Risk factors for diabetes and coronary heart disease

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This is the seventh article in the series

ABC of obesity

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Diabetes

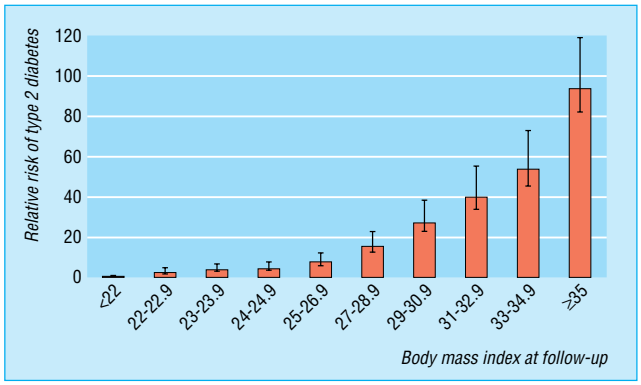
Many cross sectional and prospective studies have confirmed the association between obesity and type 2 diabetes. Most people with type 2 diabetes are overweight or obese: more than 85% of people with type 2 diabetes in southeast Scotland in 2005 had a body mass index (weight in kilograms divided by height in metres squared) of over 25. Recent evidence indicates that high waist circumference may be an even better indicator than body mass index (BMI) of increased risk of type 2 diabetes.

The risk of developing diabetes over a 14 year follow-up period (among nurses aged 30-55 years at baseline) in the nurses' health study was 49 times higher among women whose baseline BMI was >35 than among women whose baseline BMI was <22. Even a slightly raised BMI (22.0-22.9) at follow-up was associated with an age adjusted relative risk of diabetes that was three times higher than that in women with a BMI of <22.0 at follow-up.

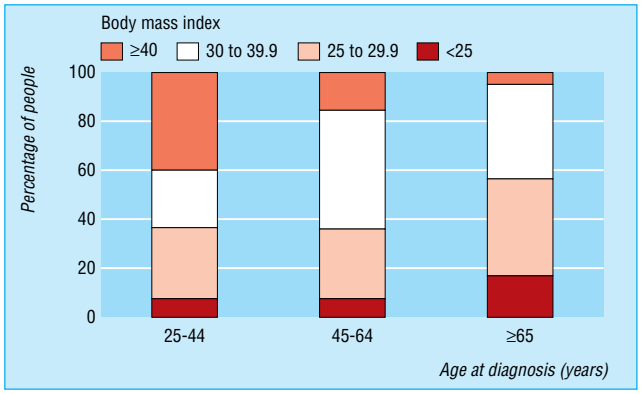
Similar findings have been reported for men from a United States cohort of 51 529 male health professionals aged 40-75 in 1986 who were followed until 1992. Those with a BMI of ≥35 had a relative risk of developing diabetes of 42 (95% confidence interval 22.0-80.6) compared with men with a BMI of <23.0 at age 21, after adjustment for age, smoking, and family history of diabetes. Moreover, earlier onset of type 2 diabetes is associated with a higher BMI, and increasing prevalence of overweight and obesity is the most important factor in the increasing number of younger people diagnosed with type 2 diabetes.

These data have been derived from mainly white populations, and ethnicity modifies the relation between BMI and risk of diabetes. In an Indian population the increasing risk of diabetes associated with increasing BMI starts at even lower BMI levels (15 to 20) than in most other ethnic groups (in whom increasing prevalence of diabetes is only observed at a BMI of >25). This difference is only partly explained by patterns of fat distribution in different ethnic groups; south Asian populations are more likely to have a greater total percentage of body fat mass and larger amount of abdominal fat (reflected by high waist circumference) than other ethnic groups at a given level of BMI. High waist circumference increases the risk of glucose intolerance and diabetes, independent of the risk reflected by high BMI.

