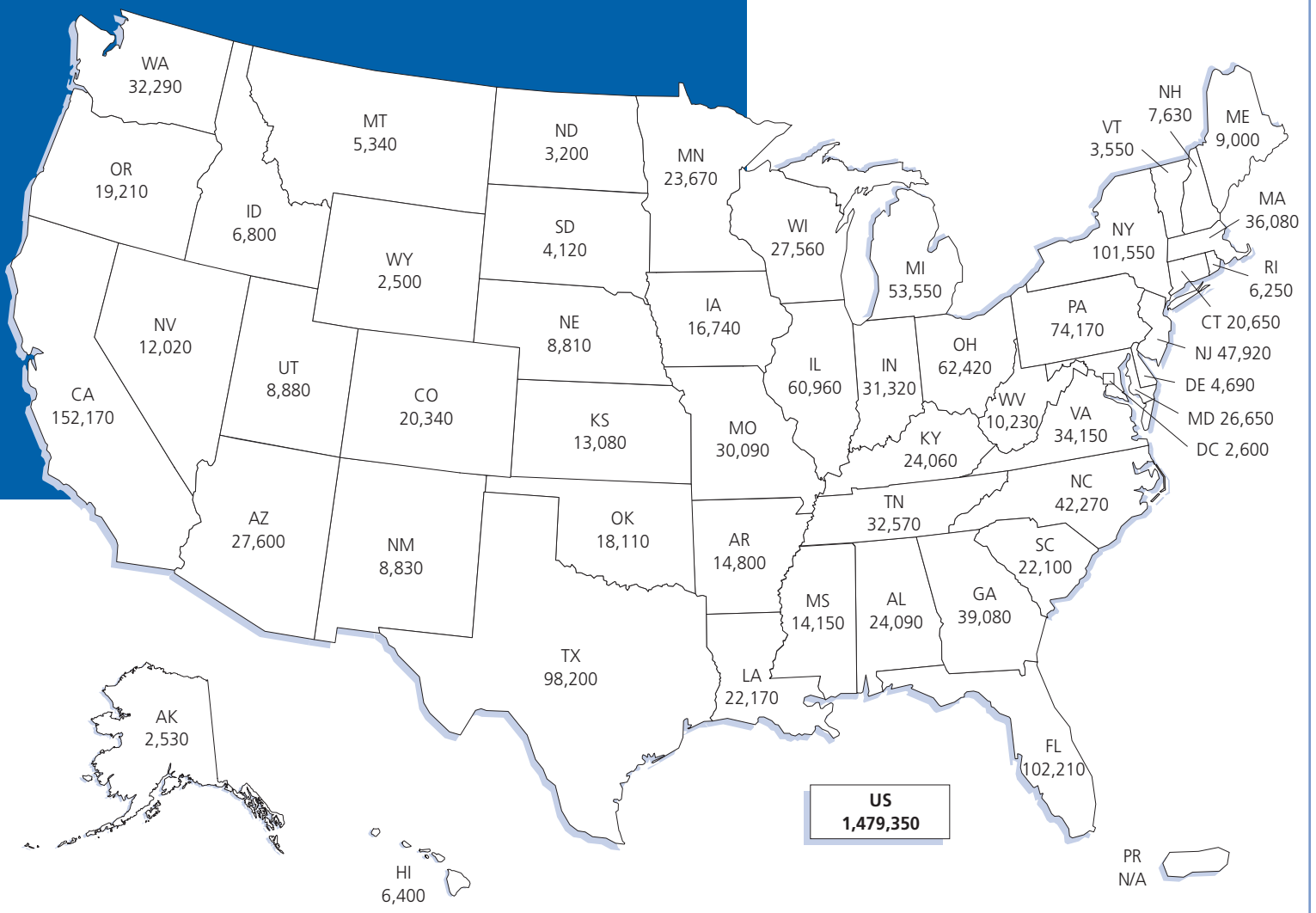
Cancer Facts & Figures 2009



Estimated number of new cancer cases for 2009, excluding basal and squamous cell skin cancers and in situ carcinomas except urinary bladder.
Note: State estimates are offered as a rough guide and should be interpreted with caution. State estimates may not add to US total due to rounding.

American Cancer Society®

Special Section:
Multiple Primary Cancers
see page 24

Contents

**Indicates a figure or table*

Cancer Facts & Figures 2009 is dedicated to **Drs. Jeanne Calle** and **Carmen Rodriguez**, outstanding leaders and scientists in the Epidemiology department at the American Cancer Society, both recently deceased. Carmen, a breast cancer survivor, died of a second primary cancer in November 2008. Jeanne died unexpectedly in February 2009, a short time after retiring from her position as vice president of Epidemiology. Jeanne's and Carmen's research and leadership made important contributions to understanding the causes and prevention of cancer. We dearly miss them as friends, mentors, and colleagues.

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This publication attempts to summarize current scientific information about cancer.
Except when specified, it does not represent the official policy of the American Cancer Society.

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Cancer: Basic Facts

What Is Cancer?

Cancer is a group of diseases characterized by uncontrolled growth and spread of abnormal cells. If the spread is not controlled, it can result in death. Cancer is caused by both external factors (tobacco, infectious organisms, chemicals, and radiation) and internal factors (inherited mutations, hormones, immune conditions, and mutations that occur from metabolism). These causal factors may act together or in sequence to initiate or promote carcinogenesis. Ten or more years often pass between exposure to external factors and detectable cancer. Cancer is treated with surgery, radiation, chemotherapy, hormone therapy, biological therapy, and targeted therapy.

Can Cancer Be Prevented?

All cancers caused by cigarette smoking and heavy use of alcohol could be prevented completely. The American Cancer Society estimates that in 2009 about 169,000 cancer deaths are expected to be caused by tobacco use. Scientific evidence suggests that about one-third of the 562,340 cancer deaths expected to occur in 2009 will be related to overweight or obesity, physical inactivity, and poor nutrition and thus could also be prevented. Certain cancers are related to infectious agents, such as hepatitis B virus (HBV), human papillomavirus (HPV), human immunodeficiency virus (HIV), *Helicobacter pylori (H. pylori),* and others, and could be prevented through behavioral changes, vaccines, or antibiotics. In addition, many of the more than 1 million skin cancers that are expected to be diagnosed in 2009 could be prevented by protection from the sun's rays and avoiding indoor tanning.

