of Political Science, University of Helsinki.

In September 1991 she started to work at the Department of Epidemiology and Health Promotion of the National Public Health Institute, Helsinki. She worked first in statistical computing in the FINMONICA-project and diabetes research projects, and from November 1992 at the MONICA Data Centre of the same department. During summer 1993 she attended a seminar on the Epidemiology and Public Health Aspects of Diabetes Mellitus in Cambridge, where she first heard of the Netherlands Institute for Health Sciences (NIHES). She participated in the NIHES Master of Science programme in 1994-95, during which she started the work described in this thesis. She completed a MSc degree in Epidemiology in 1995 and a DSc in Epidemiology in 1996. She then applied to become a PhD student at the Erasmus University of Rotterdam and was accepted. She continued her work at the MONICA Data Centre from September 1995 to February 1999 except for short leaves to complete the thesis. From June 1999 she works as an epidemiologist at the Centre for Public Health Research, Karlstad University, Sweden.

Appendix 1. Sites and key personnel of the WHO MONICA Project

Australia

University of Western Australia, Nedlands: M Hobbs[1], K Jamrozik, PL Thompson, BK Armstrong, R Parsons

University of Newcastle, Newcastle: A Dobson[1], S Leeder[2], H Alexander, R Heller

Belgium

Ghent State University, Ghent: G De Backer[1], I De Craene, F van Onsem, L van Parys, S De Henauw, D De Bacquer

Free University of Brussels, Brussels: M Kornitzer[1], L Berghmans, H Darquennes, F Kittel, R Lagasse

Interuniversity Association for the Prevention of Cardiovascular Diseases, Brussels: M Jeanjean[1], C Brohet, HE Kulbertus, S Degre, F Lavenne, D Jansens, F Lefebvre, D Beck, G Wunsch, F Bertrand, M van Houte, B Rime, G Rorive, R Hannot, A Adrienne, A Luyckx

Canada

Dalhousie University, Halifax, Nova Scotia: HK Wolf[1], RD Gregor[5]

China

Beijing Heart, Lung and Blood Vessel Research Institute, Beijing: Wu Zhaosu[1], Wu Yingkai[2], Yao Chonghua, Zhang Ruisong

Czech Republic

Institute for Clinical and Experimental Medicine, Prague: Z Škodová[1], Z Píša, L Berka, Z Cícha, J Cerovská, R Emrová, M Hoke, M Hronkova, J Pikhartová, R Poledne, P Vojtíšek, J Vorlicek, E Wiesner, D Grafnetter

Denmark

Centre of Preventive Medicine (The Glostrup Population Studies) Copenhagen University: M Schroll[1], M Kirchhoff, A Sjol, K Korsgaard Thomsen, M Madsen, TJ Joergensen

Finland

National Public Health Institute, Helsinki: J Tuomilehto[1], P Puska[2], E Vartiainen, H Korhonen, P Jousilahti

France

National Institute of Health and Medical Research (INSERM U258) Paris: P Ducimetiere[3], JL Richard[4], A Bingham, T Lang

National Institute of Health and Medical Research, Toulouse: J. Ferrieres[1], JP Cambou[2], JB Ruidavets, MP Branchu, V Delmas, P Rodier

Department of Epidemiology and Public Health, Institut Pasteur and Medical University of Lille: P Amouyel[1], D Cottel, MC Nuttens[2], N Marécaux, J Dallongeville, J-L Salomez[2], M Montaye[1], C Steclebout

Institute of Hygiene, Faculty of Medicine, Strasbourg: D Arveiler[1], P Schaffer, I Escudero, V Baas, F Pierou

Germany

Bremen Institute for Prevention Research and Social Medicine, Bremen: E Greiser[1], B Herman[5], G Stüdemann

GSF-Institute for Epidemiology, Neuherberg/Munich: U Keil[1], J Stieber, A Döring, B Filipiak, U Härtel, HW Hense

Centre for Epidemiology & Health Research, Berlin: W Barth[1], L Heinemann[1], A Assmann, S Böthig, G Voigt, S Brasche, D Quietzsch, E Classen

Department of of Clinical and Social Medicine of the University Medical Clinic, Heidelberg: E Nussel[1], E Ostor-Lamm[6], R Scheidt, W Morgenstern, M Stadler

Iceland

Heart Preventive Clinic, Reykjavik: N Sigfusson[1], II Gudmundsdottir, I Stefansdottir, Th Thorsteinsson, H Sigvaldason

