

Obesity in women – a life cycle of medical risk

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Abstract

Obesity can have an impact on health at each stage of a woman's life cycle. In young women, obesity has an impact on psychosocial health and, as they grow older, on their reproductive health. Obesity also imposes a number of serious risks during pregnancy. In older women, obesity is associated with the emergence of a number of related chronic diseases, such as type 2 diabetes and cardiovascular disease and an increased risk for many cancers. Of concern in the elderly is the increasing evidence that obesity is an independent risk factor for dementia and Alzheimer's disease. Obesity also has a marked impact on life expectancy. The medical risks associated with obesity in women are important for the woman's future generations. There is emerging evidence that nutrition during fetal and early life can influence risk for obesity and chronic diseases.

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Introduction

It is well known that obesity is a serious health problem that poses a significant challenge to both individual and public health. The latest data from the World Health Organization show that worldwide there are some 1.6 billion adults who are overweight, with a body mass index (BMI) above 25 kg/m². Of these, at least 400 million adults are obese, with a BMI above 30 kg/m². The latest prevalence figures for obesity within the European region confirm that in most countries, the number of obese women surpasses the number of obese men, sometimes as much as 2 to 1.

However, what is not generally recognised is the fact that obesity also has a greater impact on health outcomes for women than for men. This impact is seen in the physical, reproductive, psychological and social well-being of women compared to men.

One example is the well-known association between obesity and type 2 diabetes. What is rarely reported is the difference between men and women in the relationship between obesity and type 2 diabetes. The relative risk of developing type 2 diabetes for a woman with a BMI of 30 kg/m² is 28-fold compared to that of a woman with a BMI < 22 kg/m².¹ In contrast, the difference in risk between men with similar BMI values is sevenfold.²

Adolescence and young adulthood

Obesity can have an adverse impact on health at each stage of a woman's life. In young women, obesity has an impact on their psychosocial health and, as they grow older, on their reproductive health.

The social and economic consequences of obesity were demonstrated in a study of a representative sample of 10 039 American adolescent

and young adult men and women (aged 16 to 24 years). On follow-up seven years after the initial survey, women who had been overweight (defined as BMI above the 95th percentile for age and sex) at baseline had indices of socio-economic status that were worse than those of women of normal weight. The survey showed that these women were more likely to have had fewer years of education, to be living in poverty and to have lower household incomes, and that they were less likely to be married, independent of baseline socio-economic status and aptitude test scores.³ Furthermore, for each of these indices, the difference between overweight subjects and subjects of normal weight was more pronounced in women than in men (see Figure 1).

As women enter their childbearing years, obesity impacts on reproductive health. Obesity is associated with increased rates of infertility and risk for polycystic ovary syndrome (PCOS). The relationship between adolescent BMI and menstrual irregularity and ovulatory infertility was investigated in the Nurses' Health Study. The association between menstrual cycle irregularity from age 18 to 22 and BMI at age 18 was examined in the baseline cohort of over 116 000 women. Ovulatory failure was assessed in a case-control study within the main study: the cases were 2 527 married nulliparous nurses who were unable to become pregnant for at least one year because of ovulatory disorder (assessed by questionnaire and in some cases by review of medical records); controls were 46 718 married parous nurses with no history of infertility. As shown in Figure 2, as BMI at age 18 exceeded 25 kg/m², the prevalence of menstrual cycle irregularity increased and the risk of ovulatory failure increased.⁴

In women with PCOS and in women without PCOS, increased BMI was associated with an increased relative risk of infertility.⁴

Figure 1: Young adulthood
Social and economic consequences of obesity
Effect of weight status at age 16-24 over 7 years of follow-up

