Body mass index and metabolic risk factors for coronary heart disease in women

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Aims Prospective epidemiological studies demonstrate an increase in coronary heart disease mortality in women beginning at values of body mass index ≥22 kg m⁻². However, the metabolic basis for this observation has not been adequately studied in women. Our aim was to examine the association between body mass index, metabolic coronary heart disease risk factors and a predicted 10-year coronary heart disease risk score in a large occupational cohort of women in the U.K.

Methods and Results We carried out a cross-sectional survey of cardiovascular risk factors in 14,077 women, aged 30–64 years. The main outcome measures were systolic and diastolic blood pressure, serum total cholesterol, HDL cholesterol, total cholesterol/HDL cholesterol ratio, LDL-cholesterol, triglycerides, apolipoprotein A1, apolipoprotein B, lipoprotein(a), fasting blood glucose and a predicted 10-year coronary risk score. Across seven categories of body mass index, i.e. <20, 20–22, 22–24, 24–26, 26–28 and ≥30 kg m⁻², there were highly significant age-adjusted increases in the risk factors (all P<0·001), except for a decrease in HDL cholesterol and ApoA1 (all P<0·001) and no relationship with lipoprotein(a) (P=0·05). Based on a multifactorial 10-year coronary heart disease risk estimate, odds ratios for being in the highest quintile of risk for each category of body mass index, were 1 (<20 kg m⁻²), 0·91, 1·56, 2·18, 2·97, 3·83 and 4·21 (≥30 kg m⁻²).

Conclusions The significant rise in metabolic coronary heart disease risk at 22 kg m⁻² observed in this study is consistent with prospective epidemiological studies in women which have reported an increase in coronary heart disease mortality starting at 22 kg m⁻². However, body mass index was a poor discriminator of women at different levels of coronary heart disease risk. The primary goal of weight loss in individuals should be the correction of dysmetabolism, irrespective of the level of body mass index. (Eur Heart J 2001; 22: 46–55, doi:10.1053/euhj.2000.2469) © 2001 The European Society of Cardiology

Key Words: Body mass index, women, coronary heart disease, metabolic risk.

See page 10 for the Editorial comment on this article

Introduction

Obesity can be defined as ‘an excess of body fat, frequently resulting in a significant impairment of health’. A simple measure, such as body mass index, also known as Quetelet’s index (weight in kg . height⁻¹ in m²), is commonly used as a surrogate measure of obesity in epidemiological studies and in clinical practice. The increasing prevalence of obesity in many countries means that it is now considered a pandemic, and in Britain over half the population is currently overweight or obese. Between 1980 and 1998 the prevalence of obesity in women more than doubled from 8% to 21%. It follows that defining interventions for those at risk of obesity-associated diseases is an issue of considerable public health and clinical importance. As with men, studies among women show that as body mass index increases so does the risk of coronary heart disease. However, this association is either significantly attenuated or disappears after adjustment for hypertension, hyperlipidaemia, and hyperglycaemia, demonstrating that the excess coronary risk associated with obesity is largely mediated by these associated metabolic risk factors.

Conventionally applied cut-points of body mass index define desirable or ‘healthy’ weight as body mass index ≤25 kg m⁻², overweight as >25–30 and obesity as body mass index >30. Results from the Nurses Health Study show that the magnitude of overweight associated with an increase in coronary heart disease
risk is rather lower than previously thought\textsuperscript{[13]}. The relative risks (RRs) for coronary heart disease mortality corresponding to each of seven body mass index (kg m\textsuperscript{-2}) categories were as follows; 1\textperiodcentered 0 (body mass index <19), 1\textperiodcentered 0 (19-), 1\textperiodcentered 4 (22-), 1\textperiodcentered 7 (25-), 3\textperiodcentered 1 (27-), 4\textperiodcentered 6 (29-) and 5\textperiodcentered 8 (\geq 32), demonstrating increased coronary heart disease mortality at levels of body mass index hitherto regarded as healthy (\leq 25)\textsuperscript{[14]}. However, the metabolic basis for this progressive rise in coronary heart disease mortality could not be investigated in that study, because blood pressure and biochemical measurements were not available.

