Physical and Psychological Consequences of Weight Gain

Ichiro Kawachi, M.D., Ph.D.

Obesity and overweight are clearly associated with many serious conditions, including type II diabetes mellitus, hypertension, and coronary heart disease. Excess weight also increases the risk of death. Recent evidence suggests that weight gain itself, even if persons remain within the "normal" weight range, also increases the risk of medical illnesses and premature death. Persons who gain 5.0 to 7.9 kg (11 to 17.3 lb) as adults are 1.9 times more likely to develop type II diabetes mellitus and 1.25 times more likely to develop coronary heart disease than those who lose weight or maintain a stable weight after age 18 years. Gaining 11 to 20 kg (24.2 to 44 lb) or more in adulthood increases the risk of ischemic stroke 1.69 to 2.52 times. The relationship between weight gain and breast cancer has been difficult to study, primarily because postmenopausal hormone replacement therapy can mask the effect of weight gain on cancer risk. Accordingly, weight gain in adulthood has been associated with an increased risk of breast cancer only among women who have never used hormone replacement therapy. In addition to its adverse effects on disease outcomes, weight gain also impairs physical functioning, reduces quality of life, and is associated with poor mental health. These psychological and mental health consequences of weight gain can become an added burden for patients with schizophrenia and other mental disorders.
(J Clin Psychiatry 1999;60[suppl 21]:5–9)

Some 32 million women and 26 million men—or nearly one third of the adult population in the United States—are overweight, meaning they weigh at least 20% more than their desirable weight. During the past 15 years, the average weight of American adults has increased by 3.6 kg (7.9 lb).[1] Obesity and overweight are associated with a wide range of medical problems, including hypertension, type II diabetes mellitus, coronary heart disease, gallbladder disease, breast cancer, endometrial cancer, colon cancer, and osteoarthritis.[2] The medical costs of obesity (defined as a body mass index ≥ 29 kg/m^2) arising from treatment of these conditions alone amounted to an estimated $51.64 billion in 1995, or about 5.7% of national health care expenditures.[3] The 39.2 million lost work days associated with obesity was estimated to have cost an additional $3.9 billion in foregone productivity.[3] These cost estimates are conservative because they do not include the excess illness burden associated with being overweight (as opposed to being obese), nor do they take into account the disease burden resulting from weight gain within the "normal" range.

From the Department of Health and Social Behavior, Harvard School of Public Health, Boston, Mass.

Presented, in part, at the symposium "Weight Gain Associated With the Use of Psychotropic Medications," which was held August 26, 1998, Boston, Mass., and supported by an unrestricted educational grant from Janssen Pharmaceutica, L.P.

Reprint requests to: I. Kawachi, M.D., Department of Health and Social Behavior, Harvard School of Public Health, 677 Huntington Ave., Boston MA 02115.

PITFALLS IN EPIDEMIOLOGIC STUDIES OF WEIGHT GAIN

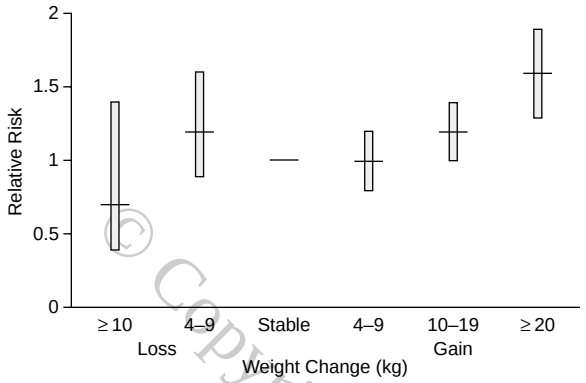
For data on the relationship between weight gain and ill health to be accurate and valid, investigators must overcome several potential pitfalls of epidemiologic studies, including reverse causation, confounding, and statistical overadjustment.

