

Obesity and Cancer: Questions and Answers

Key Points

- During the last two decades, the percentage of overweight and obese adults and children has been steadily increasing (see Question 2).
- Lack of physical activity is strongly associated with obesity (see Question 3).
- In addition to increasing the risk of coronary heart disease, stroke, high blood pressure, and diabetes, obesity increases the risk of cancers of the breast (postmenopausal), endometrium (the lining of the uterus), colon, kidney, and esophagus (see Questions 4, 6–10).
- Avoiding weight gain can lower the risk of cancers of the breast (postmenopausal), endometrium, colon, kidney, and esophagus (see Question 13).
- Regular physical activity lowers the risk of colon and breast cancers (see Question 15).

1. What is obesity?

People who are obese have an abnormally high and unhealthy proportion of body fat. To measure obesity, researchers commonly use a formula based on weight and height known as the body mass index (BMI). BMI is the ratio of weight (in kilograms) to height (in meters) squared. BMI provides a more accurate measure of obesity or being overweight than does weight alone.

Guidelines established by the National Institutes of Health (NIH) place adults age 20 and older into one of four categories based on their BMI (1):

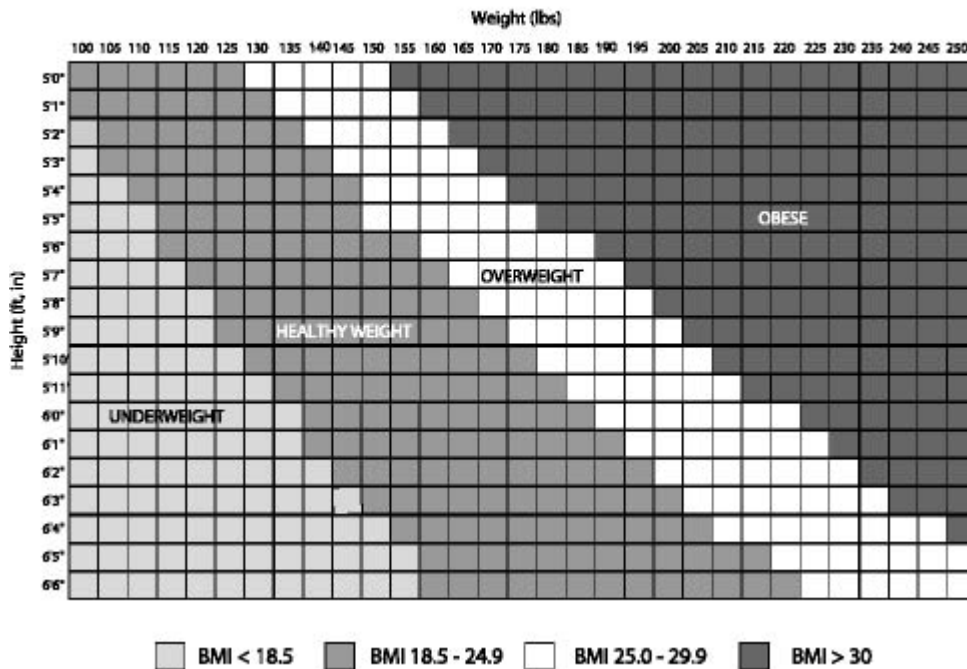
<18.5	underweight
18.5 to 24.9	healthy
25.0 to 29.9	overweight
>30.0	obese

The following chart can be used to determine BMI category. (Find the height, and move across the chart to the appropriate weight.)



X 3 0 7 0

Body Mass Index Chart, Adults 20 and Over



Compared with people in the healthy weight category, those who are overweight or obese are at greater risk for many diseases, including diabetes, high blood pressure, cardiovascular diseases, stroke, and certain cancers. Obesity lowers life expectancy.

2. How common is overweight or obesity?

Results from the 1999–2000 National Health and Nutrition Examination Survey (NHANES) show that an estimated 64 percent of U.S. adults are either overweight or obese (2). This represents an increase of 8 percentage points compared with the estimates from an earlier survey (NHANES III 1988–1994).