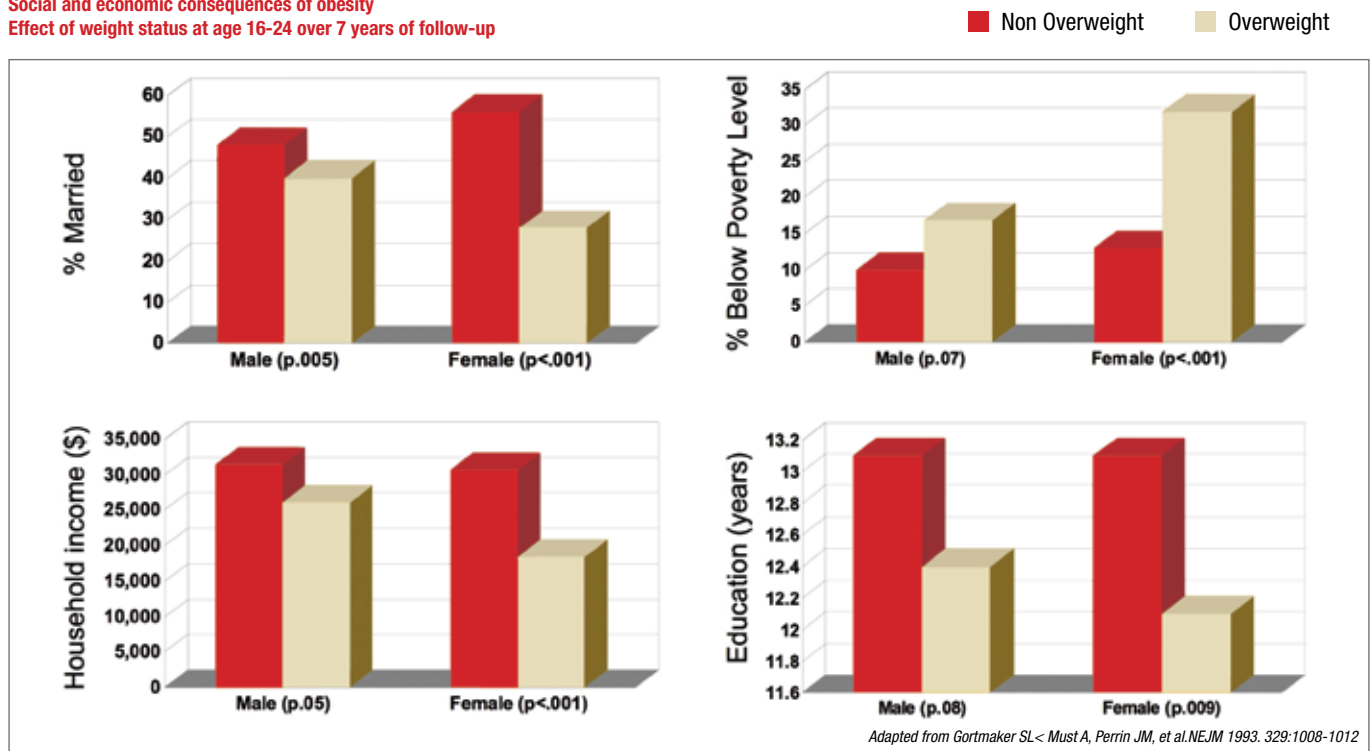
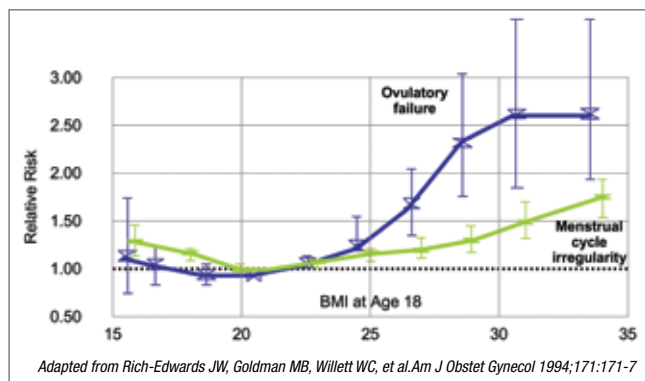


Figure 2: Relative risk of menstrual cycle irregularity and ovulatory failure at different Body mass indices (BMI)



and there is an increased risk of congenital abnormalities, foetal distress, perinatal morbidity and mortality.⁵

In 2003, the US Behavioral Risk Factor Surveillance System assessed the rate of obesity in women aged 18 to 44 years at 19.6%.⁶ This is likely to under-report the true rate of obesity, as the data come from a telephone questionnaire survey, in which respondents are likely to over-estimate their height and under-estimate their weight. Obesity is now such a widespread problem that the Institute of Medicine in the USA⁷ has made recommendations for weight gain during pregnancy for normal-weight, overweight and obese women (see Table I). There is no comparable uniform recommendation across the European Union for weight gain in pregnancy.

