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Obesity and Cancer Risk

Key Points

- During the past several decades, the percentage of overweight and obese adults and children has increased markedly.
- Obesity is associated with increased risks of cancers of the esophagus, breast (postmenopausal), endometrium (the lining of the uterus), colon and rectum, kidney, pancreas, thyroid, gallbladder, and possibly other cancer types.
- Obese people are also at higher risk of coronary heart disease, stroke, high blood pressure, diabetes, and a number of other chronic diseases.

1. What is obesity?

Obesity is a condition in which a person has an abnormally high and unhealthy proportion 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. BMI provides a more accurate measure of obesity or being overweight than weight alone.

Guidelines established by the National Institutes of Health (NIH) place adults age 20 and older into the following categories based on their BMI:

BMI	BMI Categories
Below 18.5	Underweight
18.5 to 24.9	Normal
25.0 to 29.9	Overweight
30.0 and above	Obese

The National Heart Lung and Blood Institute provides a BMI calculator at http://www.nhlbisupport.com/bmi/.

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

BMI	BMI Categories
BMI-for-age at or above sex-specific 85th percentile, but less than 95th percentile	Overweight
BMI-for-age at or above sex-specific 95th percentile	Obese

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 diseases, stroke, and certain cancers.

2. How common is overweight or obesity?

Results from the 2007-2008 National Health and Nutrition Examination Survey (NHANES) (http://wwwn.cdc.gov/nchs/nhanes/bibliography/key_statistics.aspx) show that 68 percent of U.S. adults age 20 years and older are overweight or obese. In 1988-1994, by contrast, only 56 percent of adults age 20 and older were overweight or obese.

In addition, the percentage of children who are overweight or obese has also increased. Among children and teens ages 2 to 19, 17 percent are estimated to be obese, based on the 2007–2008 survey. In 1988–1994, that figure was only 10 percent.

3. What is known about the relationship between obesity and cancer?

Obesity is associated with increased risks of the following cancer types, and possibly others as well:

- Esophagus
- Pancreas
- Colon and rectum
- Breast (after menopause)
- Endometrium (lining of the uterus)
- Kidney
- Thyroid
- Gallbladder

One study, using NCI Surveillance, Epidemiology, and End Results (SEER) data, estimated that in 2007 in the United States, about 34,000 new cases of cancer in men (4 percent) and 50,500 in women (7 percent) were due to obesity. The percentage of cases attributed to obesity varied widely for different cancer types but was as high as 40 percent for some cancers, particularly endometrial cancer and esophageal adenocarcinoma.

A projection of the future health and economic burden of obesity in 2030 estimated that continuation of existing trends in obesity will lead to about 500,000 additional cases of cancer in the United States by 2030. This analysis also found that if every adult reduced their BMI by 1 percent, which would be equivalent to a weight loss of roughly 1 kg (or 2.2 lbs) for an adult of average weight, this would prevent the increase in the number of cancer cases and actually result in the *avoidance* of about 100,000 new cases of cancer.

Several possible mechanisms have been suggested to explain the association of obesity with increased risk of certain cancers:

- Fat tissue produces excess amounts of estrogen, high levels of which have been associated with the risk of breast, endometrial, and some other cancers.

- Obese people often have increased levels of insulin and insulin-like growth factor-1 (IGF-1) in their blood (a condition known as hyperinsulinemia or insulin resistance), which may promote the development of certain tumors.

- Fat cells produce hormones, called adipokines, that may stimulate or inhibit cell growth. For example, leptin, which is more abundant in obese people, seems to promote cell proliferation, whereas adiponectin, which is less abundant in obese people, may have antiproliferative effects.

- Fat cells may also have direct and indirect effects on other tumor growth regulators, including mammalian target of rapamycin (mTOR) and AMP-activated protein kinase.

- Obese people often have chronic low-level, or “subacute,” inflammation, which has been associated with increased cancer risk.

Other possible mechanisms include altered immune responses, effects on the nuclear factor kappa beta system, and oxidative stress.

4. What is known about the relationship between obesity and breast cancer?

Many studies have shown that overweight and obesity are associated with a modest increase in risk of postmenopausal breast cancer. This higher risk is seen mainly in women who have never used menopausal hormone therapy (MHT) and for tumors that express both estrogen and progesterone receptors.

Overweight and obesity have, by contrast, been found to be associated with a reduced risk of premenopausal breast cancer in some studies.