In this study we examine the association between body mass index and a wide range of metabolic coronary heart disease risk factors, as well as the predicted risk of coronary heart disease, in a large cross-sectional survey of employed women in the U.K. The terms ‘metabolic syndrome’ or ‘insulin resistance syndrome’ are commonly used to describe a clustering of risk factors including hypertension, dyslipidaemia and abnormal glucose metabolism, which are believed to be a consequence of underlying insulin resistance\textsuperscript{[15]}. Throughout this paper we use ‘metabolic risk factors’ as a collective term for blood pressure, lipids, lipoproteins and blood glucose.

\section*{Methods}

The Marks and Spencer Cardiovascular Risk Factor Study is a cross-sectional study of cardiovascular disease risk factors in women throughout the U.K. This report is based on 14 077 women screened between June 1988 and July 1991.

\subsection*{Screening and measurements}

Details of the methods are given elsewhere\textsuperscript{[16]}. Briefly, all female Marks and Spencer (M&S) employees (excluding managers), aged 30 years and over, with a minimum of 6 months employment, were invited to participate in the ‘Healthplus’ programme; an on-site, nurse administered cardiovascular risk assessment. Participating stores were distributed across 11 distinct areas of the U.K., corresponding to the eight standard regions in England (South East; South West; East Anglia; East Midlands; West Midlands; North West; Yorkshire & Humber, and Northern), together with Wales, Scotland and Northern Ireland. The order in which the stores were visited was determined by M&S management and based entirely on operational considerations. A total of 107 stores participated and the overall response rate was 75%.

The screening assessment consisted of a brief questionnaire on personal and lifestyle factors, including personal and family history of coronary heart disease; hypertension; diabetes; smoking habits and alcohol intake; leisure-time physical activity and current drug therapy, including oral contraception, hormone replacement therapy and antihypertensive medication. Responses were entered by the nurse into a laptop computer. Height and weight (with outdoor clothing and shoes removed) were measured using a digital scales (Seca: model 707) with stadiometer, and body mass index was calculated as weight (kg)/height (m)\textsuperscript{2}. Systolic and diastolic blood pressure were measured twice using a standard mercury sphygmomanometer, with the mean value being recorded. A venous blood sample (15–20 ml) was taken at the end of the screening interview and we requested that this should be in the fasting state where possible. However, because these were working employees and fasting beyond mid-morning was inappropriate, fasting samples were only available in 37\% of subjects. Each individual screening session took 30–40 min and it took 2–3 weeks to complete screening at each store. Standard lipid, lipoprotein and blood glucose analyses were carried out using an automated system; lipoprotein (a) was determined using an enzyme immunoassay and low-density lipoprotein cholesterol was calculated in fasting samples using the Friedewald formula\textsuperscript{[17]}. Apolipoprotein A1, apolipoprotein B, lipoprotein (a) and triglycerides were measured in consecutive subjects from selected stores towards the end of the study.

\subsection*{10-year coronary heart disease risk estimates}

Because coronary heart disease risk factors tend to cluster within individuals, and coronary disease is a multifactorial disease, a measure of overall disease risk is required for each participant. The 10-year predicted probability of the development of coronary disease (10-year coronary heart disease risk) was estimated using the Framingham Heart Study coronary heart disease risk equations\textsuperscript{[18]}. Variables included in the estimate of risk were age, systolic blood pressure, total cholesterol/high density lipoprotein cholesterol (total cholesterol/HDL cholesterol) ratio, cigarette smoking and diabetes. Electrocardiographic data for left ventricular hypertrophy (ECG–left ventricular hypertrophy), which is included in the Framingham risk equations, were not available and was therefore excluded from the calculation. This would have had little impact on the results since the prevalence of ECG–left ventricular hypertrophy in a sample of asymptomatic, employed women, is negligible\textsuperscript{[19]}. Consideration was also given to the possible confounders of this relationship.

\subsection*{Possible confounders}

We examined the effect of a number of potential confounders of the relationship between body mass index and coronary heart disease risk factors. Participants were categorized as active/inactive according to whether or not they undertook regular, leisure-time physical activity.
activity at least once/week; as current (≥1 cigarette/day) or non/ex smokers; as to whether or not they had a family history of coronary heart disease before the age of 65 years; by reported alcohol consumption (0, 1–14 and ≥15 units/week); and as to whether they used hormone replacement therapy or oral contraceptives. To allow for any effect of socioeconomic status, the postcode of each subject’s home address was used to categorize her level of affluence using the quintiles of the Carstairs deprivation index[19].

