



Obesity

Part one – The greatest health threat facing mankind

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‘In the 15 minutes it will take you to read this article nine people in the USA, and one person in the UK, will have died as a direct consequence of obesity related illnesses...’

As I write this article, in the middle of 2002, the United States of America, many European states (including the United Kingdom) and other westernised nations across the globe are in the grip of an epidemic. In 1997, the problem was already so great that the World Health Organisation declared that it was the greatest health threat facing mankind. The problem is spreading through the populations of the USA and Europe, at a phenomenal speed, and it is killing people at almost unbelievable rates. Ten times more people die annually as a consequence of this problem than die in road traffic accidents.

In the UK, in 2000, approximately the same number of people died as a consequence of this condition as died from lung cancer. Indeed, the rate of death in the USA as a direct consequence of the affliction is currently the equivalent to an 11 September type event happening every four days! Yet the epidemic is almost silently progressing. Even worse, the people who suffer from this problem are often blamed for their own predicament, ridiculed and mocked by some of those who are fortunate enough not to have fallen into its grip. The pandemic is the spread of obesity and it is so great that it has even spawned a new word ‘globesity’.

Obese people carry around excessive amounts of body fat. A couple of years ago, during a radio interview, I was asked how we define obesity. ‘Surely’, the interviewer said, ‘it is just a matter of opinion’. Some people he knew were quite fat but didn’t regard themselves as being so, while he knew lots of women who were, in his opinion, dangerously thin, but they considered themselves overweight. How could we possibly study something that was so subjective? Of course, if obesity were so subjective, it would be almost

impossible to study. So how do we measure how fat somebody is? It is clear that obese people generally weigh more than thin people. But weight alone doesn’t tell us how fat we are. Our bodies consist of fat, lean and bone tissue, and the amounts of lean and bone tissue increase in relation to how tall we are. To get an indication of a person’s body fatness, therefore, we need to measure not only their body weight, but also their height, and combine these in an index of body fatness.

How fat are you?

There are several ways of combining weight and height to estimate body fatness, but the most common is to divide the weight in kilograms (W) by the height in metres (h) multiplied by itself – W/h^2 . This is called the body mass index or BMI. On this scale, people with an index over 25 and less than 30 are said to be overweight, and people with an index over 30 are defined as obese. These definitions have been adopted by the WHO. In practice, this means that a person weighing 68 kg (10 stone 12lb) and 1.73 metres high (five’ eight”) would have a body mass index of 22. If they put on 8 kg, so they weighed 76 kg (12 stones), they would fall into the overweight category; and if they piled on another 15 kg, to weigh in at 91 kg (14 stones), they would be obese.

There are several problems with this index – in particular it doesn’t work well when a person is changing their height over time, so it cannot be used to gauge the body fatness of children, who change in both their weights and heights during development. In addition, people who