Regular screening examinations by a health care professional can result in the detection and removal of precancerous growths, as well as the diagnosis of cancers at an early stage, when they are most treatable. Cancers that can be prevented by removal of precancerous tissue include cancers of the cervix, colon, and rectum. Cancers that can be diagnosed early through screening include cancers of the breast, colon, rectum, cervix, prostate, oral cavity, and skin. For cancers of the breast, colon, rectum, and cervix, early detection has been proven to reduce mortality. A heightened awareness of breast changes or skin changes may also result in detection of these tumors at earlier stages. Cancers that can be prevented or detected earlier by screening account for at least half of all new cancer cases.

Who Is at Risk of Developing Cancer?

Anyone can develop cancer. Since the risk of being diagnosed with cancer increases as individuals age, most cases occur in adults who are middle-aged or older. About 77% of all cancers are diagnosed in persons 55 years and older. Cancer researchers use the word "risk" in different ways, most commonly expressing risk as lifetime risk or relative risk.

Lifetime risk refers to the probability that an individual, over the course of a lifetime, will develop or die from cancer. In the US, men have slightly less than a 1 in 2 lifetime risk of developing cancer; for women, the risk is a little more than 1 in 3.

Relative risk is a measure of the strength of the relationship between risk factors and a particular cancer. It compares the risk of developing cancer in persons with a certain exposure or trait to the risk in persons who do not have this characteristic. For example, male smokers are about 23 times more likely to develop lung cancer than nonsmokers, so their relative risk is 23. Most relative risks are not this large. For example, women who have a first-degree relative (mother, sister, or daughter) with a history of breast cancer have about twice the risk of developing breast cancer compared to women who do not have this family history.

All cancers involve the malfunction of genes that control cell growth and division. About 5% of all cancers are strongly hereditary, in that an inherited genetic alteration confers a very high risk of developing one or more specific types of cancer. However, most cancers do not result from inherited genes but from damage to genes occurring during one's lifetime. Genetic damage may result from internal factors, such as hormones or the metabolism of nutrients within cells, or external factors, such as tobacco, chemicals, and sunlight.

How Many People Alive Today Have Ever Had Cancer?

The National Cancer Institute estimates that approximately 11.1 million Americans with a history of cancer were alive in January 2005. Some of these individuals were cancer-free, while others still had evidence of cancer and may have been undergoing treatment.

How Many New Cases Are Expected to Occur This Year?

About 1,479,350 new cancer cases are expected to be diagnosed in 2009. This estimate does not include carcinoma in situ (noninvasive cancer) of any site except urinary bladder, and does not include basal and squamous cell skin cancers. More than 1 million unreported cases of

basal and squamous cell skin cancers are expected to be diagnosed this year.

How Many People Are Expected to Die of Cancer This Year?

This year, about 562,340 Americans are expected to die of cancer, more than 1,500 people a day. Cancer is the second most common cause of death in the US, exceeded only by heart disease. In the US, cancer accounts for nearly 1 of every 4 deaths.

What Percentage of People Survive Cancer?

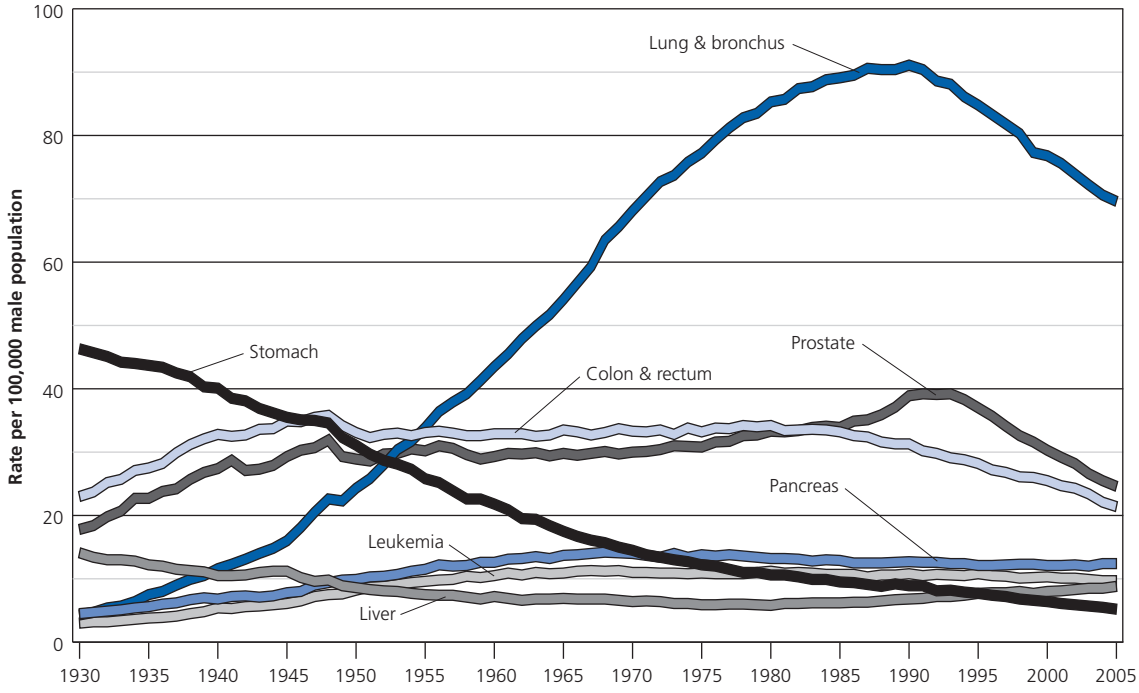
The 5-year relative survival rate for all cancers diagnosed between 1996-2004 is 66%, up from 50% in 1975-1977. (See page 18.) The improvement in survival reflects progress in diagnosing certain cancers at an earlier stage and improvements in treatment. Survival statistics vary greatly by cancer type and stage at diagnosis. Relative survival compares survival among cancer patients to that of people not diagnosed with cancer who are of the same age, race, and sex. It represents the percentage of cancer patients who are alive after some designated time period (usually 5 years) relative to persons without cancer. It does not distinguish between patients who have been cured and those who have relapsed or are still in treatment. While 5-year relative survival is useful in monitoring progress in the early detection and treatment of cancer, it does not represent the proportion of people who are cured permanently, since cancer deaths can occur beyond 5 years after diagnosis.

Although relative survival for specific cancer types provides some indication about the average survival experience of cancer patients in a given population, it may or may not predict individual prognosis and should be interpreted with caution. First, 5-year relative survival rates are based on patients who were diagnosed from 1996-2004 and do not reflect recent advances in detection and treatment. Second, factors that influence survival, such as treatment protocols, additional illnesses, and biological or behavioral differences of each individual, cannot be taken into account in the estimation of relative survival rates. For more information about survival rates, see Sources of Statistics on page 65.