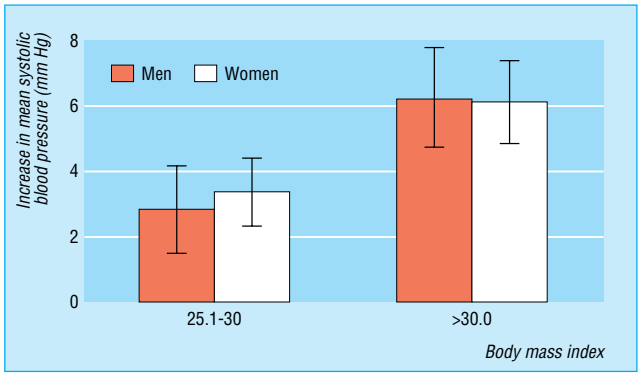
Studies in China, the US, and Finland have shown that diabetes can be prevented or delayed in people at high risk of diabetes through a combination of change in diet and lifestyle and modest weight loss. In the Swedish obesity study 69% of people with diabetes at baseline who lost weight after gastric bypass surgery did not have diabetes two years after follow-up. The challenges of maintaining weight loss and improvements in health among people with type 2 diabetes are summarised in Cochrane reviews of non-pharmacological and pharmacological interventions (see earlier article in this series).



Body mass index at follow-up and relative risk for type 2 diabetes in participants in nurses' health study. Data derived from Colditz et al (see Further Reading box)



Distribution of body mass index in people with diagnosis of type 2 diabetes in past two years, by age at diagnosis (based on 371, 1466, 1302 people aged 25-44, 45-64, and ≥65 respectively at diagnosis, in population based diabetes register in Lothian, Scotland)



Increase in mean systolic blood pressure in overweight and obese men and women compared with normal weight individuals. Data from *Health Survey for England, 2003* (www.dh.gov.uk)

Hypertension

Blood pressure increases with increasing BMI. The health survey for England 2003 found that mean systolic blood

pressure was about 6 mm Hg higher in obese men and women than in those of normal weight (BMI 18.5-25).

According to data from the third national health and nutrition examination survey (NHANES III) in the US, high blood pressure was the most common condition related to overweight and obesity that showed a marked increase with increasing categories of BMI. The prevalence of high blood pressure (defined as a doctor's diagnosis of hypertension or high blood pressure, or a mean of three readings of >140 mm Hg for systolic and >90 mm Hg for diastolic blood pressure) was 2.5 times higher in men and over three times higher in women aged <55 whose BMI was 30-34.9 than in people of the same age whose BMI was 18.5-24.9. Among people aged ≥55, the excess risk of hypertension was less marked for obese people compared with the normal weight group.

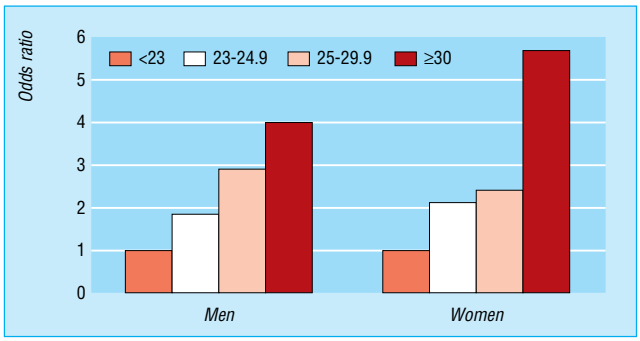
Prevalence of hypertension (as defined above) rose from 15% for the normal weight category for both men and women to 42% among obese men and 38% among obese women. Age adjusted prevalence of hypertension was higher among black than white people in each BMI category for both sexes.

These data from NHANES III show that the effect of obesity on risk of hypertension differs with age (higher relative risk among younger age groups but higher absolute risk among older age groups) and ethnicity (higher risk among black than white populations).