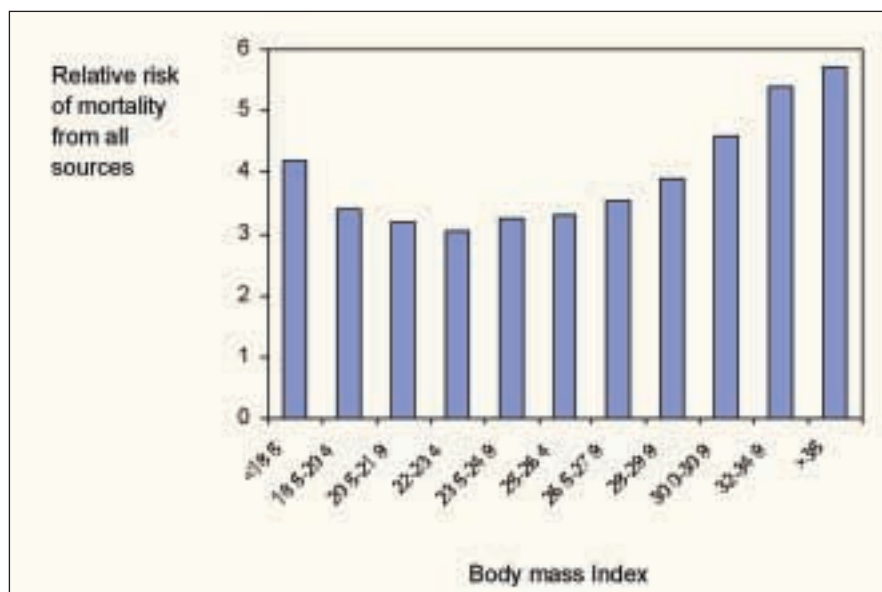


Figure 1. Risk of premature mortality as a function of Body mass index (BMI) for women (data from Calle *et al.* (1996) *New England Journal of Medicine*, **347**, 1097.

deposit large amounts of lean tissue, for example, body builders and some athletes, may also be misclassified as obese. In general, however, BMI does correlate reasonably closely in adults to their true body fatness (measured by more sophisticated scanning and imaging devices), particularly if combined with measures such as the circumferences of the waist and hips.

Other indices do exist, such as the ponderal index (W/h^3), which are perhaps more logically justified on scaling grounds (mass is a volume trait and so in theory should be divided by the linear dimension cubed, also reflecting a volume trait, to give a dimensionless index). However, the preference for BMI stems from the fact that, during the 1930s, the life insurance companies of the USA performed an analysis of the factors influencing the likelihood of a person redeeming a life insurance policy. Fraud apart, this would generally mean that a person had died. The companies performed an analysis of around five million policies issued in the 1930s. The motivation of the insurance companies in this respect was clear – if they could predict in advance who was likely to die, they could set the levels of their premiums more effectively to ensure that they made a profit. The factor they came up with as the most effective predictor of mortality was BMI. Next time you apply for life insurance you might notice that the companies still ask for your height and weight as a component of their calculation of the premium to charge you.

The relationship between fatness and mortality

The life insurance companies found that mortality had a minimum when BMI was between 20 and 25. Increases in BMI above this range were linked to increased mortality, and mortality accelerated rapidly when BMI exceeded 30 (Figure 1). On the other side of the scale, mortality also started to steeply

increase when BMI was less than 20. Much discussion has ensued about why mortality increases in this pattern at both high and low BMI. It is now widely accepted that the extent of increase in mortality at low BMI was heavily influenced by smokers. Smokers dominated the low BMI classes throughout the 1940s to 1960s, before the negative health consequences of smoking were widely acknowledged. With smokers excluded from the sample, the dramatic rise in mortality at low BMI almost disappears. This effectively means that the ‘ideal’ BMI of 20–25 is an artefact of the mixed population of smokers and non-smokers included in the analysis. Yet the notion has stuck that a BMI of 20–25 provides a useful target body weight that will minimise mortality. It is this value that slimming magazines use to calculate your ‘ideal’ weight.

The increase in mortality as BMI increases is not a consequence of a covariable factor with body weight, such as smoking. It is now clear that there is a direct link between body fatness and a whole suite of degenerative diseases (Kopelman *et al.*, 2000). The most important of these is type two diabetes (previously also known as adult onset diabetes or non-insulin dependent diabetes mellitus – NIDDM). Being overweight by 10 kg increases ones risk of developing type two diabetes by about eightfold. The difference in risk of developing type two diabetes between somebody who is heavily obese, with a BMI of 35, and somebody of ‘ideal’ BMI at 20–25 is about 60–90 fold (Figure 2). The strong link of obesity to diabetes has spawned yet another new word to describe the combined condition ‘diabesity’. Increased body fatness also leads to elevated risks of developing cardiovascular problems such as hypertension. Some cancers are increased in relation to body fatness and there is elevated susceptibility to respiratory disorders – one of the most