Nearly one-third of all adults are now classified as obese. This reflects an increase of 7.6 percentage points since 1994 (2). The data show that 31 percent of adults age 20 and older—nearly 59 million people—have a body mass index (BMI) of 30 or greater, compared with 23 percent in 1994.

In addition, the percentage of children who are overweight continues to increase. Among children and teens ages 6 to 19, 15 percent (almost 9 million) are overweight according to the 1999–2000 data, or triple what the proportion was in 1980 (3).

3. What causes obesity?

Experts have concluded that the chief causes of obesity are a sedentary lifestyle and overconsumption of high-calorie food (4):

- **Sedentary lifestyle**—Researchers have found a strong correlation between lack of physical activity and obesity (4, 5).
- **Diet**—A diet high in calories and/or fat appears to be an important factor in obesity (6).

4. What have scientists learned about the relationship between obesity and cancer?

In 2001, experts concluded that cancers of the colon, breast (postmenopausal), endometrium (the lining of the uterus), kidney, and esophagus are associated with obesity. Some studies have also reported links between obesity and cancers of the gallbladder, ovaries, and pancreas (4).

Obesity and physical inactivity may account for 25 to 30 percent of several major cancers—colon, breast (postmenopausal), endometrial, kidney, and cancer of the esophagus (4).

Preventing weight gain can reduce the risk of many cancers. Experts recommend that people establish habits of healthy eating and physical activity early in life to prevent overweight and obesity. Those who are already overweight or obese are advised to avoid additional weight gain, and to lose weight through a low-calorie diet and exercise. Even a weight loss of only 5 to 10 percent of total weight can provide health benefits (4).

5. How many people get cancer by being overweight or obese? How many die?

In 2002, about 41,000 new cases of cancer in the United States were estimated to be due to obesity. This means that about 3.2 percent of all new cancers are linked to obesity (7).

A recent report estimated that, in the United States, 14 percent of deaths from cancer in men and 20 percent of deaths in women were due to overweight and obesity (8).

6. Does obesity increase the risk of breast cancer?

The effect of obesity on breast cancer risk depends on a woman's menopausal status. Before menopause, obese women have a lower risk of developing breast cancer than do women of a healthy weight (4, 9, 10, 11, 12). However, after menopause, obese women have 1.5 times the risk of women of a healthy weight (9, 10, 13, 14).

Obese women are also at increased risk of dying from breast cancer after menopause compared with lean women (4, 11, 15, 16). Scientists estimate that about 11,000 to 18,000 deaths per year from breast cancer in U.S. women over age 50 might be avoided if women could maintain a BMI under 25 throughout their adult lives (16).

Obesity seems to increase the risk of breast cancer only among postmenopausal women who do not use menopausal hormones. Among women who use menopausal hormones, there is no significant difference in breast cancer risk between obese women and women of a healthy weight (4, 9, 11, 17).

Both the increased risk of developing breast cancer and dying from it after menopause are believed to be due to increased levels of estrogen in obese women (18). Before menopause, the ovaries are the primary source of estrogen. However, estrogen is also produced in fat tissue and, after menopause, when the ovaries stop producing hormones, fat tissue becomes the most important estrogen source (14). Estrogen levels in postmenopausal women are 50 to 100 percent higher among heavy versus lean women (11). Estrogen-sensitive tissues are therefore exposed to more estrogen stimulation in heavy women, leading to a more rapid growth of estrogen-responsive breast tumors.

Another factor related to the higher breast cancer death rates in obese women is that breast cancer is more likely to be detected at a later stage in obese women than in lean women. This is because the detection of a breast tumor is more difficult in obese versus lean women (12).

Studies of obesity and breast cancer in minority women in the United States have been limited. There is some evidence that, among African American women, the risk associated with obesity may be absent or less than that of other populations (19, 20, 21). However, a recent report showed that African American women who have a high BMI are more likely to have an advanced stage of breast cancer at diagnosis (22). Another report showed that obese Hispanic white women were twice as likely to develop breast cancer as non-obese Hispanics, but the researchers did not detect a difference in risk for obese Hispanic women before and after menopause (23).

Weight gain during adulthood has been found to be the most consistent and strongest predictor of breast cancer risk in studies in which it has been examined (4, 10, 11, 24).