Intergenerational programming

Table I: Institute of Medicine recommendations for weight gain during pregnancy

BMI (kg/m ²)	Recommended gain
< 18.5	12.5 – 18 kg
18.5 – 24.9	11.5 – 16 kg
25 – 29.9	7 – 11.5 kg
> 30	7 kg

Abbreviation: BMI: body mass index

One emerging issue of great concern in reproductive health and obesity is the intergenerational implications of childbearing in obese women. There is evidence from epidemiologic and animal studies supporting the nutritional programming of obesity and other chronic diseases in foetal and early life. Clearly, since fetuses of both genders are subject to the intrauterine environment, obesity in women in this context can impact both genders.

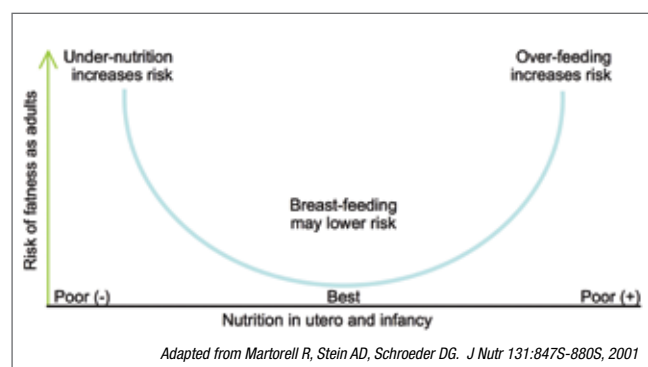
Figure 3 shows a paradigm for intergenerational programming, highlighting how the mother’s nutritional status can influence the fetus as well as the development of obesity in adult life.⁸

Obesity in pregnancy

Obesity poses a number of serious risks during pregnancy. In early pregnancy, medical complications in obese women include increased twinning and a higher rate of miscarriage; in addition, ultrasound can be difficult. During pregnancy, higher rates of pregnancy-induced hypertension and pre-eclampsia, higher rates of gestational diabetes and higher rates of venous thromboembolism are all associated with obesity. During delivery, obese women are likely to have higher rates of dystocia and, therefore, of assisted delivery and vaginal tears. There are also associated technical difficulties, with higher rates of infection, bleeding and thrombosis compared to non-obese women who have assisted deliveries and Caesarean sections. Anaesthesia poses a further challenge in obese mothers.⁵

After delivery, obese women are at increased risk for postpartum haemorrhage and infection, and also at increased risk for venous thromboembolism. Obesity in pregnancy also poses serious health risks for the fetus. Impaired glucose tolerance (IGT) in pregnant women can lead to macrosomia. There is also a risk of birth injury,

Figure 3: Paradigm for intergenerational programming



The implication is that both under-nutrition and over-nutrition – associated with gestational diabetes, maternal obesity and excessive weight gain – increase the infant's risk of later excessive body fat and the subsequent risk in adulthood of developing obesity, diabetes, hypertension and cardiovascular disease (CVD).

Gestational diabetes mellitus occurs in around 4% of all pregnancies. In overweight women, the prevalence increases significantly to 17%. Risk estimates of type 2 diabetes after gestational diabetes vary from 17 to 63% over 5 to 16 years, depending on the ethnic background of the study population and the sensitivity of the detection method used for both type 2 diabetes and gestational diabetes.^{9–11}

The emerging evidence from animal studies and human observational studies indicates a need for concern about maternal-foetal interaction and also the interaction between mother and infant in early life. This appears to be a critical period of programming that can lead to the development of increased risk for chronic disease. In a study designed to assess the hypothesis that a long-term postnatal development may be modified by metabolic experiences in utero, children of women with pregestational diabetes and gestational diabetes were reviewed annually to measure the prevalence of impaired glucose tolerance (IGT).¹² IGT was 1.2% at < 5 years, increasing to 5.4% at 5 to 9 years, and by the age of 10 to 16 years, 19.3% of the children of diabetic mothers had IGT, compared to around 2% in a control group. In other words, the children had 10 times the risk of IGT at a preadolescent age.

A relationship has also been observed between prevalence of obesity in children and their mothers' metabolic status. Children whose mothers had diabetes during pregnancy had a higher prevalence of obesity than children whose mothers had IGT (prediabetes) or were non-diabetic during pregnancy. At 15 to 19 years, 58% of the children of diabetics weighed 140% or more of their desirable weight compared to 17% of the children of non-diabetics and 25% of the children of women with prediabetes.¹³ The children of diabetic mothers were significantly more obese than those of non-diabetic mothers, regardless of maternal BMI. For the children of non-diabetic or prediabetic mothers, the relationship was also evident when the data were analysed according to the BMI of the mother; for example, in the 15 to 19 age group, the prevalence of obesity ranged from 19 to 54% according to the BMI of the mother, with the higher BMIs being associated with higher rates of obesity in the children.