The relationship between obesity and breast cancer may be affected by the stage of life in which a woman gains weight and becomes obese. Epidemiologists are actively working to address this question. Weight gain during adult life, most often from about age 18 to between the ages of 50 and 60, has been consistently associated with risk of breast cancer after menopause.

The increased risk of postmenopausal breast cancer is thought to be due to increased levels of estrogen in obese women. After menopause, when the ovaries stop producing hormones, fat tissue becomes the most important source of estrogen. Because obese women have more fat tissue, their estrogen levels are higher, potentially leading to more rapid growth of estrogen-responsive breast tumors.

The relationship between obesity and breast cancer risk may also vary by race and ethnicity. There is limited evidence that the risk associated with overweight and obesity may be less among African American and Hispanic women than among white women.

5. What is known about the relationship between obesity and endometrial cancer?

Overweight and obesity have been consistently associated with endometrial cancer, which is cancer of the lining of the uterus. Obese and overweight women have two to four times the risk of developing this disease than women of a normal weight, regardless of menopausal status. Many studies have also found that the risk of endometrial cancer increases with increasing weight gain in adulthood, particularly among women who have never used MHT.

Although it has not yet been determined why obesity is a risk factor for endometrial cancer, some evidence points to a role for diabetes, possibly in combination with low levels of physical activity. High levels of estrogen produced by fat tissue are also likely to play a role.

6. What is known about the relationship between obesity and colorectal cancer?

Among men, a higher BMI is strongly associated with increased risk of colorectal cancer. The distribution of body fat appears to be an important factor, with abdominal obesity, which can be measured by waist circumference, showing the strongest association with colon cancer risk.

An association between BMI and waist circumference with colon cancer risk is also seen in women, but it is weaker. Use of MHT may modify the association in postmenopausal women.

A number of mechanisms have been proposed to account for the association of obesity with increased colon cancer risk. One hypothesis is that high levels of insulin or insulin-related growth factors in obese people may promote colon cancer development.

High BMI is also associated with rectal cancer risk, but the increase in risk is more modest.

7. What is known about the relationship between obesity and kidney cancer?

Obesity has been consistently associated with renal cell cancer, which is the most common form of kidney cancer, in both men and women. The mechanisms by which obesity may increase renal cell cancer risk are not well understood. High blood pressure is a known risk factor for renal cell cancer, but the relationship between obesity and kidney cancer is independent of blood pressure status. High levels of insulin may play a role in the development of the disease.

8. What is known about the relationship between obesity and esophageal cancer?

Overweight and obese people are about twice as likely as people of healthy weight to develop a type of esophageal cancer called esophageal adenocarcinoma. Most studies have observed no increased risk, or even a decline in risk, with obesity for the other major type of esophageal cancer, squamous cell cancer.

The mechanisms by which obesity may increase risk of esophageal adenocarcinoma are not well understood. However, overweight and obese people are more likely than people of normal weight to have a history of gastroesophageal reflux disease or Barrett esophagus, which are associated with an increased risk of esophageal adenocarcinoma. It is possible that obesity exacerbates the esophageal inflammation that is associated with these conditions.

9. What is known about the relationship between obesity and pancreatic cancer?

Many studies have reported a slight increase in risk of pancreatic cancer among overweight and obese individuals. Waist circumference may be a particularly important factor in the association of overweight and obesity with pancreatic cancer.

10. What is known about the relationship between obesity and thyroid cancer?

Increasing weight has been found to be associated with an increase in the risk of thyroid cancer. It is unclear what the mechanism might be.

11. What is known about the relationship between obesity and gallbladder cancer?

The risk of gallbladder cancer increases with increasing BMI. The increase in risk may be due to the higher frequency of gallstones, a strong risk factor for gallbladder cancer, in obese individuals.

12. What is known about the relationship between obesity and other cancers?

The relationship between obesity and prostate cancer has been studied extensively. The results of individual studies do not suggest a consistent association between obesity and prostate cancer. However, when the data from multiple studies are pooled, analyses show that obesity may be associated with a very slight increase in the risk of prostate cancer.

In addition, several studies have found that obese men have a higher risk of aggressive prostate cancer than men of healthy weight. Generally, risk of prostate cancer has been linked to levels of certain hormones and growth factors, especially IGF-1.

Some studies have shown a weak association between increasing BMI and risk of ovarian cancer, especially in premenopausal women, although other studies have not found an association. As with some other cancers, an association between ovarian cancer and obesity may reflect increased levels of estrogens.