Statistical analyses

Individuals were grouped into seven categories of body mass index i.e., <20, 20–22, 22–24, 24–26, 26–28, and ≥30 kg · m⁻². Age-adjusted means for the risk factors in each category of body mass index were computed using linear regression, with age as a categorical variable in 10-year groups as a covariate in the models. The values for total cholesterol/HDL cholesterol ratio, fasting LDL cholesterol, fasting triglycerides, fasting blood sugar, apolipoprotein B and lipoprotein(a) were logarithmically (log10) transformed to improve normality of the distributions. Tests for trend were obtained by including body mass index as a seven-level continuous variable, and a quadratic term for the body mass index variable was used to assess non-linearity.

The 10-year coronary heart disease risk probabilities were divided into quintiles and logistic regression was used to estimate the odds ratio of being in the top quintile of risk for each category of body mass index relative to those in the <20 body mass index category, and to adjust for potential confounders. The cut-points for the quintiles of coronary heart disease risk were 0–46, 1–37, 2–64 and 5–53. Subgroup analyses were conducted to determine whether the relationship between body mass index and coronary heart disease risk was modified by age group (<50/≥50 years) or by smoking habit (current/non or ex-smoker). These variables could not be included in the logistic regression analyses as they are included in the calculation of the 10-year coronary heart disease risk.

In order to examine the ability of body mass index to discriminate between women with different levels of predicted coronary heart disease risk, we calculated the proportion (%) of women in each of four 10-year coronary heart disease risk categories (<5, 5–10, and ≥15%) for each category of body mass index. Both British and European Guidelines have consistently advocated a multifactorial approach to coronary heart disease prevention[20,21] as has the British Hypertension Society[22]. In the U.K. an absolute coronary heart disease risk of ≥15%, defines a high risk group in whom the use of drug therapies to lower blood pressure and blood lipids is recommended.

Data from 91 women who reported a previous diagnosis of coronary heart disease were excluded from all analyses, as were non-fasting values for triglycerides and blood glucose.

Results

Prevalence

Figure 1 shows the proportion of women in each body mass index category by age group. Overall, the largest proportion of women had a body mass index in the range 22–24 (26%) with the smallest (5%) in the <20 category. Overall mean and median values for body mass index were 24.8 and 24.1 kg · m⁻² respectively, and mean (SD) body mass index increased with age from 24.1 (3.7) in women aged 30–39 years, to 25.6 (3.37) in those aged 60–64 years. According to conventionally defined body mass index cut-points, 60% (n=8440) of women were in the ‘healthy’ range (body mass index ≤25), 30% (n=4242) were overweight (body mass index >25–≤30) and 9% (n=1294) were obese (body mass index >30).

Body mass index and coronary heart disease risk factors

Table 1 shows the age-adjusted relationship between body mass index and metabolic risk factors. Systolic blood pressure, diastolic blood pressure, total cholesterol, triglycerides, total cholesterol/HDL cholesterol ratio, LDL cholesterol, apolipoprotein B, and blood glucose show a statistically significant, positive trend across the categories of body mass index (all P<0.001). For HDL cholesterol there is a highly significant (P<0.001) inverse association with body mass index with a reduction of 0.31 mmol · 1⁻¹ (18%) between the lowest and highest body mass index categories. A similar, though less marked, negative association is also seen for apolipoprotein A1 (P<0.001), while the relationship with lipoprotein(a) was not statistically significant (P=0.05). Adjustment for smoking, alcohol consumption, physical activity patterns, use of oral contraceptives or hormone replacement therapy, family history of premature coronary heart disease and socioeconomic status, made little difference to these relationships.