How Is Cancer Staged?

Staging describes the extent or spread of the disease at the time of diagnosis. Proper staging is essential in deter-

Age-adjusted Cancer Death Rates,* Males by Site, US, 1930-2005



American Cancer Society, Surveillance and Health Policy Research, 2009

*Per 100,000, age adjusted to the 2000 US standard population.

Note: Due to changes in ICD coding, numerator information has changed over time. Rates for cancer of the liver, lung and bronchus, and colon and rectum are affected by these coding changes.

Source: US Mortality Data, 1960 to 2005, US Mortality Volumes, 1930 to 1959, National Center for Health Statistics, Centers for Disease Control and Prevention, 2008.

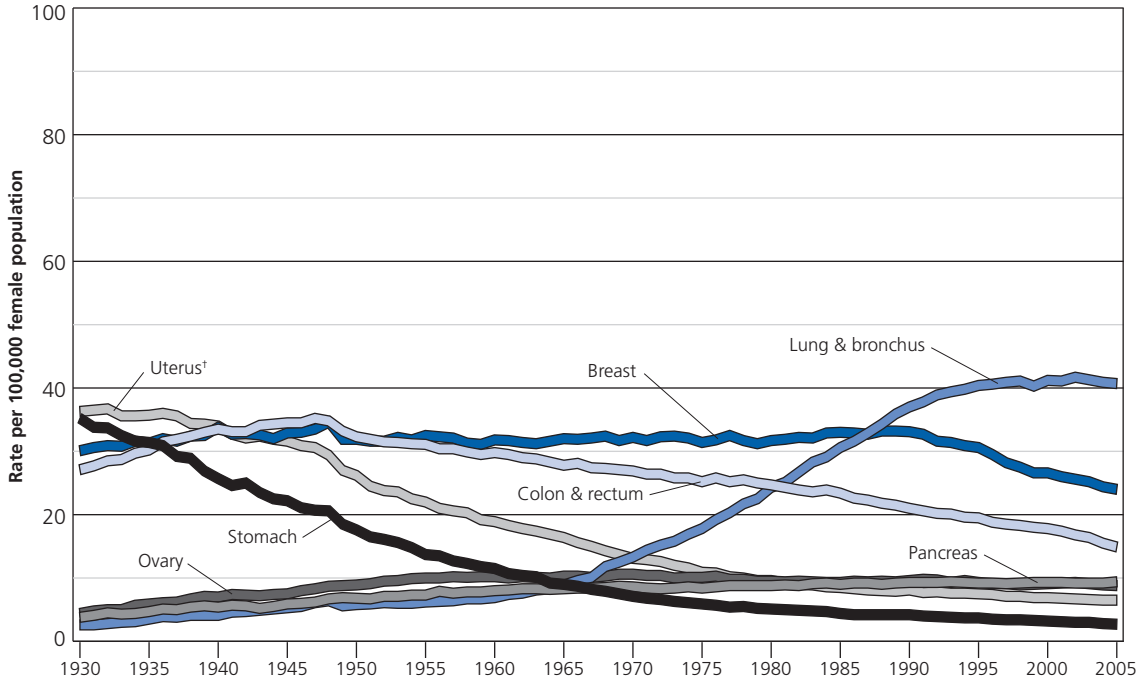
mining the choice of therapy and in assessing prognosis. A cancer's stage is based on the primary tumor's size and whether it has spread to other areas of the body. A number of different staging systems are used to classify tumors. The TNM staging system assesses tumors in three ways: extent of the primary tumor (T), absence or presence of regional lymph node involvement (N), and absence or presence of distant metastases (M). Once the T, N, and M are determined, a stage of I, II, III, or IV is assigned, with stage I being early and stage IV being advanced disease. A different system of summary staging (in situ, local, regional, and distant) is used for descriptive and statistical analysis of tumor registry data. If cancer cells are present only in the layer of cells where they developed and have not spread, the stage is in situ. If cancer cells have penetrated the original layer of tissue, the cancer is invasive. (For a description of the other summary stage categories, see Five-year Relative Survival Rates by Stage at Diagnosis, 1996-2004, page 17.) As the molecular properties of cancer have become better understood, prognostic models have been developed for some cancer sites that incorporate biological markers and genetic features in addition to anatomical characteristics.

What Are the Costs of Cancer?

The National Institutes of Health estimates overall costs of cancer in 2008 at $228.1 billion: $93.2 billion for direct medical costs (total of all health expenditures); $18.8 billion for indirect morbidity costs (cost of lost productivity due to illness); and $116.1 billion for indirect mortality costs (cost of lost productivity due to premature death).

Lack of health insurance and other barriers prevent many Americans from receiving optimal health care. According to early release estimates from the 2008 National Health Interview Survey, about 24% of Americans aged 18 to 64 years and 13% of children had no health insurance coverage for at least part of the past year. More than 36% of adults who lack a high school diploma were uninsured in the past year, compared to 23% of high school graduates and 14% of those with more than a high school education. Lack of health insurance is not only a concern of the unemployed; almost one-quarter of employed individuals (aged 18 to 64 years) were uninsured sometime during the past year. For more information on the relationship between health insurance and cancer, please see *Cancer Facts & Figures 2008* (5008.08), Special Section, available online at cancer.org.

Age-adjusted Cancer Death Rates,* Females by Site, US, 1930-2005



*Per 100,000, age adjusted to the 2000 US standard population. †Uterus cancer death rates are for uterine cervix and uterine corpus combined.

Note: Due to changes in ICD coding, numerator information has changed over time. Rates for cancer of the lung and bronchus, colon and rectum, and ovary are affected by these coding changes.

Source: US Mortality Data, 1960 to 2005, US Mortality Volumes, 1930 to 1959, National Center for Health Statistics, Centers for Disease Control and Prevention, 2008.

