



## Obesity and Cancer

### What is obesity?

Obesity is a condition in which a person has an unhealthy amount and/or distribution of body fat.

To measure obesity, researchers commonly use a scale known as the body mass index (BMI). BMI is calculated by dividing a person's weight (in kilograms) by their height (in meters) squared (commonly expressed as  $\text{kg}/\text{m}^2$ ). BMI provides a more accurate measure of obesity than weight alone, and for most people it is a fairly good (although indirect) indicator of body fatness.

Other measurements that reflect the distribution of body fat—that is, whether more fat is carried around the hips or the abdomen—are increasingly being used along with BMI as indicators of obesity and disease risks. These measurements include waist circumference and the waist-to-hip ratio (the waist circumference divided by the hip circumference).

The standard weight categories based on BMI for adults age 20 years or older are

BMI in $\text{kg}/\text{m}^2$	Weight Category
Below 18.5	Underweight
18.5 to 24.9	Normal
25.0 to 29.9	Overweight
30.0 to 39.9	Obese
40.0 or higher	Severely obese

The National Heart Lung and Blood Institute has a BMI calculator at [http://www.nhlbi.nih.gov/health/educational/lose\\_wt/BMI/bmicalc.htm](http://www.nhlbi.nih.gov/health/educational/lose_wt/BMI/bmicalc.htm).

For children and adolescents (younger than 20 years of age), overweight and obesity are based on the Centers for Disease Control and Prevention's (CDC's) BMI-for-age growth charts, which are available at [http://www.cdc.gov/growthcharts/clinical\\_charts.htm](http://www.cdc.gov/growthcharts/clinical_charts.htm):

BMI	Weight Category
BMI-for-age at or above sex-specific 85 <sup>th</sup> percentile, but less than 95 <sup>th</sup> percentile	Overweight
BMI-for-age at or above sex-specific 95 <sup>th</sup> percentile	Obese

The CDC has a BMI percentile calculator for children and teens at <http://nccd.cdc.gov/dnpabmi/Calculator.aspx>.

Compared with people of normal weight, those who are overweight or obese are at greater risk for many diseases, including diabetes, high blood pressure, cardiovascular disease, stroke, and many cancers. Extreme or severe obesity is also associated with an increased death rate; heart disease, cancer, and diabetes are responsible for most of the excess deaths (1, 2).

## How common is overweight or obesity?

Results from the National Health and Nutrition Examination Survey (NHANES) showed that in 2011–2014, nearly 70% of U.S. adults age 20 years or older were overweight or obese and more than one-third (36.5%) were obese (3). In 1988–1994, by contrast, only 56% of adults aged 20 years or older were overweight or obese.

The percentage of children and adolescents who are overweight or obese has also increased (3). In 2011–2014, an estimated 9% of 2- to 5-year-olds, 17% of 6- to 11-year-olds, and 20% of 12- to 19-year-olds were overweight or obese. In 1988–1994, those figures were only 7%, 11%, and 10%, respectively. In 2011–2014, about 17% of U.S. youth ages 2 to 19 years old were obese. In 1988–1994, by contrast, only about 10% of 2 to 19-year old were obese (4).

According to the CDC, the prevalence of obesity in the United States differs among racial/ethnic groups. For example, in 2011–2012 among adults, non-Hispanic blacks had the highest prevalence of obesity (47.8%) followed by Hispanics (42.0%), non-Hispanic whites (33.4%), and non-Hispanic Asians (10.9%) (5). Among children and adolescents ages 2–19 years, the prevalence of obesity in 2011–2012 was 21.9% among Hispanics, 19.5% among non-Hispanic blacks, 14.7% among non-Hispanic whites, and 8.6% among non-Hispanic Asians.