Body mass index and 10-year coronary heart disease risk estimates

There was a steady increase in the predicted 10-year risk of coronary heart disease with increasing body mass index, with considerable overlap of the risk distributions across the body mass index categories (Fig. 2). The median risks (%) in each of the seven body mass index categories were 0.8 (<20 kg · m⁻²), 1.1, 1.6, 2.2, 2.9, 3.5 and 3.8 (≥30 kg · m⁻²). The prevalence (%) of those in the top quintile of predicted 10-year coronary heart disease risk increased across the seven body mass index categories as follows; 9.5 (<20 kg · m⁻²), 9.7, 16, 21, 27, 32 and 35
Using a body mass index of <20 as the reference category, the odds ratio for being in the top quintile of 10-year coronary heart disease risk increased with increasing body mass index (Table 2). Adjustment for alcohol consumption, reported physical activity, oral contraception and hormone replacement therapy use, and socioeconomic status made little difference to these relative risk estimates. Subgroup analyses by age and smoking status showed that the relationship was essentially the same in women aged 30–49 years (linear trend: \( P<0.001 \)) and those aged 50–64 years (linear trend \( P<0.001 \)). Odds ratios for being in the top quintile of risk showed a steeper rise in non/ex smokers than in current smokers, although there was a significant increase in risk in both groups.

We examined the ability of body mass index to discriminate between different degrees of absolute risk \( \geq 30 \text{ kg} \cdot \text{m}^{-2} \), respectively. Using a body mass index of <20 as the reference category, the odds ratio for being in the top quintile of 10-year coronary heart disease risk increased with increasing body mass index (Table 2). Adjustment for alcohol consumption, reported physical activity, oral contraception and hormone replacement therapy use, and socioeconomic status made little difference to these relative risk estimates. Subgroup analyses by age and smoking status showed that the relationship was essentially the same in women aged 30–49 years (linear trend: \( P<0.001 \)) and those aged 50–64 years (linear trend \( P<0.001 \)). Odds ratios for being in the top quintile of risk showed a steeper rise in non/ex smokers than in current smokers, although there was a significant increase in risk in both groups.

We examined the ability of body mass index to discriminate between different degrees of absolute risk i.e. <5%, 5–10 and \( \geq 15\%\). Figure 3 shows that there is little difference in the proportion of individuals in each coronary heart disease risk category in the two lowest categories of body mass index, but thereafter there is a graded increase in the proportion of subjects in the higher risk categories across the entire range of body mass index. For example, the proportion (%) of individuals with a predicted 10-year coronary heart disease risk of 10–<15% in each body mass index category, was 1·7 (<20 kg m\(^{-2}\)), 1·8, 2·8, 4·5, 6·2, 8·6 and 9·7 (\( \geq 30 \text{ kg} \cdot \text{m}^{-2} \)).

**Discussion**

This study provides a comprehensive description of the relationship between body mass index and a range of metabolic coronary heart disease risk factors in a large sample of women in the U.K., and demonstrates the metabolic basis for the increased mortality reported in other studies at levels of body mass index hitherto regarded as healthy.