The distribution of body fat may also affect breast cancer risk. Women with a large amount of abdominal fat have a greater breast cancer risk than those whose fat is distributed over the hips, buttocks, and lower extremities (13, 25, 26). Results from studies on the effect of abdominal fat are much less consistent than studies on weight gain or BMI.

7. Does obesity increase the risk of cancer of the uterus?

Obesity has been consistently associated with uterine (endometrial) cancer. Obese women have two to four times greater risk of developing the disease than do women of a healthy weight, regardless of menopausal status (4, 27, 28, 29, 30). Increased risk has also been demonstrated among overweight women (28, 30). Obesity has been estimated to account for about 40 percent of endometrial cancer cases in affluent societies (31).

It is unclear why obesity is a risk factor for endometrial cancer; however, it has been suggested that lifetime exposure to hormones and high levels of estrogen and insulin in obese women may be contributing factors (4, 27, 28, 29, 32).

8. Does obesity increase the risk of colon cancer?

Colon cancer occurs more frequently in people who are obese than in those of a healthy weight (4, 33, 34, 35, 36, 37). An increased risk of colon cancer has been consistently reported for men with high BMIs (34, 37, 38). The relationship between BMI and risk in women, however, has been found to be weaker (4, 34, 38) or absent (39).

Unlike for breast and endometrial cancer, estrogen appears to be protective for colon cancer for women overall (40). However, obesity and estrogen status also interact in influencing colon cancer risk. Women with a high BMI who are either premenopausal or postmenopausal and taking estrogens have an increased risk of colon cancer similar to that found for men with a high BMI. In contrast, women with a high BMI who are postmenopausal and not taking estrogens do not have an increased risk of colon cancer (41).

There is some evidence that abdominal obesity may be more important in colon cancer risk (37, 38). In men, a high BMI tends to be associated with abdominal fat. In women, fat is more likely to be distributed in the hips, thighs, and buttocks. Thus, two measures of abdominal fat, waist-to-hip ratio or waist circumference, may be better predictors of colon cancer risk. Few studies have yet compared waist-to-hip ratios to colon cancer risk in women, however. One study that did find an increased risk of colon cancer among women with high waist-to-hip ratios found that the association was present only among inactive women, suggesting that high levels of physical activity may counteract the effects of increased abdominal fat (42).

A number of mechanisms have been proposed for the adverse effect of obesity on colon cancer risk. One of the major hypotheses is that high levels of insulin or insulin-related growth factors in obese people may promote tumor development (4, 43, 44).

9. Does obesity increase the risk of kidney cancer?

Studies have consistently found a link between a type of kidney cancer (renal cell carcinoma) and obesity in women (4, 30, 45, 46, 47, 48), with some studies finding risk among obese women to be two to four times the risk of women of a healthy weight.

Results of studies including men have been more variable, ranging from an association similar to that seen in women (30, 46, 49), to a weak association (48, 50, 51), to no association at all (45). A meta-analysis (where several studies are combined into a single report), which found an equal association of risk among men and women, estimated the kidney cancer risk to be 36 percent higher for an overweight person and 84 percent higher for an obese person compared to those with a healthy weight (52).

The mechanisms by which obesity may increase renal cell cancer risk are not well understood. An increased exposure to sex steroids, estrogen and androgen, is one possible mechanism (4).

10. Does obesity increase the risk of cancer of the esophagus or stomach?

Overweight and obese individuals are two times more likely than healthy weight people to develop a type of esophageal cancer called esophageal adenocarcinoma (4, 53, 54, 55, 56). A smaller increase in risk has been found for gastric cardia cancer, a type of stomach cancer that begins in the area of the stomach next to the esophagus (54, 55, 56, 57). Most studies have not observed increases in risk with obesity in another type of esophageal cancer, squamous cell cancer. An increased risk of esophageal adenocarcinoma has also been associated with weight gain, smoking, and being younger than age 59 (54, 57).

The mechanisms by which obesity increases risk of adenocarcinoma of the esophagus and gastric cardia are not well understood. One of the leading mechanisms proposed has been that increases in gastric reflux due to obesity may increase risk. However, in the few studies that have examined this issue, risk associated with BMI was similar for those with and without gastric reflux (56).