American Cancer Society, Surveillance and Health Policy Research, 2009

Estimated New Cancer Cases and Deaths by Sex, US, 2009*

	Estimated New Cases			Estimated Deaths		
	Both Sexes	Male	Female	Both Sexes	Male	Female
All sites	1,479,350	766,130	713,220	562,340	292,540	269,800
Oral cavity & pharynx	35,720	25,240	10,480	7,600	5,240	2,360
Tongue	10,530	7,470	3,060	1,910	1,240	670
Mouth	10,750	6,450	4,300	1,810	1,110	700
Pharynx	12,610	10,020	2,590	2,230	1,640	590
Other oral cavity	1,830	1,300	530	1,650	1,250	400
Digestive system	275,720	150,020	125,700	135,830	76,020	59,810
Esophagus	16,470	12,940	3,530	14,530	11,490	3,040
Stomach	21,130	12,820	8,310	10,620	6,320	4,300
Small intestine	6,230	3,240	2,990	1,110	580	530
Colon†	106,100	52,010	54,090	49,920	25,240	24,680
Rectum	40,870	23,580	17,290			
Anus, anal canal, & anorectum	5,290	2,100	3,190	710	260	450
Liver & intrahepatic bile duct	22,620	16,410	6,210	18,160	12,090	6,070
Gallbladder & other biliary	9,760	4,320	5,440	3,370	1,250	2,120
Pancreas	42,470	21,050	21,420	35,240	18,030	17,210
Other digestive organs	4,780	1,550	3,230	2,170	760	1,410
Respiratory system	236,990	129,710	107,280	163,790	92,240	71,550
Larynx	12,290	9,920	2,370	3,660	2,900	760
Lung & bronchus	219,440	116,090	103,350	159,390	88,900	70,490
Other respiratory organs	5,260	3,700	1,560	740	440	300
Bones & joints	2,570	1,430	1,140	1,470	800	670
Soft tissue (including heart)	10,660	5,780	4,880	3,820	1,960	1,860
Skin (excluding basal & squamous)	74,610	42,920	31,690	11,590	7,670	3,920
Melanoma	68,720	39,080	29,640	8,650	5,550	3,100
Other non-epithelial skin	5,890	3,840	2,050	2,940	2,120	820
Breast	194,280	1,910	192,370	40,610	440	40,170
Genital system	282,690	201,970	80,720	56,160	28,040	28,120
Uterine cervix	11,270		11,270	4,070		4,070
Uterine corpus	42,160		42,160	7,780		7,780
Ovary	21,550		21,550	14,600		14,600
Vulva	3,580		3,580	900		900
Vagina & other genital, female	2,160		2,160	770		770
Prostate	192,280	192,280		27,360	27,360	
Testis	8,400	8,400		380	380	
Penis & other genital, male	1,290	1,290		300	300	
Urinary system	131,010	89,640	41,370	28,100	18,800	9,300
Urinary bladder	70,980	52,810	18,170	14,330	10,180	4,150
Kidney & renal pelvis	57,760	35,430	22,330	12,980	8,160	4,820
Ureter & other urinary organs	2,270	1,400	870	790	460	330
Eye & orbit	2,350	1,200	1,150	230	120	110
Brain & other nervous system	22,070	12,010	10,060	12,920	7,330	5,590
Endocrine system	39,330	11,070	28,260	2,470	1,100	1,370
Thyroid	37,200	10,000	27,200	1,630	690	940
Other endocrine	2,130	1,070	1,060	840	410	430
Lymphoma	74,490	40,630	33,860	20,790	10,630	10,160
Hodgkin lymphoma	8,510	4,640	3,870	1,290	800	490
Non-Hodgkin lymphoma	65,980	35,990	29,990	19,500	9,830	9,670
Myeloma	20,580	11,680	8,900	10,580	5,640	4,940
Leukemia	44,790	25,630	19,160	21,870	12,590	9,280
Acute lymphocytic leukemia	5,760	3,350	2,410	1,400	740	660
Chronic lymphocytic leukemia	15,490	9,200	6,290	4,390	2,630	1,760
Acute myeloid leukemia	12,810	6,920	5,890	9,000	5,170	3,830
Chronic myeloid leukemia	5,050	2,930	2,120	470	220	250
Other leukemia‡	5,680	3,230	2,450	6,610	3,830	2,780
Other & unspecified primary sites‡	31,490	15,290	16,200	44,510	23,920	20,590

*Rounded to the nearest 10; estimated new cases exclude basal and squamous cell skin cancers and in situ carcinomas except urinary bladder. About 62,280 female carcinoma in situ of the breast and 53,120 melanoma in situ will be newly diagnosed in 2009. †Estimated deaths for colon and rectum cancers are combined. ‡More deaths than cases suggests lack of specificity in recording underlying causes of death on death certificates.

Source: Estimated new cases are based on 1995-2005 incidence rates from 41 states and the District of Columbia as reported by the North American Association of Central Cancer Registries (NAACCR), representing about 85% of the US population. Estimated deaths are based on data from US Mortality Data, 1969-2006, National Center for Health Statistics, Centers for Disease Control and Prevention, 2009.

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Estimated New Cancer Cases for Selected Cancer Sites by State, US, 2009*