Reverse causation refers to the possibility that prior illness might have caused the weight change, rather than weight change causing illness. For example, clinical depression can lead to weight gain, so investigators must exclude prior depression when examining weight gain and changes in mental health. Similarly, many diseases can cause weight loss, which might lead investigators to erroneously conclude that loss of weight is associated with ill health.

Confounding variables can bias results, again leading to erroneous conclusions if these confounders are not adequately addressed. For example, cigarette smokers tend to gain less weight over time than do nonsmokers,[4] yet cigarette smoking clearly causes ill health.[5] If investigators do not adjust for confounding by smoking status, their results will underestimate the excess risks of ill health associated with weight gain.

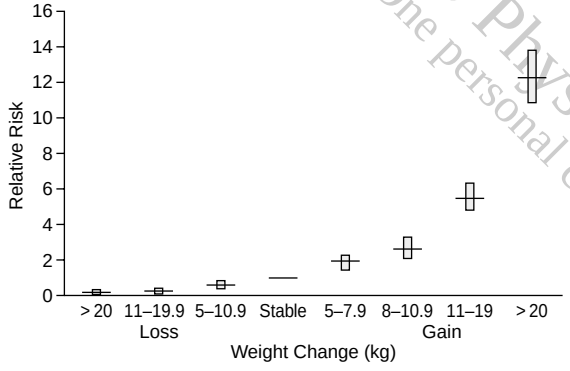
Researchers also must be wary of possible statistical overadjustment. Inappropriate statistical adjustment typically occurs when investigators adjust for the biological effects of weight gain, such as hypertension or hyperglycemia, when analyzing the relationship between weight gain and risk of coronary heart disease (CHD). Both hy-

Figure 1. Weight Change Since Age 18 Years and Relative Risk of Death From All Causes in Women Who Never Smoked[a]



[a]Data from reference 8. p < .001 for trend across categories of weight change.

Figure 2. Weight Change Since Age 18 Years and Relative Risk of Diabetes Mellitus[a]



[a]Data from reference 11. p < .001 for trend across categories of weight change.

pertension and hyperglycemia are variables in the causal pathway leading from weight gain to CHD, and controlling for these conditions is equivalent to adjusting for the mechanisms by which weight gain is believed to cause CHD.

WEIGHT GAIN AND TOTAL MORTALITY

The relationship between excess body weight and increased risk of death was first noted by the life insurance industry.[6] Since then, an impressive number of studies have corroborated this relationship.[7] In addition, the Harvard Nurses' Health Study[8] provides evidence of an association between weight change and increased risk of death. The Nurses' Health Study is an ongoing cohort study of 121,700 female registered nurses residing in the United States. It was established in 1976 to examine predictors of morbidity and mortality.

In one report from the study based on 12 years of follow-up,[8] the authors examined the association between weight change and mortality after excluding women with prior illness at baseline (to avoid reverse causation) and stratifying the remaining women according to smoker status (to prevent bias from confounding). As shown in Figure 1, women who had never smoked and reported gaining 10 kg (22 lb) or more since age 18 years were at significantly increased risk of death in middle age ($p < .001$ for trend across categories of weight change). Women who gained 20 kg (44 lb) or more since age 18 years were 1.6 times (95% confidence interval [CI], 1.3 to 1.9) more likely to die from all causes than those who maintained a stable weight (defined as within ± 5 kg [11 lb] of weight at age 18 years) as adults. Patients with significant weight gain as adults were at particularly high risk of death from CHD and all cancers.[8]