It is becoming apparent, therefore, that a woman's nutritional and metabolic status during pregnancy can programme her daughter or son, and in the case of the daughter when she reaches childbearing age, she can in turn impose an effect on the next generation. Therefore, obesity in pregnancy may affect several generations to come and should therefore be avoided.

Mature and ageing women

As women age, one sees the emergence of obesity-related chronic diseases, such as type 2 diabetes, hypertension and CVD.¹⁴ There is also increased risk for several of the major cancers.

CVD now ranks as the world's top cause of death, causing one-third of all deaths globally.¹⁵ It is also the largest single cause of death among women worldwide. In Western countries, more women than men die every year of CVD. However, across all cultures and settings, men outnumber women in the ratio of three or four to one regarding premature (that is before 75 years of age) mortality from coronary heart disease.¹⁶ Studies have identified a number of factors that may protect women against CVD, with the greatest emphasis on

- higher high-density lipoprotein (HDL) cholesterol
- greater increase in HDL cholesterol in unfavourable dietary circumstances, such as when there is more than 30 to 35% total fat intake in the diet
- pear-shaped rather than apple-shaped obesity
- better lifestyle
- lesser sympathetic response to stress
- lower blood viscosity, and
- more favourable values for most classical and novel CVD risk factors

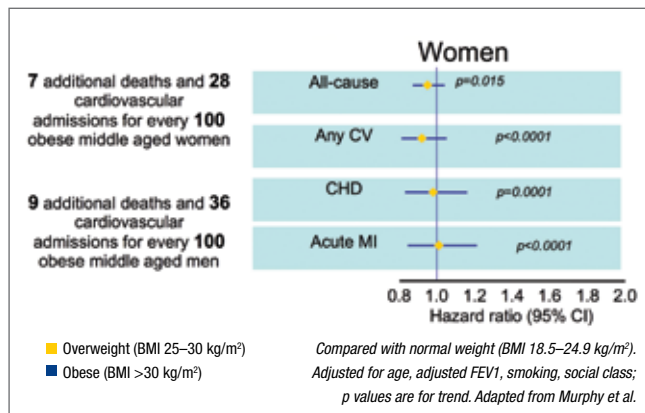
However, ageing gradually erodes the female advantage. Epidemiological studies have shown that the prevalence and incidence of CVD among both men and women increase with age,¹⁷ and that the gender difference narrows at older ages. An increase in risk-factor levels is associated with the age-related increase in CVD in both sexes, but this increase is larger in women.¹⁸ Difference in serum total cholesterol level, blood pressure, BMI and diabetes prevalence have been shown to explain about 50 to 60% of the age-related increase in coronary heart disease risk in women, compared to only about one-third of the increase in men.¹⁸

Recent data from the Renfrew-Paisley study, which recruited 15 406 individuals in Scotland between 1972 and 1976, serve to emphasise the importance of obesity as a CVD risk factor in women.¹⁹ In this analysis, mortality and other outcomes after 20 years were calculated according to baseline BMI. While being overweight did not increase the relative risks for all-cause mortality, cardiovascular mortality or coronary disease, all of these were very clearly increased in obese individuals (see Figure 4). In terms of absolute rates of CVD, the Renfrew-Paisley study showed that after adjusting for age, forced expiratory volume in 1 second, smoking and social class, compared to women of normal weight (BMI 18.5 – 24.9 kg/m²), for every 100 obese women followed for 20 years there were seven additional cases of fatal cardiovascular hospitalisations attributable to obesity. The equivalent numbers among men were similar: nine additional cases of fatal CVD and thirty-six additional cardiovascular hospitalisations attributable to obesity. This study therefore also emphasises the magnitude of the health threat posed by obesity.

The increased risk for cancer associated with obesity was illustrated in the American Cancer Society study, which followed over 900 000 individuals between 1982 and 1998. Increased body weight was associated with increased death rates for all cancers combined, and for cancers at multiple specific sites. Cancer in women showed significant trends of increasing risk with higher BMI for death from cancers of the breast, uterus, cervix and ovary.²⁰

Of concern in the elderly is the risk that obesity imposes for impaired cognitive function and Alzheimer's disease, and the negative implications that obesity has in terms of life expectancy.