**Body mass index and coronary heart disease risk factors**

Mean systolic blood pressure and diastolic blood pressure increased consistently with each body mass index category, the magnitude of this relationship being comparable to that seen with age. This association was recognised early last century and has been repeatedly demonstrated\[^{23-25}\].
<table>
<thead>
<tr>
<th>Number</th>
<th>SBP (mmHg)*</th>
<th>DBP (mmHg)*</th>
<th>TC (mmol . l⁻¹)</th>
<th>HDL-C (mmol . l⁻¹)</th>
<th>TG (mmol . l⁻¹)</th>
<th>Apo A1 (mg . dl⁻¹)</th>
<th>Apo B (mg . dl⁻¹)</th>
<th>Lp(a) (mg . dl⁻¹)</th>
<th>Glucose (mmol . l⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20</td>
<td>110.6</td>
<td>69.2</td>
<td>5.02</td>
<td>1.68</td>
<td>0.78</td>
<td>6188</td>
<td>688</td>
<td>3733</td>
<td>4.88</td>
</tr>
<tr>
<td>20–22</td>
<td>111.2</td>
<td>69.6</td>
<td>(4.94–5.01)</td>
<td>(1.65–1.71)</td>
<td>(0.73–0.82)</td>
<td>(520–560)</td>
<td>(552–587)</td>
<td>(574–582)</td>
<td>(4.77–4.91)</td>
</tr>
<tr>
<td>22–24</td>
<td>111.9</td>
<td>70.4</td>
<td>(5.07–5.16)</td>
<td>(1.61–1.65)</td>
<td>(0.76–0.82)</td>
<td>(565–600)</td>
<td>(573–597)</td>
<td>(574–582)</td>
<td>(4.84–4.92)</td>
</tr>
<tr>
<td>24–26</td>
<td>114.0</td>
<td>71.9</td>
<td>(5.16–5.25)</td>
<td>(1.57–1.60)</td>
<td>(0.76–0.82)</td>
<td>(619–653)</td>
<td>(605–633)</td>
<td>(674–682)</td>
<td>(4.85–4.93)</td>
</tr>
<tr>
<td>26–28</td>
<td>116.7</td>
<td>73.8</td>
<td>(5.29–5.38)</td>
<td>(1.52–1.55)</td>
<td>(0.82–0.89)</td>
<td>(619–653)</td>
<td>(605–633)</td>
<td>(674–682)</td>
<td>(4.85–4.93)</td>
</tr>
<tr>
<td>28–30</td>
<td>118.7</td>
<td>75.3</td>
<td>(5.31–5.42)</td>
<td>(1.48–1.50)</td>
<td>(0.87–0.97)</td>
<td>(619–653)</td>
<td>(605–633)</td>
<td>(674–682)</td>
<td>(4.85–4.93)</td>
</tr>
<tr>
<td>≥ 30</td>
<td>123.1</td>
<td>78.5</td>
<td>(5.45–5.59)</td>
<td>(1.42–1.50)</td>
<td>(1.03–1.17)</td>
<td>(619–653)</td>
<td>(605–633)</td>
<td>(674–682)</td>
<td>(4.85–4.93)</td>
</tr>
</tbody>
</table>

*Subjects not taking antihypertensive medication.  
†Geometric means  
‡test for linear trend: all P<0.001 except for lipoprotein (a) P=0.05  
§test for significance of quadratic term: all P<0.001 except for total cholesterol (TC) P=0.003, LDL cholesterol (LDL-C) P=0.001, and HDL cholesterol (HDL-C), total cholesterol/HDL cholesterol (TC/HDL-C), apolipoprotein A1 (Apo A1), apolipoprotein B (Apo B), lipoprotein (a) (Lp(a)) P>0.20.  
SBP=systolic blood pressure; DBP=diastolic blood pressure.
The positive association between body mass index and total cholesterol, LDL cholesterol, fasting blood glucose and triglycerides, and the inverse association with HDL cholesterol, has been consistently observed in other cross-sectional studies in both women and men[7,26,27]. The association between body mass index and apolipoproteins in women is less well described, but our finding of a strong positive association between body mass index and apolipoprotein B, and an inverse association with apolipoprotein A1, has also been reported in the Whitehall II study[28].

Our results show no association between body mass index and lipoprotein(a), an observation consistent with earlier reports on smaller groups of women[29,30] although some studies have reported a positive relationship[31,32].

Our findings are consistent with a number of recent studies which have attempted to define healthy weight in relation to the prevalence of risk factors, rather than cardiovascular events. In these reports, healthy adiposity corresponds to a body mass index at, or close to, 22 kg \(m^{-2}\) in women[7,33-35].

**Body mass index and coronary heart disease risk**

The probability of being in the highest quintile of a multifactorial 10-year coronary heart disease risk estimate based on a Framingham algorithm increases across the body mass index range, starting at a body mass index of 22 kg \(m^{-2}\). This corresponds to the threshold at which coronary heart disease mortality increases in the Nurses Health Study[14]. Therefore some of the excess risk associated with increasing body weight — even that within the ‘healthy’ range \((\leq 25)\) — can be explained by adverse changes in blood pressure, lipids, lipoproteins, and blood glucose. Other components of the insulin resistance (or metabolic) syndrome, including haemostatic factors, may also contribute to an increased risk of coronary heart disease[15].