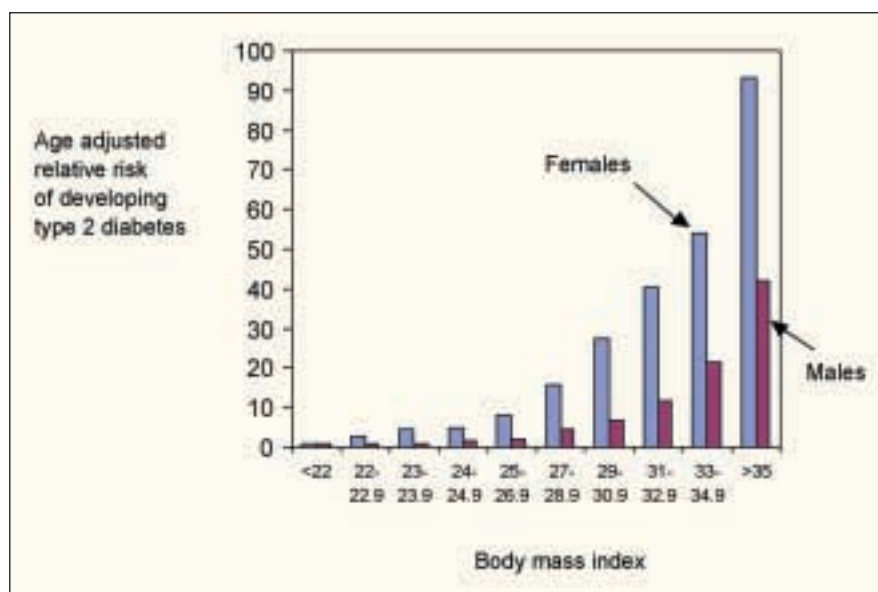


Figure 2. The risk of developing type two diabetes in women and men (age adjusted) as a function of body mass index. Risk is expressed relative to the risk for someone of BMI=22. (Data for females from Colditz *et al.* (1996) *Arch. Int Medicine*, **122**, 431–4 and for males from Chen *et al.* (1994) *Diabetes care*, **17**, 961–9.) In both sexes, type two diabetes risk increases enormously with increasing body mass index but the effect is more profound in females than males.

serious of which is sleep apnea. In this condition, subjects literally stop breathing while they are asleep, resulting in dangerous build-up of oxygen debt. Studies of patients admitted to obesity clinics reveal that obese people are not only more likely suffer from these major debilitating diseases, but they are also more likely to be depressed and taking antidepressant medications, suffer problems with their joints and suffer ailments that one would not immediately associate with obesity – such as skin disorders.

The cut-off points for overweight, at a BMI of 25, and for obesity, at a BMI of 30, are not, therefore, just convenient markers on the continuous scale of body fatness, but real indicators of the initial shallow and subsequent dramatic rise in mortality risk as body fatness increases. If your body mass index is greater than 25 then you have a statistically significant increased risk of mortality. If you are obese, with a BMI above 30, then on average your expected lifespan is reduced by a full nine years compared with somebody with a BMI of 20–25 (National Audit Office report, 2001). Premature mortality due to obesity-related illnesses in the UK accounts for about 30 000 deaths annually (lung cancer deaths are around 33 000), while in the USA the figure is about 10 times greater at 300 000 premature deaths each year. Put another way, in the 15 minutes it will take you to read this article nine people in the USA, and one person in the UK, will have died as a direct consequence of obesity related illnesses.

Trends in the prevalence of obesity

The prevalence of obesity and being overweight has increased dramatically in the last 30–50 years. In 1980, the percentage of the UK population that was classed as obese amounted to seven per cent of the population. By 2000, this had increased to around 20%, a threefold expansion in the obese population (Figure 3). Overweight subjects comprised about 20% of the 1980 population, but by 2000 this was about 45%. In combination then, obese and overweight persons comprise the majority of contemporary UK society.

In the United States, the situation is very similar – although the progression of obesity is about three to four years ahead of the problem in the UK. Figures from the Center for Disease Control in Atlanta, Georgia, show that

the prevalence of obesity has expanded progressively across almost the entire US mainland so that now almost all the US states have a prevalence between 20 and 24% (Figure 4). In some sub-populations the problem is worse than in others. Blacks in the USA appear to be particularly susceptible to the problem of obesity, and the prevalence across the entire US in black populations runs at about five per cent higher than white populations in the same areas. Socio-economic class is also a correlated factor to development of obesity in both the USA and UK. The lowest educated groups have a prevalence of obesity that runs about five per cent higher than more educated sub-populations.