11. Does obesity increase the risk of prostate cancer?

Of the more than 35 studies on prostate cancer risk, most conclude that there is no association with obesity (4, 44, 58, 59, 60). Some report that obese men are at higher risk than men of healthy weight, particularly for more aggressive tumors (61, 62, 63). One study found an increased risk among men with high waist-to-hip ratios, suggesting that abdominal fat may be a more appropriate measure of body size in relation to prostate cancer (64).

Studies examining BMI and prostate cancer mortality have had conflicting results (8, 65, 66).

Despite the lack of association between obesity and prostate cancer incidence, a number of studies have examined potential biological factors that are related to obesity, such as insulin-related growth factors, leptin, and other hormones. Results of these studies are inconsistent, but generally, risk has been linked to men with higher levels of leptin (67), insulin (68), and IGF-1 (insulin-like growth factor-1) (69).

12. Is there any evidence that obesity is linked to cancer of the gallbladder, ovaries, or pancreas?

An increased risk of gallbladder cancer has been found to be associated with obesity, particularly among women (70, 71, 72). This may be due to the higher frequency of gallstones in obese individuals, as gallstones are considered a strong risk factor for gallbladder cancer. However, there is not enough evidence to draw firm conclusions.

It is unclear whether obesity affects ovarian cancer risk. Some studies report an increased risk among obese women (73, 74, 75), whereas others have found no association (76, 77). A recent report found an increased risk in women who were overweight or obese in adolescence or young adulthood; no increased risk was found in older obese women (78).

Studies evaluating the relationship between obesity and pancreatic cancer have been inconsistent (79, 80, 81, 82). One recent study found that obesity increases the risk of pancreatic cancer only among those who are not physically active (80). A recent meta-analysis reported that obese people may have a 19 percent higher risk of pancreatic cancer than those with a healthy BMI. The results, however, were not conclusive (83).

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

The most conclusive way to test if avoiding weight gain will decrease the risk of cancer is through a controlled clinical trial. At present, there have been no controlled clinical trials on the effect on cancer related to avoiding weight gain. However, many observational studies have shown that avoiding weight gain lowers the risk of cancers of the colon, breast (postmenopausal), endometrium, kidney, and esophagus. There is limited evidence for thyroid cancers, and no substantial evidence for all other cancers (4, 84).

14. Does losing weight lower the risk of cancer?

There is insufficient evidence that intentional weight loss will affect cancer risk for any cancer. A very limited number of observational studies have examined the effect of weight loss, and a few found some decreased risk for breast cancer among women who have lost weight. However, most of these studies have not been able to evaluate whether the weight loss was intentional or related to other health problems (4, 24, 25, 85).

One recent study that examined the effect of intentional weight loss found that women who experienced intentional weight loss of 20 or more pounds and were not currently overweight had cancer rates at the level of healthy women who never lost weight. However, unintentional weight loss episodes were not associated with decreased cancer risk (86).

15. Does regular physical activity lower the risk of cancer?

There have been no controlled clinical trials on the effect of regular physical activity on the risk of developing cancer. However, observational studies have examined the possible association between physical activity and a lower risk of developing colon or breast cancer:

- **Colon cancer:** In 2002, a major review of observational trials found that physical activity reduced colon cancer risk by 50 percent. This risk reduction occurred even with moderate levels of physical activity (4). For example, one study showed that even moderate exercise, such as brisk walking for 3 to 4 hours per week, can lower colon cancer risk (42).

A limited number of studies have examined the effect of physical activity on colon cancer risk for both lean and obese people. Most of these studies have found a protective effect of physical activity across all levels of BMI (4).

- **Breast cancer:** The pattern of the association between physical activity and breast cancer risk is somewhat different. Most studies on breast cancer have focused on postmenopausal women. A recent study from the Women's Health Initiative found that physical activity among postmenopausal women at a level of walking about 30 minutes per day was associated with a 20 percent reduction in breast cancer risk. However, this reduction in risk was greatest among women who were of normal weight. For these women, physical activity was associated with a 37 percent decrease in risk. The protective effect of physical activity was not found among overweight or obese women (87).