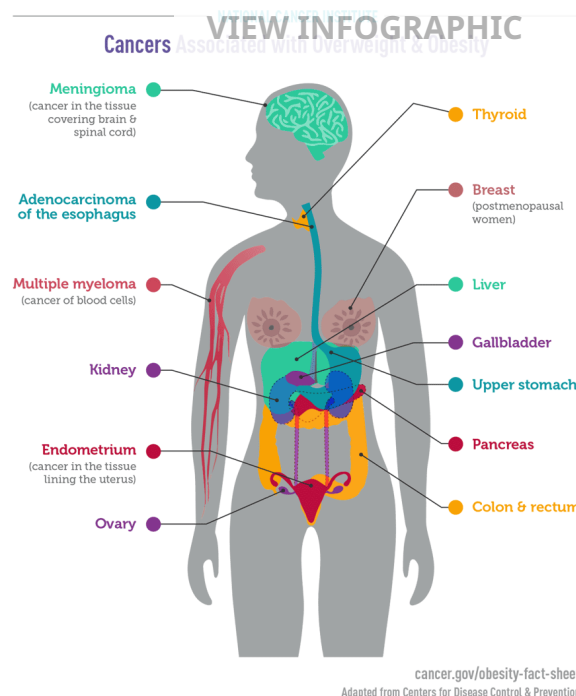
The CDC has state-level estimates of obesity prevalence among U.S. adults available at <http://www.cdc.gov/obesity/data/prevalence-maps.html>.

## What is known about the relationship between obesity and cancer?

Nearly all of the evidence linking obesity to cancer risk comes from large cohort studies, a type of observational study. However, data from observational studies can be difficult to interpret and cannot definitively establish that obesity causes cancer. That is because obese or overweight people may differ from lean people in ways other than their body fat, and it is possible that these other differences—rather than their body fat—are what explains their different cancer risk.

Despite the limitations of the study designs, there is consistent evidence that higher amounts of body fat are associated with increased risks of a number of cancers (6), including:

- **Endometrial cancer:** Obese and overweight women are two to about four times as likely as normal-weight women to develop endometrial cancer (cancer of the lining of the uterus), and extremely obese women are about seven times as likely to develop the more common of the two main types of this cancer (7). The risk of endometrial cancer increases with increasing weight gain in adulthood, particularly among women who have never used menopausal hormone therapy (8).
- **Esophageal adenocarcinoma:** People who are overweight or obese are about twice as likely as normal-weight people to develop a type of esophageal cancer called esophageal adenocarcinoma, and people who are extremely obese are more than four times as likely (9).
- **Gastric cardia cancer:** People who are obese are nearly twice as likely as normal-weight people to develop cancer in the upper part of the stomach, that is, the part that is closest to the esophagus (10).
- **Liver cancer:** People who are overweight or obese are up to twice as likely as normal-weight people to develop liver cancer. The association between overweight/obesity and liver cancer is stronger in men than women (11, 12).
- **Kidney cancer:** People who are overweight or obese are nearly twice as likely as normal-weight people to develop renal cell cancer, the most common form of kidney cancer (13). The association of renal cell cancer with obesity is independent of its association with high blood pressure, a known risk factor for kidney cancer (14).
- **Multiple myeloma:** Compared with normal-weight individuals, overweight and obese individuals have a slight (10% to 20%) increase in the risk of developing multiple myeloma (15).
- **Meningioma:** The risk of this slow-growing brain tumor that arises in the membranes surrounding the brain and the spinal cord is increased by about 50% in people who are obese and about 20% in people who are overweight (16).
- **Pancreatic cancer:** People who are overweight or obese are about 1.5 times as likely to develop pancreatic cancer as normal-weight people (17).



- **Colorectal cancer:** People who are obese are slightly (about 30%) more likely to develop colorectal cancer than normal-weight people (18).

A higher BMI is associated with increased risks of colon and rectal cancers in both men and in women, but the increases are higher in men than in women (18).

- **Gallbladder cancer:** Compared with normal-weight people, people who are overweight have a slight (about 20%) increase in risk of gallbladder cancer, and people who are obese have a 60% increase in risk of gallbladder cancer (19, 20). The risk increase is greater in women than men.
- **Breast cancer:** Many studies have shown that, in postmenopausal women, a higher BMI is associated with a modest increase in risk of breast cancer. For example, a 5-unit increase in BMI is associated with a 12% increase in risk (21). Among postmenopausal women, those who are obese have a 20% to 40% increase in risk of developing breast cancer compared with normal-weight women (22). The higher risks are seen mainly in women who have never used menopausal hormone therapy and for tumors that express hormone receptors. Obesity is also a risk factor for breast cancer in men (23).