Similar patterns of increases in the levels of obesity have been reported in almost all westernised societies. In addition, in the past decade, there are signs that this problem has achieved truly global distribution, with many Asian, South American and African nations also reporting that rates of obesity are increasing rapidly. Perhaps most worrying is the dramatic increase in rates of overweight and obese children. This increase is so great that the age of first occurrence of diseases like type two diabetes has steadily fallen, so that now there are records of this disease developing in teenagers. Indeed the decline in age of onset has been so great that it is no longer appropriate to call type two diabetes 'adult onset' diabetes.

The health consequences of obesity have profound economic ramifications. These have generally been partitioned into direct healthcare costs and costs that accrue to the wider economy because of time and productivity lost to sickness and premature mortality. In the UK, these costs were quantified by the National Audit Office (figures for 2000, published 2001) to be about £500 million annually in direct healthcare costs to the National Health Service. The additional costs to the wider economy were quantified at around two billion pounds. I recently spoke with a chairman of a National Health Trust who considered that, if the expansion of obesity continued at its present rate, by 2010 the entire resources of his trust would be soaked up in the treatment of its consequences. In the USA, the total economic costs of obesity in 1997 were estimated at around US\$97 Bn annually. Similar data are available for most western societies, which indicate that the current costs of obesity generally run at about five to eight percent of health care spending.

The good news is that the effects of obesity on health are not permanent but can be reversed if the person in question loses weight. This is important, because it is not entirely clear yet what the mechanisms are by which obesity predisposes a person to disease.

Based on the correlative evidence alone it could be possible that obesity does not cause the elevated risk of disease, but it is rather a consequence of a genetic pleiotropy. That is, a genetic problem leads a person not only to develop obesity, but the same genetic problem, in association with a western lifestyle, independently causes the disease risks. In this latter case, simply reducing the level of body fatness in a person would do nothing to the underlying cause of the elevated risk of disease. However, several recent studies have consistently shown improvements in associated health outcomes for people who were obese but have sustained weight loss for protracted periods. It

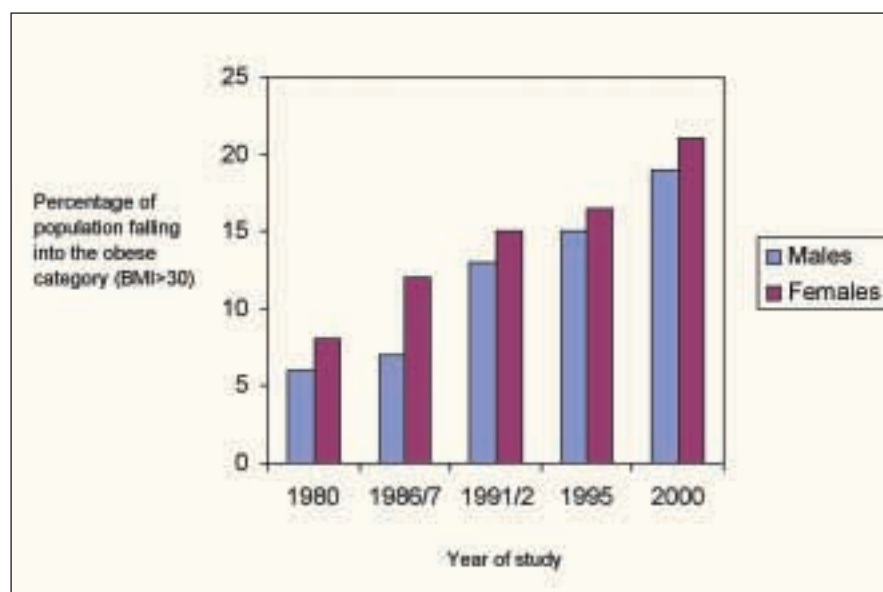


Figure 3. Prevalence of obesity (BMI > 30) in England between 1980 and 2000 for both males and females. Data from various sources.