WEIGHT GAIN AND INDIVIDUAL CAUSES OF MORBIDITY

Hypertension

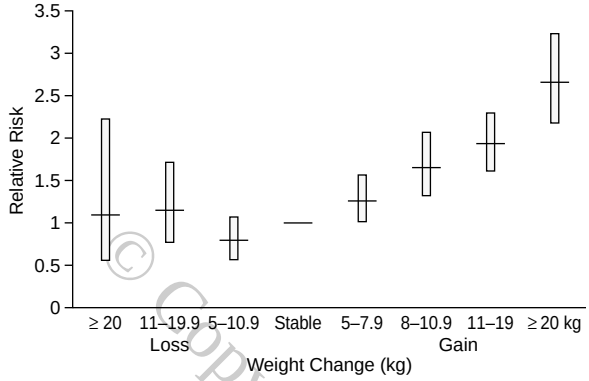
In the Framingham Heart Study, weight gain was clearly associated with increases in blood pressure; a 15% gain in weight increased systolic blood pressure by 18%.[9] In the Nurses' Health Study, even fairly modest degrees of weight gain were associated with measurable increases in the risk of hypertension.[10] The relative risk of developing hypertension among women who gained 2.1 to 4.9 kg (4.6 to 10.8 lb) over 2 or more years was 1.38 (95% CI, 1.28 to 1.48) compared with women who maintained their weight within ± 2 kg (4.4 lb). Twenty-one percent of the new cases of hypertension in this cohort were attributable to weight gain occurring during midlife.[10]

Several biologically plausible mechanisms may explain how increased body weight is related to an increased risk of hypertension. These mechanisms include enhanced sympathetic nervous system activity, increased plasma renin activity, and increased insulin resistance (which in turn enhances renal sodium reabsorption).[2]

Type II Diabetes Mellitus

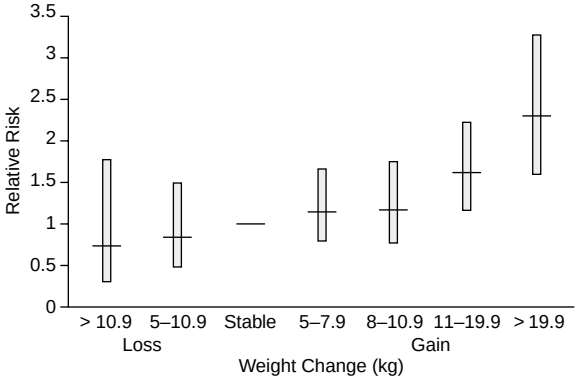
One of the diseases most strongly and consistently associated with overweight and weight gain is type II, or non-insulin-dependent, diabetes mellitus. Using data from the Nurses' Health Study, Colditz et al.[11] reported that women who gained 5.0 to 7.9 kg (11 to 17.3 lb) as adults were 1.9 times (95% CI, 1.5 to 2.3) more likely to develop type II diabetes than those who maintained a stable weight in adulthood (Figure 2). Until recently, a weight gain of up to 9 kg (19.8 lb) after age 35 years was sanctioned as falling within the desirable range.[12] Thus, a person who gained 7 kg (15.4 lb) as an adult would remain within the desirable range of weight gain according to 1990 guidelines[12] but would increase his or her risk of diabetes 2-fold.

Figure 3. Weight Change Since Age 18 Years and Relative Risk of Coronary Heart Disease[a]



[a]Data from reference 14. $p < .001$ for trend across categories of weight change.

Figure 4. Weight Change Since Age 18 Years and Relative Risk of Ischemic Stroke[a]



[a]Data from reference 16. $p < .001$ for trend across categories of weight change.

For people who gain more than 9 kg (19.8 lb) as adults, the risks are even greater. Women in the Nurses' Health Study who gained 20 kg (44 lb) or more in adulthood were 12.3 times (95% CI, 10.9 to 13.8) more likely to develop diabetes than those who kept their weight stable.[11] Similarly, in the Rancho Bernardo Study, Holbrook et al.[13] reported that a weight gain of 4.5 kg (10 lb) or more between ages 40 and 60 years significantly increased the risk of diabetes in both men (relative risk, 1.4; $p < .05$) and women (relative risk, 1.7; $p < .02$).