Some evidence links obesity to liver cancer and to some types of lymphoma and leukemia, but additional studies are needed to confirm these associations.

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

The most conclusive way to test whether avoiding weight gain or losing weight will decrease the risk of cancer is through a controlled clinical trial. A number of NIH-funded weight loss trials have demonstrated that people can lose weight and that losing weight reduces their risk of developing chronic diseases, such as diabetes, while improving their risk factors for cardiovascular disease.

However, previous trials and the results of an NCI workshop have demonstrated that it would not be feasible to conduct a weight loss trial of cancer prevention. The reason is that the effect of weight loss on the prevention of other chronic diseases would be demonstrated—and the trial consequently stopped so that the public could be informed of the benefits—before the effect on the prevention of cancer would become evident.

Therefore, most data about whether losing weight or avoiding weight gain prevents cancer come mainly from cohort and case-control studies. Data from these types of studies, called observational studies, can be difficult

to interpret because people who lose weight or avoid weight gain may be different in other ways from people who do not, just as obese people may differ from lean people in other ways than BMI. That is, it is possible that these other differences explain their different cancer risk.

Nevertheless, many observational studies have shown that people who have a lower weight gain during adulthood have a lower risk of:

- Colon cancer
- Breast cancer (after menopause)
- Endometrial cancer

A more limited number of observational studies have examined the relationship between weight loss and cancer risk, and a few have found decreased risks of breast cancer and colon cancer among people who have lost weight. However, most of these studies have not been able to evaluate whether the weight loss was intentional or related to underlying health problems.

Stronger evidence comes from studies of patients who have undergone bariatric surgery to lose weight. Obese people who have bariatric surgery appear to have lower rates of obesity-related cancers than obese people who did not have bariatric surgery. It is important to note that whereas most lifestyle weight loss interventions result in weight losses of 7-10 percent of body weight, weight loss from bariatric surgery combined with lifestyle changes generally results in weight loss of 30 percent.

14. How is NCI studying and supporting research on obesity and cancer risk, and supporting research to understand the populations most at risk?

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. The Institute has also issued a number of competitive funding opportunities related to obesity and cancer risk. In addition, NCI is an active participant in the NIH Obesity Research Task Force and played an active role in the development of the 2011 Strategic Plan for NIH Obesity Research (http://www.obesityresearch.nih.gov/About/strategic-plan.aspx). NCI-supported projects are outlined below.

NCI-Funded Initiatives	
Transdisciplinary Research on Energetics and Cancer (TREC) (http://cancercontrol.cancer.gov/trec/)	The 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 Initiative helps scientists conduct research across multiple disciplines and trains new and established researchers capable of carrying out this kind of integrated research.
Breast Cancer Surveillance Consortium (BCSC) (http://breastscreening.cancer.gov)	The BCSC is a research resource for studies designed to assess the delivery and quality of breast cancer screening, and related patient outcomes. Through the BCSC, NCI is funding studies to examine why there are lower rates of breast cancer screening among obese adults.
National Collaborative on Childhood Obesity Research (NCCOR) (http://www.nccor.org/)	NCCOR brings together four of the nation's leading funders of childhood obesity research: the CDC, NIH, Robert Wood Johnson Foundation, and the U.S. Department of Agriculture. NCI has been an active and leading participant in NCCOR activities related to measurement, surveillance, and policy evaluation.