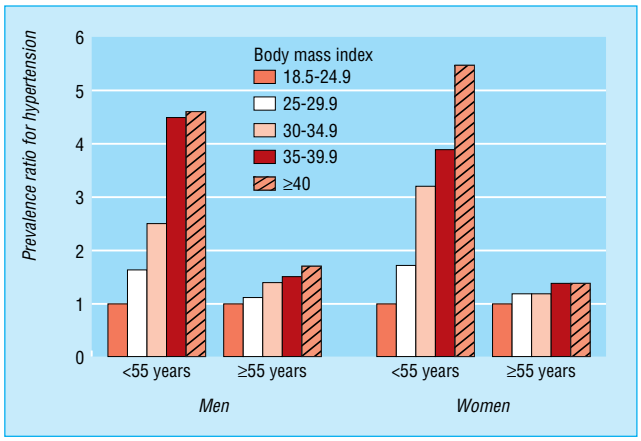
Evidence from both American and British populations suggests a stronger relation between blood pressure and central obesity than between blood pressure and peripheral or general fat distribution. Systolic blood pressure was found to increase in a linear manner across the whole range of waist to hip ratio, independently of age, BMI, and other covariates in 9936 men and 12 154 women aged 45-79 years who took part in the Norfolk component of the European Prospective Investigation into Cancer and Nutrition (EPIC-Norfolk). These data were obtained from cross sectional studies, but the clear relation between obesity and subsequent hypertension has also been shown in prospective studies. Interpreting the results of cross sectional studies can be difficult because of potential bias.

Dyslipidaemia

Obesity is associated with both higher levels of total cholesterol and an unfavourable lipid pattern, with low concentrations of HDL (high density lipoprotein) cholesterol and high triglyceride concentrations. This dyslipidaemic pattern is particularly marked in people with central obesity.



Odds ratios for hypertriglyceridaemia (triglycerides >1.7 mmol/l) by sex and BMI category. Data derived from cross sectional study of 6318 Taiwanese (3540 men, 2778 women) attending health screening centres in southern Taiwan in 2002-3 (Tsai et al. *Am J Epidemiol* 2004;160:557-65)

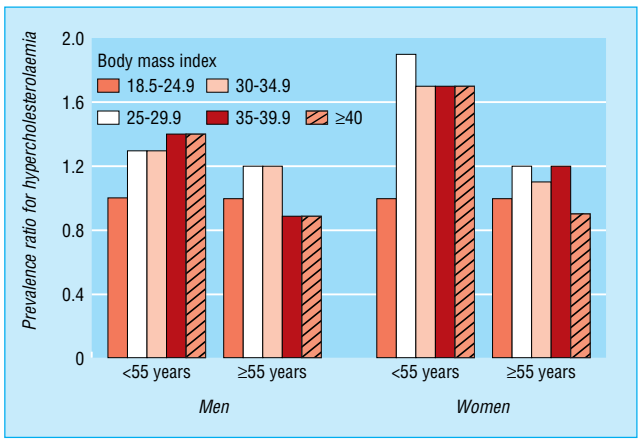


Prevalence ratios for hypertension (that is, a doctor's diagnosis or three readings of ≥140/90 mm Hg) by sex, age, and BMI category. Data derived from cross sectional data from the NHANES III study (Must et al (see Further Reading box))

Weight gain and hypertension

- Weight gain is associated with an increased risk of developing hypertension, but "weight cycling" (repeated gain and loss of weight) does not seem to be
- Long term reductions in blood pressure and reduced risk of hypertension have been achieved with modest weight loss among people aged 30 to 54 who were overweight and had high normal blood pressure levels at baseline
- The number of drugs required to control blood pressure has been shown to be lower among people in a weight loss intervention group

Some of the effect of obesity on blood pressure may be permanent: one study found that blood pressure decreased initially after gastric surgery but after eight years the prevalence of hypertension had returned to the preoperative level



Prevalence ratios for hypercholesterolaemia (that is, a doctor's diagnosis or a measurement of ≥6.2 mmol/l) by sex, age, and BMI category. Data derived from cross sectional data from the NHANES III study (Must et al (see Further Reading box))

In NHANES III, participants were considered to have hypercholesterolaemia if they reported a doctor's diagnosis or if their total cholesterol concentration was higher than 6.2 mmol/l. Trends in hypercholesterolaemia with increasing BMI were less marked than for hypertension. The prevalence of hypercholesterolaemia in this study was highest among the overweight group (BMI 25-29.9) and slightly lower in the obese groups but was still about 50% higher in men and women who were obese than in those of normal weight. The prevalence of high blood cholesterol concentration in each BMI category was lower in black and Hispanic than in white populations.