State	All Sites	Female Breast	Uterine Cervix	Colon & Rectum	Uterine Corpus	Leukemia	Lung & Bronchus	Melanoma of the Skin	Non-Hodgkin Lymphoma	Prostate	Urinary Bladder
Alabama	24,090	2,970	190	2,480	510	590	4,040	930	950	2,800	960
Alaska	2,530	370	†	250	70	70	350	80	110	360	120
Arizona	27,600	3,470	210	2,680	660	810	3,960	1,460	1,250	3,530	1,460
Arkansas	14,800	1,820	130	1,540	310	420	2,580	500	680	2,140	610
California	152,170	21,740	1,350	14,680	4,230	4,570	17,910	9,080	7,140	20,790	6,870
Colorado	20,340	2,840	150	1,860	530	720	2,240	1,260	920	3,070	940
Connecticut	20,650	2,790	110	1,950	660	540	2,720	1,260	920	2,400	1,120
Delaware	4,690	600	†	440	140	120	800	220	190	550	220
Dist. of Columbia	2,600	340	†	260	80	50	370	70	90	380	90
Florida	102,210	12,650	800	10,420	2,590	3,180	17,790	4,920	4,640	12,380	5,490
Georgia	39,080	5,370	340	3,750	930	1,080	6,150	2,040	1,560	5,210	1,400
Hawaii	6,400	870	50	710	200	160	740	320	260	860	220
Idaho	6,800	810	†	630	170	250	820	380	330	1,170	340
Illinois	60,960	7,610	480	6,430	1,960	1,940	9,180	2,010	2,900	7,590	3,100
Indiana	31,320	3,710	220	3,260	970	930	5,360	1,170	1,420	3,250	1,550
Iowa	16,740	2,080	90	1,800	500	590	2,620	910	750	2,330	870
Kansas	13,080	1,790	90	1,290	400	380	2,110	610	600	1,970	620
Kentucky	24,060	2,840	180	2,620	590	690	4,650	1,260	980	2,910	1,070
Louisiana	22,170	2,700	190	2,330	430	660	3,650	630	960	3,160	910
Maine	9,000	1,080	50	870	270	270	1,390	480	360	1,130	500
Maryland	26,650	3,660	190	2,620	840	640	4,060	1,310	1,120	3,580	1,110
Massachusetts	36,080	4,800	200	3,380	1,140	1,000	5,120	2,030	1,610	4,200	2,010
Michigan	53,550	6,480	320	5,020	1,700	1,690	8,190	2,240	2,470	7,010	2,810
Minnesota	23,670	3,280	140	2,520	810	890	3,310	890	1,130	4,910	1,200
Mississippi	14,150	1,820	130	1,480	270	360	2,340	380	540	1,990	540
Missouri	30,090	3,880	220	3,100	870	880	5,600	1,260	1,250	3,620	1,450
Montana	5,340	640	†	520	140	170	730	220	240	810	270
Nebraska	8,810	1,200	60	950	270	290	1,230	420	400	1,410	450
Nevada	12,020	1,350	110	1,240	270	380	1,910	480	480	1,660	630
New Hampshire	7,630	1,010	†	730	240	210	1,100	460	310	910	420
New Jersey	47,920	6,440	410	4,590	1,620	1,380	6,250	2,530	2,160	6,060	2,640
New Mexico	8,830	1,090	80	810	210	310	970	460	360	1,400	350
New York	101,550	13,530	870	9,970	3,510	3,140	13,550	3,710	4,540	12,520	5,360
North Carolina	42,270	5,470	340	4,230	1,030	1,150	6,670	2,190	1,730	6,130	1,790
North Dakota	3,200	410	†	350	90	110	420	110	140	560	180
Ohio	62,420	7,340	390	6,060	1,930	1,950	10,690	2,080	2,800	6,510	2,990
Oklahoma	18,110	2,340	140	1,860	400	580	3,220	690	820	2,190	770
Oregon	19,210	2,680	110	1,780	570	490	2,610	1,220	910	2,510	1,020
Pennsylvania	74,170	9,380	500	7,590	2,550	2,200	10,480	3,440	3,330	8,130	4,160
Rhode Island	6,250	810	†	590	190	180	900	340	260	650	370
South Carolina	22,100	2,820	170	2,150	520	590	3,680	1,090	870	2,910	880
South Dakota	4,120	530	†	440	120	140	590	180	180	740	230
Tennessee	32,570	3,970	240	3,490	720	1,000	5,370	1,410	1,370	4,790	1,380
Texas	98,200	13,090	980	9,800	2,220	3,470	14,150	3,820	4,530	13,130	3,720
Utah	8,880	1,080	60	770	250	330	620	600	440	1,570	360
Vermont	3,550	480	†	330	120	100	500	200	140	540	190
Virginia	34,150	4,850	240	3,380	1,020	840	5,330	1,790	1,450	4,830	1,430
Washington	32,290	4,520	190	2,890	960	990	4,130	1,970	1,540	4,680	1,660
West Virginia	10,230	1,180	70	1,070	330	290	2,030	450	420	1,210	510
Wisconsin	27,560	3,480	160	2,770	1,000	980	3,960	1,040	1,310	2,770	1,530
Wyoming	2,500	300	†	240	70	70	320	130	110	390	130
United States	1,479,350	192,370	11,270	146,970	42,160	44,790	219,440	68,720	65,980	192,280	70,980

* Rounded to nearest 10. Excludes basal and squamous cell skin cancers and in situ carcinomas except urinary bladder. † Estimate is fewer than 50 cases.

Note: These estimates are offered as a rough guide and should be interpreted with caution. State estimates may not sum to US total due to rounding and exclusion of state estimates fewer than 50 cases.

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Estimated Cancer Deaths for Selected Cancer Sites by State, US, 2009*

State	All Sites	Brain/ Nervous System	Female Breast	Colon & Rectum	Leukemia	Liver	Lung & Bronchus	Non-Hodgkin Lymphoma	Ovary	Pancreas	Prostate
Alabama	9,900	200	700	940	340	280	3,140	290	270	550	510
Alaska	830	†	60	70	†	†	220	†	†	50	†
Arizona	10,260	280	740	970	410	360	2,820	350	290	630	580
Arkansas	6,230	130	410	580	250	190	2,160	200	130	400	340
California	54,600	1,460	4,030	4,830	2,200	2,450	12,750	1,900	1,580	3,740	2,780
Colorado	6,740	200	520	670	300	210	1,670	230	210	430	350
Connecticut	6,990	150	480	550	270	210	1,810	220	180	540	390
Delaware	1,860	50	110	150	70	50	590	50	†	110	90
Dist. of Columbia	970	†	70	100	50	†	240	†	†	60	60
Florida	41,270	810	2,730	3,460	1,650	1,300	12,210	1,560	970	2,470	2,280
Georgia	14,970	320	1,130	1,370	550	400	4,660	460	400	870	800
Hawaii	2,270	†	140	210	80	120	570	80	50	170	100
Idaho	2,450	90	160	200	120	80	630	80	50	200	160
Illinois	23,220	470	1,770	2,260	950	700	6,460	770	600	1,560	1,150
Indiana	12,820	290	860	1,130	520	350	4,000	420	340	770	520
Iowa	6,360	160	400	600	300	150	1,760	280	170	380	330
Kansas	5,290	150	370	510	200	140	1,620	180	150	330	210
Kentucky	9,410	150	590	840	320	240	3,430	300	210	500	390
Louisiana	8,810	210	690	910	310	330	2,700	310	210	530	450
Maine	3,190	80	180	260	110	80	980	90	70	200	160
Maryland	10,320	200	810	940	390	320	2,880	300	260	690	550
Massachusetts	13,140	270	870	1,070	490	420	3,610	430	350	880	540
Michigan	20,450	490	1,350	1,720	820	610	5,840	710	520	1,250	820
Minnesota	9,020	230	600	760	370	260	2,380	320	240	580	410
Mississippi	6,090	160	430	600	220	190	2,030	180	140	350	300
Missouri	12,620	270	890	1,100	530	360	4,100	430	290	750	660
Montana	1,980	50	120	170	90	50	550	70	50	120	120
Nebraska	3,360	80	210	350	150	80	890	130	90	190	200
Nevada	4,600	120	330	500	140	160	1,340	130	120	280	230
New Hampshire	2,620	70	170	220	100	70	750	60	60	170	130
New Jersey	16,480	320	1,470	1,580	610	540	4,190	610	450	1,080	660
New Mexico	3,300	80	240	320	120	150	710	110	90	220	210
New York	34,190	790	2,550	3,110	1,380	1,210	8,780	1,430	970	2,360	1,470
North Carolina	18,550	330	1,310	1,410	640	470	5,630	530	430	1,090	860
North Dakota	1,300	†	80	120	50	†	370	†	†	90	100
Ohio	24,350	550	1,790	2,210	890	640	7,300	740	580	1,430	1,200
Oklahoma	7,420	170	520	600	290	200	2,390	240	170	380	280
Oregon	7,380	210	500	610	290	210	2,140	330	220	470	390
Pennsylvania	28,690	550	2,070	2,550	1,080	790	8,090	1,090	760	1,920	1,440
Rhode Island	2,220	50	130	160	90	70	560	70	60	120	100
South Carolina	9,100	190	640	780	330	250	2,880	310	210	530	420
South Dakota	1,640	†	100	150	60	†	450	70	50	100	100
Tennessee	13,340	350	910	1,140	480	350	4,520	440	310	730	570
Texas	36,030	850	2,570	3,140	1,430	1,650	9,780	1,300	890	2,120	1,700
Utah	2,760	100	260	240	130	70	480	130	90	190	170
Vermont	1,150	†	80	120	60	†	350	†	†	70	60
Virginia	13,920	290	1,140	1,270	500	390	4,250	410	380	880	620
Washington	11,210	380	790	940	450	410	3,090	410	340	710	680
West Virginia	4,530	90	280	430	140	110	1,500	180	120	210	140
Wisconsin	11,170	260	750	900	500	320	2,910	400	300	710	500
Wyoming	990	†	60	100	†	†	260	†	†	60	†
United States	562,340	12,920	40,170	49,920	21,870	18,160	159,390	19,500	14,600	35,240	27,360