Coronary Heart Disease

Among the 11,818 women aged 30 to 55 years enrolled in the Nurses' Health Study who were followed for 14 years, CHD developed in 1292.[14] Women who gained weight from age 18 years until the beginning of the study follow-up period (in 1976) were at significantly greater risk for CHD than those who maintained a stable weight (within ± 5 kg [11 lb] of their weight at age 18 years). The relative risk of CHD was 1.25 (95% CI, 1.01 to 1.55) for women who gained 5.0 to 7.9 kg (11 to 17.3 lb), 1.64 (95% CI, 1.33 to 2.04) for an 8.0 to 10.9 kg (17.6 to 24.0 lb) gain, 1.92 (95% CI, 1.61 to 2.29) for an 11.0 to 19.0 kg (24.2 to 41.8 lb) gain, and 2.65 (95% CI, 2.17 to 3.22) for a gain of 20 kg (44 lb) or more (Figure 3). For each kilogram of weight gained, the risk of CHD increased by 3.1% (95% CI, 2.6 to 3.6). The excess risk of CHD associated with weight gain was apparent even among women whose body mass index remained within the normal range (between 18 and 25 kg/m^2).[14] Twenty-seven percent of the overall incidence of CHD in this cohort could be attributed to weight gains of 5 kg (11 lb) or more after age 18 years. These findings are strengthened by the design of the Nurses' Health Study. Investigators excluded women with preexisting coronary heart disease at baseline and extensively controlled for potential confounding factors, including smoking status, menopausal status, use of postmenopausal hormone replacement therapy, body mass index at age 18 years, and parental history of heart disease.[15]

Without doubt, the association between weight gain and risk of CHD is partly mediated by the known links between weight gain and risk factors for CHD, such as hypertension and diabetes mellitus. Being overweight also is associated with lipid abnormalities, including high triglyceride levels and low high-density lipoprotein cholesterol levels,[15] which also increase the risk of CHD.

Stroke

Stroke has recently been added to the list of deleterious health outcomes associated with weight gain. Rexrode et al.[16] examined this association in a 16-year follow-up analysis of data from the Nurses' Health Study. Using multivariate analyses that adjusted for body mass index at age 18 years, they found that weight gain from age 18 years until the start of the study follow-up was associated with a relative risk for ischemic stroke of 1.60 (95% CI, 1.16 to 2.21) for a gain of 11 to 19.9 kg (24.2 to 43.8 lb) and 2.28 (95% CI, 1.59 to 3.26) for a gain of 20 kg (44 lb) or more ($p < .001$ for trend) (Figure 4). When the investigators statistically controlled for hypertension, diabetes, and hypercholesterolemia in the women who gained the most weight as adults, the relative risk of ischemic stroke decreased from 2.52 to 1.45, suggesting that these are the mechanisms by which weight gain increases the risk of stroke. Although weight change was not associated with an increased risk of hemorrhagic stroke ($p = .2$ for trend), a direct relationship was observed between weight gain and risk of total stroke ($p < .001$ for trend). An increased risk of stroke has also been reported for men who gain more than 9 kg (19.8 lb) as adults.[17]

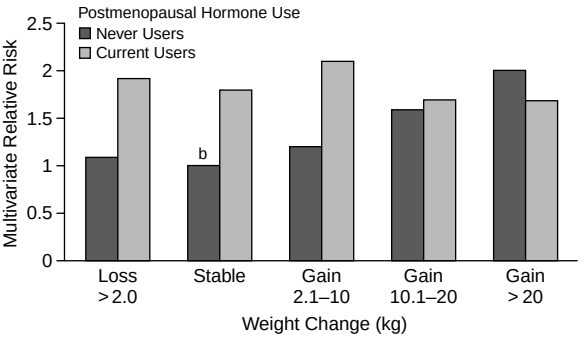
Breast Cancer

The relationship between weight, weight change, and breast cancer risk is complex. Among premenopausal