Mean concentrations of HDL cholesterol decreased with increasing BMI in both sexes and were higher in black than in white populations. The effect of BMI on HDL cholesterol and triglyceride concentrations is more marked than on total cholesterol. The association of waist circumference with lipids and novel markers of lipid associated risk (such as apolipoprotein B or lipoprotein subfractions) is at least as good as that between BMI and lipids.

Smoking

The relation between obesity and smoking is complex: smoking is associated with lower BMI; smoking cessation is linked with weight gain. In many developed countries, however, smoking and obesity are generally associated with lower socioeconomic status and often occur together. Studies examining the effects of BMI that do not take into account smoking habit may be biased and underestimate the harmful effects of increasing BMI.

In addition, smoking seems to be associated with an altered pattern of fat distribution and increased waist circumference. A cross sectional study of Dutch women showed that BMI decreased but that waist to hip ratio increased with increasing number of cigarettes smoked per day. The EPIC-Norfolk study also collected lifestyle data using questionnaires and anthropometric measurements. Current smokers had the highest waist to hip ratios and "never smokers" had the lowest waist to hip ratios after adjustment for age, BMI, alcohol intake, total energy intake, physical activity, and education.

A study of trends in obesity in Texas found that, although smoking cessation was associated with weight gain, the contribution of smoking cessation to trends in overweight and obesity was small. The benefits of smoking cessation may be partly offset by weight gain, although, at least in women, this may not be associated with an increase in fat accumulation.

National survey data from the US suggest that obesity has roughly the same association with chronic health conditions as does 20 years of ageing and that this is considerably greater than the effect of smoking.

The effect of obesity on hospital costs and drug use (36% increase and 77% increase respectively) is considerably greater than for smoking (21% increase and 28% increase respectively).

The National Audit Office estimated that in England in 1998, 10% of deaths were attributable to smoking and 6% to obesity. As smoking levels decline and prevalence of obesity increases, the relative importance of these factors will probably change. A recent analysis from the Framingham study showed that obesity and smoking each reduce life expectancy after the age 40 years, more so if combined together.

Competing interests: SHW has received a fee for speaking from Bayer. CDB has received honorariums and educational grants from several pharmaceutical companies involved in selling and developing treatments for obesity, cardiovascular disease, and diabetes. For series editors' competing interests, see the first article in this series.

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Clinical trials have shown the benefits of weight loss to improve dyslipidaemia, and exercise seems to have an additional benefit over the effects of a low fat diet. One review has reported that every kilogram of weight loss is associated with the following changes in lipid concentrations: fasting serum cholesterol −1.0%, LDL (low density lipoprotein) cholesterol −0.7%, triglycerides −1.9%, HDL cholesterol 0.2%

Lifestyle modification before drugs

- In 14 statin trials the mean LDL cholesterol concentration was 3.8 mmol/l and the average reduction in LDL cholesterol concentration was 1.1 mmol/l
- An average of over 40 kg of weight loss would be required to achieve an equivalent LDL reduction
- Clearly, to achieve cholesterol targets, many people require drug therapy as well as trying to lose weight. Weight loss alone can be very effective in improving lipid patterns in some overweight people
- Given the additional health benefits of weight loss and the potential side effects of drugs, lifestyle modification should always be tried first

Effects of obesity and smoking on life expectancy after age 40 on basis of follow-up data from Framingham study. Adapted from Peeters et al (see Further Reading box)

Study group*	Comparison group*	Years of life lost after age 40 relative to comparison group	
		Men	Women
≥30, non-smokers	18.5-24.9, non-smokers	5.8	7.1
≥30, smokers	BMI 18.5-24.9, smokers	6.7	7.2
≥30, smokers	BMI 18.5-24.9, non-smokers	13.7	13.3

*Body mass index and smoking status.

Further reading

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The ABC of Obesity is edited by Naveed Sattar (nsattar@clinmed.gla.ac.uk), professor of metabolic medicine, and Mike Lean, professor of nutrition, University of Glasgow. The series will be published as a book by Blackwell Publishing in early 2007.