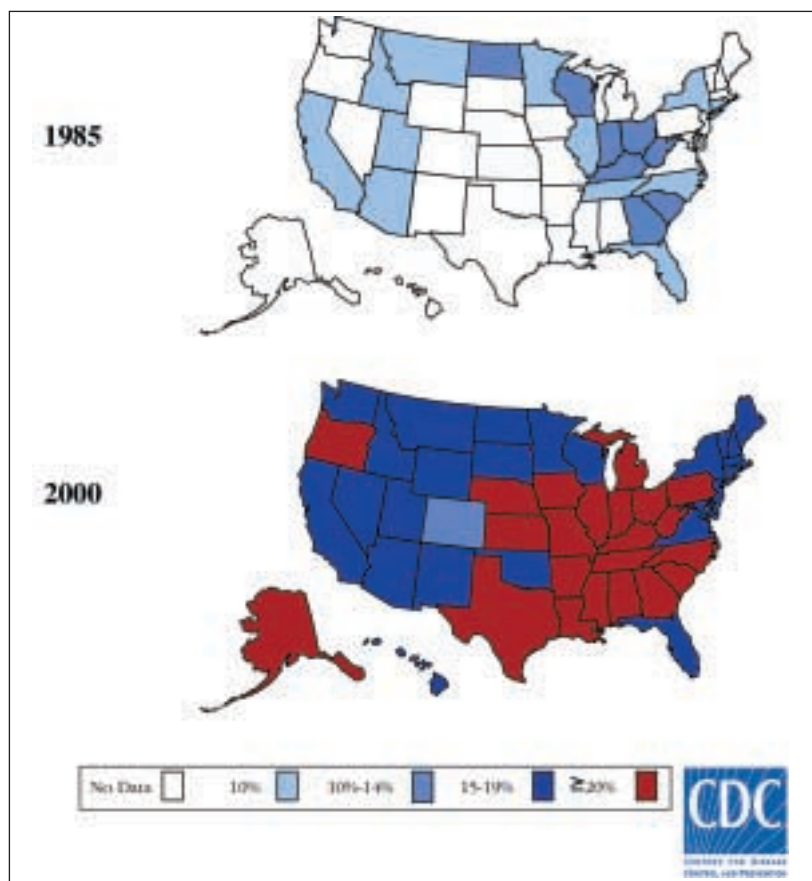


Figure 4. Maps showing the prevalence of obesity in the United States of America in 1985 and 2000 (maps provided by the Center for Disease Control in Atlanta Georgia and used with permission). (Data from Mokdad et al. (2001) *J Am Med Assoc*, **286**, 10.)

would appear that it is obesity itself that causes the elevated disease risks and not a shared underlying problem.

The mechanisms by which obesity leads to the development of disease are an area of very active investigation.

The argument being that, since it is not obesity itself that is the issue, but the health problems obesity generates, if we understand the causal nature of the link between obesity and these health problems, we might then be able to develop therapies that break the link. This approach has some attractive features to it because it means people could continue to pursue a western lifestyle and all the positive things that includes, without any of the negative consequences.

There are two basic alternatives that have been proposed to link obesity with diabetes. The first suggests that since obese people have much higher circulating levels of free-fatty acids, these might compete with circulating glucose in muscles. This leads to persistently elevated circulating glucose levels, elevated insulin secretion and ultimately insulin resistance. The alternative suggestion is that some molecules produced by fat tissue actively interact with insulin to generate the insulin resistance or promote insulin sensitivity. Some important products of adipose tissue in this respect are tumour necrosis factor-alpha (TNF α) and adiponectin. A novel compound, discovered in 2001 and produced by adipose tissue, was called resistin and it generated a brief surge of interest since it appeared to also directly affect insulin resistance in rodents. However, interest in this compound has now waned as it does not appear to be produced by human adipose tissue.