In premenopausal women, by contrast, overweight and obesity have been found to be associated with a 20% decreased risk of breast tumors that express hormone receptors (22).

- **Ovarian cancer:** Higher BMI is associated with a slight increase in the risk of ovarian cancer, particularly in women who have never used menopausal hormone therapy (24). For example, a 5-unit increase in BMI is associated with a 10% increase in risk among women who have never used menopausal hormone therapy (24).
- **Thyroid cancer:** Higher BMI (specifically, a 5-unit increase in BMI) is associated with a slight (10%) increase in the risk of thyroid cancer (25).

## How might obesity increase the risk of cancer?

Several possible mechanisms have been suggested to explain how obesity might increase the risks of some cancers.

- Obese people often have chronic low-level inflammation, which can, over time, cause DNA damage that leads to cancer. Overweight and obese individuals are more likely than normal-weight individuals to have conditions or disorders that are linked to or that cause chronic local inflammation and that are risk factors for certain cancers (26). For example, chronic local inflammation induced by gastroesophageal reflux disease or Barrett esophagus is a likely cause of esophageal adenocarcinoma. Obesity is a risk factor for gallstones, a condition characterized by chronic gallbladder inflammation, and a history of gallstones is a strong risk factor for gallbladder cancer (27). Chronic ulcerative colitis (a chronic inflammatory condition) and hepatitis (a disease of the liver causing inflammation) are risk factors for different types of liver cancer (28).
- Fat tissue (also called adipose tissue) produces excess amounts of estrogen, high levels of which have been associated with increased risks of breast, endometrial, ovarian, and some other cancers.
- Obese people often have increased blood levels of insulin and insulin-like growth factor-1 (IGF-1). (This condition, known as hyperinsulinemia or insulin resistance, precedes the development of type 2 diabetes.)

High levels of insulin and IGF-1 may promote the development of colon, kidney, prostate, and endometrial cancers (29).

- Fat cells produce adipokines, hormones that may stimulate or inhibit cell growth. For example, the level of an adipokine called leptin, which seems to promote cell proliferation, in the blood increases with increasing body fat. And another adipokine, adiponectin—which is less abundant in obese people than in those of normal weight—may have antiproliferative effects.
- Fat cells may also have direct and indirect effects on other cell growth regulators, including mammalian target of rapamycin (mTOR) and AMP-activated protein kinase.

Other possible mechanisms by which obesity could affect cancer risk include changes in the mechanical properties of the scaffolding that surrounds breast cells (30) and altered immune responses, effects on the nuclear factor kappa beta system, and oxidative stress (31).

## How many cancer cases may be due to obesity?

A population-based study using BMI and cancer incidence data from the GLOBOCAN project estimated that, in 2012 in the United States, about 28,000 new cases of cancer in men (3.5%) and 72,000 in women (9.5%) were due to overweight or obesity (32). The percentage of cases attributed to overweight or obesity varied widely for different cancer types but was as high as 54% for gallbladder cancer in women and 44% for esophageal adenocarcinoma in men.

A 2016 study summarizing worldwide estimates of the fractions of different cancers attributable to overweight/obesity reported that, compared with other countries, the United States had the highest fractions attributable to overweight/obesity for colorectal cancer, pancreatic cancer, and postmenopausal breast cancer (33).

## Does avoiding weight gain or losing weight decrease the risk of cancer?

Most of the data about whether avoiding weight gain or losing weight reduces cancer risk comes from cohort and case-control studies. As with observational studies of obesity and cancer risk, these studies can be difficult to interpret because people who lose weight or avoid weight gain may differ in other ways from people who do not.

Nevertheless, when the evidence from multiple observational studies is consistent, the association is more likely to be real. Many observational studies have provided consistent evidence that people who have lower weight gain during adulthood have lower risks of colon cancer, kidney cancer, and—for postmenopausal women—breast, endometrial, and ovarian cancers (34).

Fewer studies have examined possible associations between weight loss and cancer risk. Some of these have found decreased risks of breast, endometrial, colon, and prostate cancers among people who have lost weight. However, most of these studies were not able to evaluate whether the weight loss was intentional or unintentional (and possibly related to underlying health problems).