Since 10-year coronary heart disease risk increases across the entire body mass index range, using conventionally defined body mass index cut points to identify those at high risk of coronary heart disease would lead
to considerable individual misclassification. For example, in this study 84% of women with a body mass index $\geq 25$ kg.m$^{-2}$ (‘healthy’) had a predicted 10-year coronary heart disease risk of $<5\%$, as did 60% of those with a body mass index $\geq 30$ kg.m$^{-2}$ (‘obese’). The substantial overlap of low and high coronary heart disease risk across the body mass index categories confirms that body mass index used alone is a poor discriminator of coronary heart disease risk. This is not surprising given that the mechanism underlying the adverse metabolic consequences of obesity — including hypertension and dyslipidaemia — is insulin resistance and hyperinsulinaemia, which are considered to be a consequence of abdominal fat deposition$^{[36,37]}$. By comparison, fat in the buttock and thigh area is less metabolically active and associated with fewer health risks$^{[38,39]}$. Body mass index does not distinguish between the contribution to body weight of fat tissue and that of muscle, bone and water$^{[9,40]}$, nor does it provide any information regarding fat distribution$^{[41]}$. Hence there is considerable variability in body composition for any given body mass index, and some individuals with low body mass indices have as much fat as individuals with high body mass indices$^{[42]}$.

It is therefore important to distinguish between those who are overweight but metabolically normal. The key clinical issue is not overweight per se, but rather the metabolic consequences of excess adiposity, as concentrating on weight alone can lead to inappropriate and unrealistic interventions.

### Table 2 Odds ratios (95% confidence intervals) for prevalence of being in the top quintile of 10 year probability of developing coronary heart disease* by body mass index category

<table>
<thead>
<tr>
<th>Body mass index (kg.m$^{-2}$)</th>
<th>Unadjusted</th>
<th>Fully adjusted†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds ratio</td>
<td>Odds ratio</td>
</tr>
<tr>
<td></td>
<td>(95% CI)</td>
<td>(95% CI)</td>
</tr>
<tr>
<td>&lt;20</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>20–</td>
<td>0.90 (0.67–1.20)</td>
<td>0.91 (0.68–1.22)</td>
</tr>
<tr>
<td>22–</td>
<td>1.58 (1.20–2.06)</td>
<td>1.56 (1.19–2.05)</td>
</tr>
<tr>
<td>24–</td>
<td>2.21 (1.69–2.90)</td>
<td>2.18 (1.66–2.86)</td>
</tr>
<tr>
<td>26–</td>
<td>3.16 (2.40–4.16)</td>
<td>2.97 (2.25–3.92)</td>
</tr>
<tr>
<td>28–</td>
<td>4.20 (3.16–5.59)</td>
<td>3.83 (2.87–5.11)</td>
</tr>
<tr>
<td>≤30</td>
<td>4.76 (3.60–6.29)</td>
<td>4.21 (3.18–5.59)</td>
</tr>
</tbody>
</table>

* Determined using the Framingham risk equations$^{[18]}$.
† Adjusted for alcohol consumption, vigorous physical activity, hormone replacement therapy, oral contraceptive use and socio-economic status; additional term for family history of premature coronary heart disease was not statistically significant.
‡ Based on model including linear term for body mass index.
§ Likelihood ratio test.

*Figure 3* The prevalence of individuals in each body mass index category, according to four levels of predicted 10-year coronary heart disease risks, i.e. $<5\%$, 5–10% and $\geq 15\%$. The total number of subjects in each body mass index category is shown at the top of the bars and the total number in each coronary heart disease risk category is shown under the legend.
Public health implications

In terms of coronary heart disease prevention our data show that a healthy body weight in women corresponds to a body mass index of $<22 \text{ kg} \cdot \text{m}^{-2}$—substantially below the currently recommended healthy upper limit of $\leq 25$. However, because body mass index is a poor predictor of metabolic risk in individuals, recommending a new target of $22 \text{ kg} \cdot \text{m}^{-2}$ for all women would be both unrealistic and unnecessary. Instead, we suggest that those women with a body mass index $\geq 22-30 \text{ kg} \cdot \text{m}^{-2}$ who have an adverse metabolic profile, should be specifically targeted to lose fat weight. All women with a body mass index $>30 \text{ kg} \cdot \text{m}^{-2}$ should be encouraged to lose weight since, even if they are at low risk of coronary heart disease, they are predisposed to a variety of other obesity-associated morbidities.