Blocking the signals that link obesity to diabetes may be an effective therapy for obesity-mediated diabetes, but this approach is likely to only address each disease consequence one at a time. Hence while it is a valid research strategy, a much more useful approach is to actually try to solve the root cause itself and thus eliminate all the disease consequences at once

– approaches I will discuss in the following two articles in this series.

Despite all the medical evidence suggesting associations between obesity and health, there are some groups who believe that the obesity problem is an issue of personal freedom and choice. These groups promote the notion that obese people (particularly women) should be proud of their body images and should not feel shoehorned by society into conforming to an 'ideal' body pattern that doesn't suit them (Box 1). Perhaps the strongest argument to counter these claims is the fact that obesity shows little sex biased differences. In fact, slightly more men than women in the UK are overweight, but slightly more women than men are obese. At the very least, these personal freedom notions undermine the importance of the health issue. At worst, they positively promote women in particular to adopt or sustain lifestyles that are detrimental to their

Box 1. Obesity and personal freedom

The whole debate about obesity as an issue of personal freedom started in the late 1960s and early 1970s, before we were fully aware of the links between obesity and health problems. At that time, criticisms were raised about the promotion by the fashion industry of slenderness as the beautiful ideal (a criticism that has been reiterated recently amid suggestions that this promotion encourages impressionable teenagers to develop eating disorders such as anorexia and bulimia nervosa). The famous quote that 'you can never be too rich or too thin' perhaps crystallises this concept. In particular during the 1970s, several books such as *Fat is a feminist issue* by Susie Orbach and *The tyranny of slenderness* by Kim Chernin suggested that women were being encouraged to be thin to conform to an ideal promoted by the men who controlled the fashion industry. Consequently, breaking this domination, by eating to achieve a non-conventional body weight was a method of expressing ones feminist credentials.

The evidence in this regard was promoted by the fact that, looking beyond western society and also looking at western society in the distant past provided alternative ideals that were regarded as beautiful. In particular, it is often noted that the paintings by artists such as Rubens frequently depict feminine subjects that have body mass indices that would certainly class them as overweight if not obese. Even as recently as the 1950s, it was noted that icons of beauty such as Marilyn Monroe wore dress sizes that would be considered unacceptable by the modern fashion industry. These arguments about the ephemerality of male notions of beauty therefore led to the suggestion that women should escape the contemporary fashion – *The tyranny of slenderness* (which would in any case only be a transient phenomenon) and eat to please themselves.

This notion has not been completely dispelled by the modern knowledge of the very clear links between body fatness and the risk of developing grave life-threatening illnesses. Magazines such as *Dimensions* (www.dimensionsmagazine.com) promote strongly the idea that obesity is not a health issue but an issue of personal freedom. This year, Susie Orbach has a sequel to her classic *Fat is a feminist issue*, which makes updated personal freedom claims over the whole issue of eating and body weight. It suggests that simply eating whatever we wish, whenever we feel hungry, and until we feel full, is the most sensible way to eat.

health. Obesity is a serious health threat costing western economies billions of pounds and blighting the lives of millions of people (male and female), leading them into serious illness and premature mortality. It is the job of biologists to further our understanding of this phenomenon and devise solutions to it.

In the next two articles in this series I will explore how our understanding of the biological basis of the regulation of body weight has blossomed in the past decade, principally through the use of animal models and molecular biology. In the final article, I will detail, in the light of this knowledge, why contemporary solutions to the problem are failing to stem the tide of obesity. And how, in the coming decades, we will potentially use this knowledge to devise sophisticated interventions that will alleviate the problem, and save millions of people from illness and premature death.

Further reading

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Websites

www.ietf.org

International Obesity Task force

www.abdn.ac.uk/acero

Aberdeen Centre for Energy regulation and obesity

www.nutrition.org

British Nutrition Foundation

www.aso.org

UK Association for the study of obesity

www.naaso.org

North American Association for the study of obesity

www.obesity.org

American Obesity Organisation

www.obesity.chair.ulaval.ca

University of LaVal, Canada, Obesity resource

Euroobesity-online

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