Stronger evidence for a relationship between weight loss and cancer risk comes from studies of people who have undergone bariatric surgery (surgery performed on the stomach or intestines to induce weight loss). Obese people who have bariatric surgery appear to have lower risks of obesity-related cancers than obese people who do not have bariatric surgery (35).

Nevertheless, the follow-up study of weight and breast cancer in the Women's Health Initiative (36) found that for women who were already overweight or obese at baseline, weight change (either gain or loss) was not associated with breast cancer risk during follow-up. However, for women who were of normal weight at baseline, gaining more than 5% of body weight was associated with increased breast cancer risk.

## How does obesity affect cancer survivorship?

Most of the evidence about obesity in cancer survivors comes from people who were diagnosed with breast, prostate, or colorectal cancer. Research indicates that obesity may worsen several aspects of cancer survivorship, including quality of life, cancer recurrence, cancer progression, and prognosis (survival) (37, 38).

For example, obesity is associated with increased risks of treatment-related lymphedema in breast cancer survivors (39) and incontinence in prostate cancer survivors treated with radical prostatectomy (40). In a large clinical trial of patients with stage II and stage III rectal cancer, those with a higher baseline BMI (particularly men) had an increased risk of local recurrence (41). Death from multiple myeloma is 50% more likely for people at the highest levels of obesity compared with people at normal weight (42).

Several randomized clinical trials in breast cancer survivors have reported weight loss interventions that resulted in both weight loss and beneficial changes in biomarkers that have been linked to the association between obesity and prognosis (43, 44). However, there is little evidence about whether weight loss improves cancer recurrence or prognosis (45). The NCI-sponsored [Breast Cancer WEight Loss \(BWEL\) Study](#), a randomized phase III trial that is currently recruiting participants, will compare recurrence rate in overweight and obese women who take part in a weight loss program after breast cancer diagnosis with that in women who do not take part in the weight loss program.

## What research is being done on obesity and cancer?

Several areas of research are exploring mechanisms that link obesity and cancer (29, 46). One research area involves understanding the role of the microbes that live in the human gastrointestinal tract (collectively called the gut microbiota, or microbiome) in both type 2 diabetes and obesity. Both conditions are associated with dysbiosis, an imbalance in the collection of these microbes. For example, the gut microbiomes of obese people are different from, and less diverse than, those of non-obese people. Imbalances in the gut microbiota are associated with inflammation, altered metabolism, and genotoxicity, which may in turn be related to cancer. Experiments in mice show that the microbiome may influence the efficacy of some types of cancer treatment, particular immunotherapy (47, 48). Researchers are beginning to think about ways to change the microbiota of cancer patients to improve their outcomes.

Another area of investigation is the role of insulin receptor signaling in cancer. Many cancer cells express elevated levels of IR-A, a form of the insulin receptor that has a high affinity for insulin and related growth

factors. Researchers are investigating how these factors contribute to metabolic disease and cancer and which may be useful targets for therapeutic interventions to prevent obesity-related cancers.

Researchers are also trying to understand why the association between obesity and the risks of some cancers vary among racial/ethnic groups. For example, obesity has been found to be more strongly associated with an increased risk of prostate cancer among African American men than among white men (49). This observation might reflect a difference in the biological effects of obesity between these two groups, such as a difference in the effects of obesity on inflammation or insulin secretion.

NCI supports research on obesity and cancer risk through a variety of activities, including large cooperative initiatives, web and data resources, extramural and intramural epidemiologic studies, basic science, and dissemination and implementation resources. For example, the [Transdisciplinary Research on Energetics and Cancer \(TREC\) initiative](#) links four research centers and a coordination center to investigate how the combined effects of obesity, poor diet, and low levels of physical activity increase cancer risk.

The [NCI Cohort Consortium](#) is an extramural–intramural partnership within NCI’s Division of Cancer Control and Population Sciences that combines more than 50 prospective cohort studies from around the world with more than seven million participants. The studies are gathering information on energy balance–related factors from each cohort. The large size of the study will allow researchers to get a better sense of how obesity-related factors relate to [less common cancers](#), such as cancers of the thyroid, gallbladder, head and neck, and kidney.

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