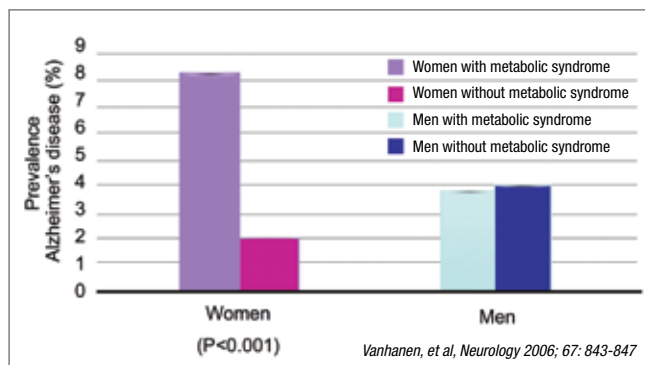
Figure 4: 20-year mortality risk associated with obesity in the Renfrew-Paisley study show that compared with normal-weight individuals, (BMI 18.5 – 24.9 kg/m²), obesity (BMI ³ 30 kg/m²) was associated with an increased adjusted risk of all-cause mortality, cardiovascular death (CV), coronary heart disease (CHD) and acute myocardial infarction (MI) compared with women of normal weight. Being overweight (BMI 25-30 kg/m²) was not associated with an increased risk



A population-based study of 959 men and women aged 69 to 78 years found a strong association between the metabolic syndrome (defined according to National Cholesterol Education Program criteria) and the risk for Alzheimer's disease in women (see Figure 5). The prevalence of probable or possible Alzheimer's disease was 8.3% in women with the metabolic syndrome and 1.9% in women without the metabolic syndrome. The association was not demonstrated in men, in whom the prevalence was 3.8 and 3.9% respectively.²¹ However, the sample included few cases of Alzheimer's disease (45 overall) and it also had a smaller sample of men (337 compared to 622 women) and, therefore, the validity of the data regarding men is not as strong as that regarding women.

There is emerging evidence that obesity is also an independent risk factor for cognitive dysfunction and Alzheimer's disease. Cross-sectional and longitudinal studies have demonstrated an increased risk for dementia and Alzheimer's disease in obese individuals. In one study of 1 449 individuals, obesity (BMI > 30 kg/m²) at midlife was associated with increased risk of dementia and Alzheimer's disease in later life, after adjusting for socio-demographic variables.²² Midlife obesity, high total cholesterol and high systolic blood pressure were all significant risk factors for dementia, and had additive effects.

Risk of Alzheimer's disease in elderly patients, with or without the Metabolic syndrome



In another study, 392 adults aged 70 without dementia were followed up for 18 years.²³ The findings suggested that overweight at age 70 is a risk factor for dementia, particularly Alzheimer's disease, in women. Dementia risk was associated with a BMI \geq 25 kg/m². BMI was, on average, 3.6 higher among those who developed Alzheimer's

disease than those who did not. A similar association was not found in men. In addition, at least one longitudinal study has demonstrated that overweight and obesity are associated with abnormalities in areas of the brain that are associated with Alzheimer's disease, with temporal lobe brain atrophy being observed on computerised tomography scans.²⁴

Impact on life expectancy

Obesity and overweight in adulthood have been reported to be associated with important reductions in life expectancy. Data from the longitudinal Framingham Heart Study were analysed to assess the implications of obesity (as measured by BMI) at age 40 on life expectancy. The analysis showed that in 40-year-old non-smokers (without previously diagnosed CVD) obesity was associated with 7.1 years of life lost in women and 5.8 years of life lost in men, compared to people of normal weight at age 40.²⁵ The difference between men and women was not statistically significant, but the trend to increased effect for women was of interest. With the double burden of obesity and smoking, obese female smokers lost 13.3 years and obese male smokers lost 13.7 years compared to non-smokers of normal weight.²⁶

Summary

Obesity has negative consequences for women's health throughout the life cycle, with important psychosocial, economic and biologic implications. In addition, obesity in women has the potential of having an intergenerational impact if overweight and obese mothers transmit risk for chronic disease during their pregnancies.

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