Evidence from randomized trials shows that even moderate weight loss (10%), can significantly decrease the severity of obesity-associated risk factors. Hence the primary goal of weight loss in all subjects should be normalization of the metabolic risk factor profile, regardless of the level of body mass index.

It follows that measurement of coronary heart disease risk factors should be a routine part of the initial assessment of the overweight and obese, an approach consistent with recent guidelines from the US National Institutes of Health. This policy is also consistent with recent guidelines from the US National Institutes of Health. They recommend a target or optimal weight based on body mass index. Most approaches to weight loss recommend a target or optimal weight based on body mass index alone, because of an implicit assumption that body mass index is a reliable surrogate marker for coronary heart disease risk. Our data show that this assumption is unwarranted and that body mass index should not be used as the sole basis for intervention in individuals. Weight loss interventions should be targeted at those with a body mass index $\geq 22 \text{ kg} \cdot \text{m}^{-2}$ who also have an adverse risk factor profile, although all women with a body mass index $>30 \text{ kg} \cdot \text{m}^{-2}$ should be encouraged to lose weight. Successful weight loss should be defined in terms of a reduction in metabolic risk, which can often be achieved by relatively modest weight loss, and is more likely to be successful than repeated attempts to attain a target ideal weight based on a body mass index of $<25 \text{ kg} \cdot \text{m}^{-2}$.

Strengths and limitations

This is a large study of cardiovascular risk factors in women across the U.K. Other studies which have included women are smaller, have included only a limited number of risk factors, or are restricted to relatively limited geographical locations.

A limitation of our analysis is the use of a 10-year coronary heart disease risk score rather than actual coronary heart disease outcome. This use of a proxy outcome measure (inevitable in a cross-sectional study) may lead to misclassification in either direction, although the efficacy of the Framingham risk equations in distinguishing high from low risk individuals has been demonstrated in diverse populations.

A number of studies have suggested that the use of a measure of fat distribution, such as the waist:hip ratio or waist circumference alone, may provide a better assessment of coronary heart disease risk than the use of body mass index alone. In the present survey, waist and hip measurements were not available so we were unable to investigate the value of anthropometric measures other than body mass index.

Finally, there is the issue of selection bias; women who are employed tend to be healthier than those who are not. Furthermore, only a proportion of subjects eligible to participate in the study actually did so and these women may differ from non-participants in a number of important respects. Nevertheless, there is little biological evidence to suggest that the observed relationships between body mass index and the variables examined here would be materially different in other groups of women.

Conclusion

This study demonstrates a biological basis for the rise in coronary heart disease mortality observed in women at levels of body mass index hitherto regarded as ‘healthy’. The association between body mass index and increasing coronary heart disease risk in women is partly explained by a rise in blood pressure and an increasingly adverse lipid and lipoprotein profile across the whole range of body mass index. Most approaches to weight loss recommend a target or optimal weight based on body mass index alone, because of an implicit assumption that body mass index is a reliable surrogate marker for coronary heart disease risk. Our data show that this assumption is unwarranted and that body mass index should not be used as the sole basis for intervention in individuals. Weight loss interventions should be targeted at those with a body mass index $\geq 22 \text{ kg} \cdot \text{m}^{-2}$ who also have an adverse risk factor profile, although all women with a body mass index $>30 \text{ kg} \cdot \text{m}^{-2}$ should be encouraged to lose weight. Successful weight loss should be defined in terms of a reduction in metabolic risk, which can often be achieved by relatively modest weight loss, and is more likely to be successful than repeated attempts to attain a target ideal weight based on a body mass index of $<25 \text{ kg} \cdot \text{m}^{-2}$.

We thank the women who participated in this study; the nurses who carried out the Healthplus screening programme; Marks and Spencer Health Services & Occupational Health Department for their support; Wei Dong and Stephen Browne for initial organisation of the study data; Simon Stevenson for providing the Carstairs index data; Neil McLennan for obtaining postcodes and Chris Frost and Elaine Meilahn for comments on an earlier draft of the paper. Biochemical analyses were carried out at Medical Diagnostic Laboratories, London, except for lipoprotein (a) which was analysed at Innogenetics N.V. Canadastraat 21–Haven 1009, 2070 Zwijndrecht, Belgium.

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References