Italy

National Institute of Health, Rome: A Menotti[3], S Giampaoli, A Verdecchia

S. M. Goretti Hospital, Latina: G Righetti[1], B De Pasquale, P Di Raimo, E Forte, A Majetta

Institute of Cardiology, Regional Hospital, Udine: D Vanuzzo[1], GA Feruglio[2], L Pilotto, GB Cignacco, M Scarpa, R Marini, G Zilio, M Spanghero,G Zanatta

Research Centre on Chronic Degenerative Diseases of the University of Milan: GC Cesana[1], M Ferrario[1], R Sega, P Mocarelli, G De Vito, F Valagussa

Lithuania

Kaunas Medical Academy, Institute of Cardiology: J Bluzhas[1], S Domarkiene, A Tamosiunas, R Reklaitiene

New Zealand

University of Auckland, Auckland: R Beaglehole[1], R Jackson, R Bonita, A Stewart, D Mahon, W Bingley

Poland

Medical Adademy and Jagiellonian University, Kraków: A Pajak[1], J Sznajd [2], E Kawalec, T Pazucha, M Malczewska, I Mórawska

National Institute of Cardiology, Warsaw, Department of Cardiovascular Epidemiology and Prevention: S Rywik[1], G Broda[5], HW Growska, B Pardo, P Kurjata

Romania

Medical Institute, Fundeni Hospital, Bucharest: C Carp[1], I Orha[1], E Apetrei, C Ginghina, I Coman, C Dashievici, P Dumitru, I Zatreanu, A Dumitrescu, T Ionescu, I Stoian, I Cinca

Russian Federation

National Research Centre for Preventive Medicine, Moscow: T Varlamova[1], A Britov, V Konstantinov, T Timofeeva, A Alexandri, O Konstantinova

Institute of Internal Medicine, Novosibirsk: Yu P Nikitin[1], S Malyutina, T Gagulin

Spain

Institute of Health Studies, Department of Health and Social Security, Barcelona: S Sans[1], Ll Balanà, G Paluzie, I Balaguer-Vintró[2]

Sweden

Ostra Hospital Preventive Cardiology Unit, Göteborg: L Wilhelmsen[1], P Harmsen, A Rosengren, G Lappas

Department of Internal Medicine, Kalix Lasarett, Kalix: V Lundberg, F Huhtasaari[1]

Umeå University Hospital, Department of Medicine: M Peltonen, B Stegmayr, K Asplund[1]

Switzerland

Institute of Social and Preventive Medicine, University of Lausanne: M Rickenbach, V Wietlisbach, D Hausser, B Tullen, F Paccaud

Institute of Social and Preventive Medicine, University of Zurich: F Gutzwiller[1]

Department of Social Affairs, Cantonal Health Office of Ticino: F Barazzoni, F Mainieri, G Domenighetti

United Kingdom

The Queen's University of Belfast, Northern Ireland: AE Evans[1], EE McCrum, T Falconer, S Cashman, C Patterson, M Kerr, D O'Reilly, A Scott, M McConville, I McMillan

University of Dundee, Scotland: H Tunstall-Pedoe[1], WCS Smith[6], R Tavendale, K Barrett, C Brown, M Shewry, I Crombie, M Kenicer

Royal Infirmary, Glasgow, Scotland: C Morrison[5], G Watt[6]

USA

Stanford Center for Research in Disease Prevention, Stanford University, California: SP Fortmann[1], A Varady, MA Winkleby, D Jatulis, M Hull

Yugoslavia

Novi Sad Health Centre: M Planojevic[1], D Jakovljevic[2], A Svircevic, M Mirilov, T Strasser

MONICA Management Centre - World Health Organization, Geneva: I Martin[7], I Gyarfas[8], Z Pisa[8], SRA Dodu[8], S Böthig[8], MJ Watson, M Hill

MONICA Data Centre - National Public Health Institute, Helsinki, Finland: K Kuulasmaa[7], J Tuomilehto[8], A Molarius, E Ruokokoski, V Moltchanov, H Tolonen

MONICA Steering Committee: M Ferrario (Chair), K Asplund (Publications coordinator), R Beaglehole, A Evans, H Tunstall-Pedoe (Rapporteur), I Martin (MMC), K Kuulasmaa (MDC), A Shatchkute (WHO, Copenhagen). Consultants: A Dobson, P Amouyel
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[1] Principal Investigator
[2] Former Principal Investigator
[3] Country Co-ordinator
[4] Former Country Co-ordinator
[5] Co-Principal Investigator
[6] Former Co-Principal Investigator
[7] Responsible Officer
[8] Former Responsible Officer