16. What biological mechanisms are thought to be involved in explaining the link between obesity and cancer?

The biological mechanism that explains how obesity increases cancer risk may be different for different cancers. (See Questions 6–11.) The exact mechanisms are not known for any of the cancers. However, possible mechanisms include alterations in sex hormones (e.g., estrogen, progesterone, and androgens), and insulin and IGF-1 in obese people that may account for their increased risk for cancers of the breast, endometrium, and colon. Sex-hormone binding globulin, the major carrier protein for certain sex hormones in the plasma, may also be involved in the altered risk for these cancers in obese people (4, 32, 58, 88).

17. What are current research needs?

Although there has been extensive research with large populations looking at the possible link between obesity and cancer, few clinical trials have studied the effect of weight control, physical activity, and energy balance (the calories consumed compared with those burned) on cancer. For some cancers, such as colon and breast, it is not clear whether the increased cancer risk in obese people is due to the extra weight; a high-fat, high-calorie diet; a lack of physical activity; or a combination of these factors.

The 2002 International Agency for Research on Cancer (IARC) report on weight control, physical activity, and cancer (4) made several recommendations for future trials:

- Conduct long-term intervention studies on the effect of dietary changes on weight gain and cancer risk;
- Conduct long-term intervention studies on the effect of patterns of physical activity (the intensity, frequency, and duration of various sorts of physical activity) in relation to weight gain and cancer risk;
- Conduct long-term intervention studies on the combined effects of changes in diet and physical activity on obesity and cancer risk; and
- Conduct community intervention studies to prevent weight gain and promote physical activity.

Several international reports have concluded that controlling the obesity epidemic will require substantial investments by many segments of society. Efforts to increase physical activity and promote healthy eating are needed in families, day care centers, schools, and work sites. The efforts of community services such as health care and public education are needed, as well as transportation systems that encourage walking and the use of bicycles (4).

18. Is the National Cancer Institute (NCI) currently studying the possible link between obesity and cancer?

Several NCI-funded studies are investigating the relationship between obesity and cancer, including breast, ovarian, endometrial, prostate, colorectal, and esophageal cancers. Some of the studies with women include the following:

- The Four Corners Breast and Endometrial Cancer Study is focusing on the effects of obesity and weight changes on breast and endometrial cancer risk among Hispanic, Native American, and non-Hispanic white women (89).
- A study of white, African American, and Latina women is investigating whether phytoestrogen consumption can modify the risk of endometrial cancer associated with obesity (90).
- The Black Women's Health Study is considering the effect of risk factors, including obesity, on breast cancer risk (91).
- The Health, Eating, Activity and Lifestyle (HEAL) Breast Cancer Prognosis Study is examining the interrelationships between diet, weight, physical activity, hormones, breast cancer prognosis, and quality of life in a multi-ethnic cohort of 1,200 breast cancer survivors (<http://appliedresearch.cancer.gov/surveys/heal/>).

The Division of Cancer Epidemiology and Genetics (DCEG), one of NCI's intramural research divisions, is conducting a series of large-scale epidemiologic studies on the influence of obesity and physical inactivity on several major cancers. These include cohort studies within clinical trials, such as the Alpha-Tocopherol Beta-Carotene Study; the Prostate, Lung, Colorectal, and Ovarian Cancer study; and the Polyp Prevention Trial. In addition, DCEG is studying energy balance in cohort and case-control studies in Sweden, China, and the United States; these include the NIH-AARP (National Institutes of Health-American Association of Retired Persons) Diet and Health Study, a prospective cohort study of nutrition in relation to major cancers among over half a million American men and women, and the Cohort Consortium, a new effort that combines several prospective cohort studies from around the world, gathering information on energy balance-related factors from each cohort.

NCI is also developing and supporting research initiatives to improve the measurement of diet and physical activity in the population, understand health professionals' knowledge and practices about obesity treatment, and support the establishment of centers in nutrition, energetics, and physical activity and cancer outcomes. Some of these initiatives are cosponsored with other parts of the NIH (<http://grants.nih.gov/grants/guide/pa-files/PA-01-017.html>).