* Rounded to nearest 10. †Estimate is fewer than 50 deaths.

Note: State estimates may not sum to US total due to rounding and exclusion of state estimates fewer than 50 deaths.

Source: US Mortality Data, 1969-2006, National Center for Health Statistics, Centers for Disease Control and Prevention, 2009.

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Cancer Incidence Rates* by Site and State, US, 2001-2005

	All Sites		Breast	Colon & Rectum		Lung & Bronchus		Non-Hodgkin Lymphoma		Prostate	Urinary Bladder	
State	**Male**	**Female**	**Female**	**Male**	**Female**	**Male**	**Female**	**Male**	**Female**	**Male**	**Male**	**Female**
Alabama†	555.6	377.6	114.2	62.2	41.9	109.5	52.5	20.5	14.0	150.7	31.1	7.7
Alaska†	533.2	410.6	127.9	61.3	46.0	82.4	62.8	23.5	16.1	151.3	39.4	7.2
Arizona	461.7	363.0	109.8	49.4	36.3	69.8	48.8	18.6	13.2	116.6	35.0	8.7
Arkansas†	558.2	381.5	114.0	59.2	43.6	113.4	59.0	21.9	15.1	158.1	33.1	8.9
California†	518.2	396.4	124.7	53.8	39.8	67.0	47.5	22.6	15.5	152.6	34.4	8.3
Colorado†	512.7	401.7	125.9	51.5	41.0	63.0	46.0	21.4	16.3	159.4	35.0	9.1
Connecticut†	589.5	454.3	137.4	65.2	47.9	82.5	58.8	25.5	17.8	166.6	44.6	12.5
Delaware†	601.7	438.6	126.4	62.6	46.4	97.8	66.2	22.5	16.7	175.5	42.4	11.0
Dist. of Columbia‡	—	—	—	—	—	—	—	—	—	—	—	—
Florida†	549.3	410.1	116.7	67.7	43.4	91.4	60.8	21.9	15.5	143.1	38.7	10.0
Georgia†	571.3	395.2	120.6	60.1	42.6	104.1	53.4	20.6	14.2	163.6	33.0	8.1
Hawaii†	484.9	385.9	126.0	62.4	42.5	67.8	38.9	18.9	12.7	129.3	25.1	6.2
Idaho†	543.5	399.0	118.2	52.0	38.5	69.6	46.7	21.5	17.2	168.8	38.4	8.5
Illinois†	580.1	426.8	124.1	68.0	48.5	93.1	57.8	23.8	16.3	159.5	40.8	10.4
Indiana†	552.3	414.9	117.7	64.6	47.3	105.3	62.2	22.6	16.0	136.9	37.2	9.3
Iowa†	560.9	428.3	125.4	67.2	50.5	89.3	52.4	23.5	17.0	147.3	40.6	9.8
Kansas‡	—	—	—	—	—	—	—	—	—	—	—	—
Kentucky†	612.5	447.1	120.5	70.3	51.4	136.2	76.2	22.4	16.9	144.4	38.1	9.8
Louisiana†	624.9	409.5	120.9	70.1	48.3	111.3	58.2	22.9	16.2	180.2	35.6	8.7
Maine†	621.6	460.6	130.6	67.7	49.1	99.8	65.7	24.5	18.6	166.8	48.7	12.9
Maryland‡	—	—	—	—	—	—	—	—	—	—	—	—
Massachusetts†	604.0	455.9	133.8	67.6	48.4	86.0	63.0	24.1	17.1	170.2	46.5	12.9
Michigan†	608.0	440.2	127.0	61.0	45.7	94.3	61.3	25.0	18.5	186.4	42.5	10.7
Minnesota†	568.8	418.6	129.3	57.9	43.1	71.4	49.2	26.4	18.1	185.9	40.0	10.5
Mississippi (2002-2005)	555.6	365.5	105.8	62.9	45.2	110.1	50.9	19.9	13.0	161.9	28.3	7.4
Missouri†	545.3	414.6	123.0	64.7	46.1	105.4	61.8	21.8	15.9	131.5	36.2	9.2
Montana†	561.2	412.3	122.6	55.4	41.5	78.2	57.9	23.2	15.0	182.4	41.9	9.3
Nebraska†	557.0	417.9	127.8	68.5	48.0	84.5	48.8	24.0	16.9	157.3	37.8	10.0
Nevada†	539.9	415.8	116.0	56.9	43.1	84.3	69.5	21.9	15.0	148.7	43.0	11.2
New Hampshire†	586.7	451.9	132.3	61.7	46.9	82.3	61.5	24.4	18.1	162.7	47.9	13.5
New Jersey†	612.5	451.5	129.8	68.3	50.0	80.9	56.0	25.9	17.7	183.9	46.0	12.2
New Mexico†	490.7	367.7	111.7	50.8	35.4	59.1	38.5	18.4	14.0	149.3	28.0	7.0
New York†	575.7	432.7	124.6	63.4	47.2	80.5	53.7	24.3	16.9	165.9	42.1	11.2
North Carolina‡	—	—	—	—	—	—	—	—	—	—	—	—
North Dakota†	543.8	396.7	122.5	68.3	44.1	74.9	47.1	22.6	15.3	170.8	36.7	9.9
Ohio	543.8	413.6	121.9	62.7	45.8	97.2	58.9	22.8	16.2	145.6	38.7	9.7
Oklahoma†	551.3	409.2	126.4	61.2	43.9	107.4	63.8	22.3	16.2	147.0	33.8	8.1
Oregon†	533.4	430.0	134.7	54.4	41.7	79.9	60.4	24.1	17.5	151.4	40.3	10.4
Pennsylvania†	593.9	444.0	125.7	68.4	49.6	91.6	55.7	24.8	17.3	161.4	44.6	11.3
Rhode Island†	616.7	446.9	127.5	67.8	46.8	94.5	59.5	25.0	16.7	161.6	51.6	12.9
South Carolina†	589.6	395.2	119.2	63.5	44.9	103.8	52.3	20.6	14.5	172.3	32.6	7.7
South Dakota†	568.5	406.0	125.5	63.8	46.7	80.3	45.0	22.4	17.4	183.0	39.7	8.3
Tennessee§	496.9	377.4	115.3	57.7	42.2	105.0	56.4	19.4	14.2	120.3	31.5	7.8
Texas†	546.5	390.9	116.3	59.5	40.5	90.4	51.2	22.2	16.1	146.6	30.2	7.4
Utah†	493.1	348.2	112.9	46.3	34.1	39.6	22.4	22.9	15.8	185.0	29.1	6.4
Vermont‡	—	—	—	—	—	—	—	—	—	—	—	—
Virginia	515.6	376.4	119.5	56.7	42.3	86.1	51.9	19.6	13.1	154.1	32.1	8.3
Washington†	571.2	447.7	138.9	54.6	41.4	80.5	60.0	26.9	18.4	167.7	41.6	10.4
West Virginia†	576.0	433.6	115.3	70.6	51.7	117.0	69.4	22.3	16.0	139.4	40.0	11.4
Wisconsin‡	—	—	—	—	—	—	—	—	—	—	—	—
Wyoming†	515.5	394.8	117.9	49.4	43.6	62.6	47.2	20.6	16.3	171.2	41.5	9.5
United States	562.3	417.3	123.6	61.2	44.8	87.3	55.4	23.2	16.3	158.2	38.4	9.8