women, body weight is consistently inversely related to the risk of breast cancer,[18] meaning that overweight premenopausal women are at less risk than their healthy weight counterparts. This relationship might be explained by the greater frequency of anovulatory cycles among overweight women, which, in turn, lowers circulating levels of estradiol and progesterone. Among postmenopausal women, however, plasma estrogen levels are derived mainly from adipose tissue. Endogenous estrogen levels in overweight and obese postmenopausal women can be up to 50% to 100% higher than those in lean postmenopausal women.[19] Thus, it is somewhat puzzling why epidemiologic studies have not consistently found a positive relationship between overweight and increased risk of breast cancer.

The reason for this apparent paradox may lie in the use of hormone replacement therapy among postmenopausal women. The use of hormone replacement therapy, which is itself linked to an increased risk of breast cancer,[20] seems to mask the relationship between weight gain and breast cancer risk in postmenopausal women. In the Nurses' Health Study,[21] weight gain in adulthood among postmenopausal women was associated with an increased risk of breast cancer only among women who never used hormone replacement therapy. In these women, the relative risk of breast cancer was 1.99 (95% CI, 1.43 to 2.76) for those who gained more than 20 kg (44 lb) as adults ($p < .001$ for trend) (Figure 5). Among current users of hormone replacement therapy, no relationship between weight gain and increased risk of breast cancer was seen. Among premenopausal women in the Nurses' Health Study, there was a borderline statistically significant relationship between weight gain and a decreased risk of breast cancer ($p = .07$ for trend).[21]

Figure 5. Weight Change Since Age 18 Years and Relative Risk of Breast Cancer Among Postmenopausal Women Who Currently Use or Have Never Used Hormone Replacement Therapy[a]



[a]Data from reference 21.
[b]Reference group.

WEIGHT GAIN AND QUALITY OF LIFE

Increasing evidence suggests that being overweight and gaining weight have psychosocial consequences. Overweight and obese people are stigmatized and discriminated against in various areas of daily life, including education, employment, and health care.[22] Unfortunately, few studies have examined the consequences of weight gain on psychological well-being; most studies conducted to date enrolled obese patients who were already seeking treatment or had received counseling services. Rumpel et al.[23] are among the few investigators to examine the relationship between weight gain and psychological well-being in a nonobese population. In their study, based on data from 3747 women enrolled in the National Health and Nutrition Examination Surveys epidemiologic follow-up study, psychological health was assessed using the General Well-Being Scale.[24] Among both normal-weight and overweight women, those who gained 5 kg (11 lb) or more over a 10-year period were more likely to report lower overall well-being, as well as a higher negative affect and a lower positive affect (odds ratio, ~ 1.5).

Weight gain not only adversely affects psychological functioning but also impairs physical functioning. In the British Whitehall II Study, which enrolled 6895 men and 3413 women, Stafford et al.[25] reported that weight gain in adulthood increased the likelihood of being in the bottom quintile based on a validated physical functioning scale (the 10-item physical functioning subscale of the SF-36 Health Status Survey).

CONCLUSION

Obesity and overweight are established risk factors for morbidity and mortality. In addition, we are now finding that weight gain in adulthood also has physical and psychological consequences. The adverse effects of weight gain on mental health can become an added burden for patients with schizophrenia or other types of mental illness. A weight gain during adulthood of 10 kg (22 lb) or more, even among persons who remain within the "normal" weight range, increases the risk of a variety of illnesses, ranging from cardiovascular diseases to cancer, and compromises the patient's quality of life.