Research and Policy Resources	
National Health and Nutrition Examination Survey (NHANES) (http://www.cdc.gov/nchs/nhanes.htm)	In collaboration with the National Center for Health Statistics, which is part of the CDC, NCI is supporting the use of activity monitors to collect objective physical activity, sleep, and strength data for NHANES.
Genes, Environment and Health Initiative (GEI) (http://gei.nih.gov/)	This trans-NIH includes an NCI-led component that invests in new technology to measure environmental toxins, dietary intake, and physical activity and to determine an individual's biological response to those influences on the level of the genome, the proteome, and the metabolome.
Measures Registry (http://nccor.org/measures) Catalogue of Surveillance Systems (http://nccor.org/css/)	In partnership with NCCOR, NCI has developed these two online resources to help researchers and clinicians identify validated measures and datasets relevant to obesity and health behaviors and environmental factors.
Cancer Control PLANET (Plan, Link, Act, Network With Evidence-Based Tools) (http://cancercontrolplanet.cancer.gov/)	The modules on Cancer Control PLANET include science-based information on interventions related to diet and physical activity that can help planners, program staff, and researchers design, implement, and evaluate science-based cancer control programs.
Population Studies	
Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (http://prevention.cancer.gov/plco) Polyp Prevention Trial (http://clinicaltrials.gov/ct2/show/NCT00339625)	Researchers are looking at groups of people within these studies to learn more about the influence of obesity and physical activity on all major cancer types, as well as some of the less common cancers.
NIH-AARP Diet and Health Study (http://dietandhealth.cancer.gov/)	This is a prospective cohort study of nutrition in relation to major cancers among over half a million American men and women. Results from this large cohort have already contributed to our understanding of the relationship between obesity and non-Hodgkin lymphoma, as well as prostate, endometrial, pancreatic, bladder, kidney, thyroid, and colorectal cancer.
Nurses' Health Study (http://clinicaltrials.gov/ct2/show/NCT00005152) Iowa Women's Health Study (http://www.cancer.umn.edu/research/programs/peiowa.html) Health Professionals Follow-up Study (http://clinicaltrials.gov/ct2/show/NCT00005182) Women's Health Initiative (http://clinicaltrials.gov/ct2/show/NCT00000611?term=women%27s+health+initiative&rank=5)	These large studies conducted by researchers around the country, with support from NCI, have made important contributions to understanding the association between weight and cancer.

Cohort Consortium (http://epi.grants.cancer.gov/Consortia/cohort.html)	This joint intramural/extramural initiative combines more than 20 prospective cohort studies from around the world, which have enrolled more than two million participants collectively. 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 thyroid and gallbladder cancer.
Multiethnic Cohort Study (http://www.crch.org/multiethniccohort/) Southern Community Cohort Study (http://www.southerncommunitystudy.org/) Black Women's Health Study (http://www.bu.edu/bwhs/index.htm) Adventist Health Study 2 (http://www.llu.edu/public-health/health/index.page?) California Teachers Study (http://www.calteachersstudy.org/)	In light of concerns about the potential for differential effects of obesity in diverse populations, NCI supports research that has the potential to examine obesity and cancer associations in non-white populations.
Other Research Projects and Funding Announcements	
Studies of Energy Balance and Cancer in Humans (http://grants.nih.gov/grants/guide/pa-files/PA-09-148.html) Exploratory Grants for Behavioral Research in Cancer Control (http://grants.nih.gov/grants/guide/pa-files/PA-09-130.html)	Competitive funding opportunities to encourage grant applications for research on obesity and cancer risk.
Improving Diet and Physical Activity Assessment (http://grants.nih.gov/grants/guide/pa-files/PAR-09-224.html) Obesity Policy Research: Evaluation and Measures (http://grants.nih.gov/grants/guide/pa-files/pa-10-028.html)	These funding opportunities relate to improving the measurement of obesity and related behaviors and risk factors and the evaluation of interventions.
Provocative Questions Request for Applications (http://provocativequestions.nci.nih.gov/rfa)	These funding opportunities relate to better understanding molecular and cellular mechanisms that underlie the link between cancer risk and obesity.
Energy Balance Funding Opportunities (http://cancercontrol.cancer.gov/energy_balance/funding.html)	NCI's Division of Cancer Control and Population Sciences funds researchers around the world to learn more about how modifiable factors, such as obesity, can be changed to alter cancer risk.

Selected References

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Related Resources

- *Physical Activity and Cancer* (http://www.cancer.gov/cancertopics/factsheet/prevention/physicalactivity)
- Energy Balance: Weight and Obesity, Physical Activity, Diet Home Page (http://www.cancer.gov/cancertopics/prevention/energybalance)
- MedlinePlus Obesity Page (http://www.nlm.nih.gov/medlineplus/obesity.html)
- Prevention, Genetics, Causes Home Page (http://www.cancer.gov/cancertopics/prevention-genetics-causes)

How can we help?

We offer comprehensive research-based information for patients and their families, health professionals, cancer researchers, advocates, and the public.

- ***Call*** NCI's Cancer Information Service at 1–800–4–CANCER (1–800–422–6237)
- ***Visit*** us at http://www.cancer.gov or http://www.cancer.gov/espanol
- ***Chat*** using LiveHelp, NCI's instant messaging service, at http://www.cancer.gov/livehelp
- ***E-mail*** us at cancergovstaff@mail.nih.gov
- ***Order*** publications at http://www.cancer.gov/publications or by calling 1–800–4–CANCER
- ***Get help*** with quitting smoking at 1–877–44U–QUIT (1–877–448–7848)