* Per 100,000, age adjusted to the 2000 US standard population. Rates for Alabama, Louisiana, Mississippi, and Texas are for cases diagnosed through June 2005.
† This state's registry has submitted 5 years of data and passed rigorous criteria for each single year's data, including completeness of reporting, non-duplication of records, percent unknown in critical data fields, percent of cases registered with information from death certificates only, and internal consistency among data items.
‡ This state's registry did not submit incidence data to the North American Association of Central Cancer Registries (NAACCR) for 2001-2005.
§ Case ascertainment for this state's registry is incomplete for the years 2001-2005.

Source: NAACCR, 2008. Data are collected by cancer registries participating in the National Cancer Institute's SEER program and the Centers for Disease Control and Prevention's National Program of Cancer Registries.

American Cancer Society, Surveillance and Health Policy Research, 2009

Cancer Death Rates* by Site and State, US, 2001-2005

	All Sites		Breast	Colon & Rectum		Lung & Bronchus		Non-Hodgkin Lymphoma		Pancreas		Prostate
State	Male	Female	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male
Alabama	271.7	163.6	26.0	23.9	15.2	94.8	41.6	9.1	6.0	12.4	9.1	33.0
Alaska	226.7	155.9	20.5	21.6	14.8	67.1	44.2	8.3	4.9	12.2	9.0	26.1
Arizona	201.3	142.0	22.2	19.5	13.5	57.2	36.9	8.5	5.7	10.8	8.0	23.2
Arkansas	266.8	166.2	24.4	25.0	16.8	99.0	47.1	9.7	5.5	12.3	9.0	28.9
California	206.4	150.5	23.7	19.8	14.3	54.8	36.3	8.8	5.4	11.6	9.2	25.0
Colorado	199.3	145.4	22.6	20.0	15.1	51.0	33.6	8.7	5.6	11.0	8.9	26.5
Connecticut	225.1	158.6	25.1	20.7	15.5	62.0	40.2	9.4	5.9	13.3	9.9	27.0
Delaware	252.8	171.0	25.1	23.8	16.7	80.5	48.7	9.9	5.8	11.5	9.5	29.4
Dist. of Columbia	275.5	169.4	31.0	27.0	18.1	76.3	36.1	9.1	4.5	14.4	10.6	43.8
Florida	219.9	149.9	23.0	20.3	14.2	69.8	41.7	8.8	5.4	11.6	8.5	22.3
Georgia	250.9	158.3	24.7	22.7	15.7	86.0	39.8	8.3	5.4	12.5	9.0	30.6
Hawaii	189.4	123.0	18.0	21.1	11.8	49.8	26.2	7.4	4.4	11.9	9.6	18.8
Idaho	208.4	147.6	22.1	18.2	13.4	55.9	34.9	9.2	6.0	11.4	9.9	29.0
Illinois	245.6	167.3	26.2	25.8	17.2	74.3	41.9	9.6	6.2	13.1	9.9	28.1
Indiana	257.7	171.1	25.0	25.7	17.0	87.2	47.4	10.3	6.7	12.9	9.5	27.8
Iowa	231.3	156.1	23.1	23.7	16.5	72.6	38.4	10.1	6.6	11.5	9.4	27.5
Kansas	231.9	157.3	24.3	22.4	16.2	73.7	41.5	10.4	6.5	12.2	8.9	25.0
Kentucky	286.9	180.5	25.6	26.6	18.9	111.5	55.9	9.9	6.2	12.0	9.1	26.9
Louisiana	285.9	178.0	29.7	28.5	17.9	95.9	46.3	9.8	6.4	13.8	10.7	32.2
Maine	256.0	173.8	23.5	22.8	17.0	79.5	48.4	9.6	6.6	13.7	9.6	28.1
Maryland	241.4	167.6	27.4	24.1	16.9	73.1	44.1	8.9	5.6	12.9	10.2	29.3
Massachusetts	237.8	166.2	24.8	23.3	16.5	67.3	44.5	9.5	6.4	13.3	10.0	26.4
Michigan	240.2	165.7	25.3	22.4	15.9	74.5	44.1	10.5	6.7	12.7	9.3	26.5
Minnesota	219.2	153.0	23.0	19.8	14.7	59.5	37.3	10.1	6.3	11.8	9.0	28.6
Mississippi	282.6	165.8	26.9	25.5	17.9	101.3	43.2	8.6	5.3	13.1	9.7	36.2
Missouri	252.1	168.6	26.6	24.4	16.7	87.2	46.0	9.8	6.3	12.6	9.0	24.3
Montana	222.0	162.0	23.8	20.5	13.8	64.9	44.6	9.8	5.8	11.1	8.8	29.2
Nebraska	220.6	152.4	24.0	23.5	16.9	66.9	36.2	9.1	6.2	11.2	7.9	25.1
Nevada	229.4	171.6	25.3	24.6	16.8	68.3	51.9	7.6	5.4	11.7	9.5	26.6
New Hampshire	237.6	164.2	24.3	23.0	16.1	67.4	44.8	9.6	6.4	11.2	10.7	28.3
New Jersey	232.4	169.2	27.8	24.9	17.9	64.8	40.4	9.7	6.0	12.5	10.0	26.2
New Mexico	203.4	140.9	22.1	20.6	13.8	48.8	29.7	7.8	5.1	11.2	8.9	26.9
New York	217.1	156.8	25.6	23.1	16.5	61.0	37.6	8.6	5.4	12.4	9.9	26.0
North Carolina	251.8	160.1	25.4	22.1	15.5	85.1	41.3	9.0	5.8	12.8	9.2	29.9
North Dakota	216.3	149.6	24.0	22.0	16.5	60.5	34.1	9.1	5.7	11.7	8.7	28.1
Ohio	254.9	171.2	27.6	24.9	17.5	82.4	45.2	9.9	6.4	12.3	9.2	27.9
Oklahoma	252.2	164.5	25.4	24.3	16.0	87.6	46.1	9.8	5.8	12.0	8.3	24.9
Oregon	228.2	166.9	24.5	21.0	15.1	66.5	46.7	10.3	7.0	12.3	9.7	27.7
Pennsylvania	246.4	168.0	27.0	25.4	17.3	73.7	40.5	10.2	6.5	12.8	9.5	26.9
Rhode Island	243.3	164.4	23.5	23.0	17.1	72.8	42.7	9.3	6.2	11.6	9.8	27.0