REFERENCES

1. Kuczmarski RJ, Flegal KM, Campbell SM, et al. Increasing prevalence of overweight among US adults: the National Health and Nutrition Examination Surveys 1960 to 1991. JAMA 1994;272:205–211
2. Pi-Sunyer FX. Medical hazards of obesity. Ann Intern Med 1993;119: 655–660
3. Wolf AM, Colditz GA. Current estimates of the economic cost of obesity in the United States. Obes Res 1998;6:97–106
4. Kawachi I, Troisi RJ, Rotnitzky AG, et al. Can physical activity minimize weight gain following smoking cessation? a prospective study. Am J Public Health 1996;86:999–1004
5. Kawachi I, Colditz GA, Stampfer MJ, et al. Smoking cessation in relation to total mortality rates in women: a prospective cohort study. Ann Intern Med 1993;119:992–1000

6. Society of Actuaries. Blood Pressure Study of 1979. Chicago, Ill: Society of Actuaries/Association of Life Insurance Medical Directors of America; 1980
7. Bray GA. Health hazards of obesity. Endocrinol Metab Clin North Am 1996;25:907–919
8. Manson JE, Willett WC, Stampfer MJ, et al. Body weight and mortality among women. N Engl J Med 1995;333:677–685
9. Kannel WB, Brand N, Skinner JJ Jr, et al. The relation of adiposity to blood pressure and development of hypertension: the Framingham Study. Ann Intern Med 1967;67:48–59
10. Huang Z, Willett WC, Manson JE, et al. Body weight, weight change, and risk for hypertension in women. Ann Intern Med 1998;128:81–88
11. Colditz GA, Willett WC, Rotnitzky A, et al. Weight gain as a risk factor for clinical diabetes mellitus in women. Ann Intern Med 1995;122:481–486
12. Department of Agriculture, Department of Health and Human Services. Nutrition and Your Health: Dietary Guidelines for Americans. 3rd ed. Washington, DC: Government Printing Office; 1990
13. Holbrook TL, Barrett-Connor E, Wingard DL. The association of lifetime weight and weight control patterns with diabetes among men and women in an adult community. Int J Obes 1989;13:723–729
14. Willett WC, Manson JE, Stampfer MJ, et al. Weight, weight change, and coronary heart disease in women: risk within the "normal" weight range. JAMA 1995;273:461–465
15. Grundy SM, Barnett JP. Metabolic and health complications of obesity. Dis Mon 1990;36:641–696
16. Rexrode KM, Hennekens CH, Willett WC, et al. A prospective study of body mass index, weight change, and risk of stroke in women. JAMA 1997;277:1539–1545
17. Heyden S, Hames CG, Bartel A, et al. Weight and weight history in relation to cerebrovascular and ischemic heart disease. Arch Intern Med 1971;128: 956–960
18. Ursin G, Longnecker MP, Haile RW, et al. A meta-analysis of body mass index and risk of premenopausal breast cancer. Epidemiology 1995;6: 137–141
19. Hankinson SE, Willett WC, Manson JE, et al. Alcohol, height, and adiposity in relation to estrogen and prolactin levels in postmenopausal women. J Natl Cancer Inst 1995;87:1297–1302
20. Colditz GA, Hankinson SE, Hunter DJ, et al. The use of estrogens and progestins and risk of breast cancer in postmenopausal women. N Engl J Med 1995;332:1589–1593
21. Huang Z, Hankinson SE, Colditz GA, et al. Dual effects of weight and weight gain on breast cancer risk. JAMA 1997;278:1407–1411
22. Gortmaker SL, Must A, Perrin JM, et al. Social and economic consequences of overweight in adolescence and young adulthood. N Engl J Med 1993;329:1008–1012
23. Rumpel C, Ingram DD, Harris TB, et al. The association between weight change and psychological well-being in women. Int J Obes 1994;18: 179–183
24. Fazio AF. A concurrent validation study of the NCHS General Well-Being Schedule. Vital and Health Statistics. Series 2, No. 73. DHEW Publication No. HRA 78-1347. Washington, DC: National Center for Health Sciences; 1977
25. Stafford M, Hemingway H, Marmot M. Current obesity, steady weight change and weight fluctuation as predictors of physical functioning in middle aged office workers: the Whitehall II study. Int J Obes 1998;22: 23–31