Other studies being conducted or funded by NCI use animal models to study obesity and cancer. One such study is examining the role of body fat mass on cancer progression in a mouse model of prostate cancer. The Center for Cancer Research, one of NCI's intramural research divisions, is conducting studies examining mechanisms of energy modulation, specifically caloric restriction, fasting, physical activity, diet-induced obesity, and genetically induced obesity, frequently using animal models of cancer.

NCI is supporting the training of new scientists through programs such as the Nutrition and Obesity Training Program at the University of California, Los Angeles and grants to individual new scientists, who are studying topics such as Culturally Proficient Smoking and Weight Control Treatment, Exploration and Intervention in Weight Gain Associated With Adjuvant Chemotherapy for Breast Cancer, and Visceral Adipose Tissue and Colorectal Neoplasia.

Because the delivery of research results is important, NCI has ongoing programs to move obesity-related research into practice. For example, NCI's Division of Cancer Control and Population Sciences is supporting the integration of diet and physical activity science into comprehensive cancer control planning. Cancer Control PLANET (Plan, Link, Act, Network With Evidence-Based Tools) provides access to data and resources that can help planners, program staff, and researchers design, implement, and evaluate science-based cancer control programs. The modules on Cancer Control PLANET include science-based information on interventions related to diet, physical activity, and NCI's 5 A Day For Better Health Program (<http://www.fruitsandveggiesmatter.gov/>), which has incorporated messages on the importance of maintaining a healthy weight and a physically active lifestyle in its public awareness efforts. These messages are a key component of a recent NCI campaign, "9 A Day Campaign for African American Men," to increase

African American men's consumption of fruits and vegetables. As the national health authority for 5 A Day, the NCI provides leadership through the implementation of a national media campaign, support of state 5 A Day programs, coordination of national partnership efforts and activities, and funding of nutrition behavior change research.

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Related Resources

- The National Heart, Lung, and Blood Institute (NHLBI) Obesity Education Initiative seeks to reduce the risk of heart disease and overall morbidity and mortality from heart disease by reducing the prevalence of overweight and physical inactivity. The NHLBI Web site has information for health professionals as well as patients and the general public.

Address: Post Office Box 30105
Bethesda, MD 20824-0105
Telephone: 301-592-8573
Fax: 301-592-8563
Internet
Web site: <http://www.nhlbi.nih.gov>

- The Weight-control Information Network (WIN) is a national public information service of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). WIN assembles and distributes information and publications about weight control, obesity, and nutritional disorders.

Address: One Win Way
Bethesda, MD 20892-3665
Telephone: 1-877-946-4627
202-828-1025
Fax: 202-828-1028
E-mail: win@info.niddk.nih.gov
Internet
Web site: <http://win.niddk.nih.gov/index.htm>

- The U.S. Preventive Services Task Force recommended that clinicians, using BMI, screen all adults for obesity and offer obese patients intensive counseling and behavioral interventions. For more information, visit the Agency for Healthcare Research and Quality Web site at <http://www.ahrq.gov/clinic/3rduspstf/obesity/obesrr.htm> on the Internet.
- The Centers for Disease Control and Prevention published the first Surgeon General's report on physical activity and health, a comprehensive review of the research on physical activity and health. The report can be found at <http://www.cdc.gov/nccdphp/sgr/index.htm> on the Internet.
- BMI is calculated either as weight in pounds divided by height in inches squared multiplied by 703, or as weight in kilograms divided by height in meters squared. An online BMI calculator can be found at <http://www.cdc.gov/healthyweight/assessing/bmi/index.html> on the Internet.
- A major clinical trial, the Women's Health Initiative Dietary Modification trial, is testing whether low-fat diet will lower breast cancer risk (<http://www.nhlbi.nih.gov/whi/ctos.htm>).
- The NCI Health, Eating, Activity, and Lifestyle (HEAL) Study is designed to look at the associations between physical activity, eating habits, weight patterns, diet, hormones, and prognostic factors for breast cancer among the early stage breast cancer participants. For more information, visit <http://appliedresearch.cancer.gov/surveys/heal/> on the Internet.

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Related NCI materials and Web pages:

- National Cancer Institute Fact Sheet 4.24, *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/energybalance>)
- 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)

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