South Carolina	263.7	159.0	25.3	23.7	15.9	88.9	40.1	8.2	5.7	12.7	9.4	32.4
South Dakota	228.2	150.8	22.9	23.4	15.8	67.6	35.9	8.8	6.1	11.4	10.4	28.8
Tennessee	272.4	170.9	26.2	25.0	16.5	99.9	46.7	10.1	6.4	12.5	9.6	29.3
Texas	232.3	152.6	23.8	21.9	14.7	72.7	38.5	8.8	5.8	11.8	8.7	25.5
Utah	172.5	117.9	23.1	15.9	11.8	33.7	16.9	9.2	5.2	10.9	7.3	26.5
Vermont	226.2	156.2	24.2	23.1	16.5	64.6	39.2	9.9	5.5	10.5	8.0	28.3
Virginia	244.8	162.5	26.5	23.4	15.7	76.8	42.5	8.7	5.6	12.4	9.3	30.1
Washington	222.8	162.7	23.6	19.7	14.6	65.2	45.2	10.3	6.1	12.4	9.8	26.8
West Virginia	265.6	178.2	25.1	27.0	18.8	92.8	50.6	10.4	6.3	10.9	7.7	25.0
Wisconsin	230.8	157.6	24.0	22.0	15.0	64.3	38.4	9.6	6.1	12.6	9.8	28.8
Wyoming	211.2	157.4	22.6	19.7	17.0	58.8	38.0	7.9	7.7	12.1	9.6	25.8
United States	234.4	159.9	25.0	22.7	15.9	72.0	41.0	9.3	5.9	12.2	9.3	26.7

*Per 100,000, age adjusted to the 2000 US standard population.

Source: US Mortality Data 1960-2005, National Center for Health Statistics, Centers for Disease Control and Prevention, 2008.

American Cancer Society, Surveillance and Health Policy Research, 2009

Selected Cancers

Breast

New cases: An estimated 192,370 new cases of invasive breast cancer are expected to occur among women in the US during 2009; about 1,910 new cases are expected in men. Excluding cancers of the skin, breast cancer is the most frequently diagnosed cancer in women. After continuously increasing for more than two decades, female breast cancer incidence rates decreased by 2.2% per year from 1999-2005. This decrease may reflect reductions in the use of menopausal hormone therapy (MHT), previously known as hormone replacement therapy, following the publication of results from the Women's Health Initiative in 2002, which linked MHT use to increased risk of heart diseases and breast cancer. It may also reflect a slight drop in mammography utilization, which may delay the diagnosis of some tumors. According to the National Health Interview Survey, mammography rates in women 40 and older decreased from 70.1% in 2000 to 66.4% in 2005.

In addition to invasive breast cancer, 62,280 new cases of in situ breast cancer are expected to occur among women in 2009. Of these, approximately 85% will be ductal carcinoma in situ (DCIS). In situ breast cancer incidence rates have stabilized since 2000.

Deaths: An estimated 40,610 breast cancer deaths (40,170 women, 440 men) are expected in 2009. Breast cancer ranks second as a cause of cancer death in women (after lung cancer). Death rates for breast cancer have steadily decreased in women since 1990, with larger decreases in women younger than 50 (a decrease of 3.2% per year) than in those 50 and older (2.0% per year). The decrease in breast cancer death rates represents progress in both earlier detection and improved treatment.

Signs and symptoms: The earliest sign of breast cancer is often an abnormality detected on a mammogram, before it can be felt by the woman or a health care professional. Larger tumors may become evident as a painless mass. Less common symptoms include persistent changes to the breast, such as thickening, swelling, distortion, tenderness, skin irritation, redness, or scaliness, or nipple abnormalities, such as ulceration, retraction, or spontaneous discharge. Typically, breast pain results from benign conditions and is not an early symptom of breast cancer.

Risk factors: Aside from being female, age is the most important risk factor for breast cancer. Potentially modifiable risk factors include being overweight or obese after menopause, use of MHT (especially combined estrogen and progestin therapy), physical inactivity, and consumption of one or more alcoholic beverages per day. (Many studies have also shown that being overweight adversely affects survival for postmenopausal women with breast cancer.) Medical findings that predict higher risk include high breast tissue density (a mammographic measure of the amount of glandular tissue relative to fatty tissue in the breast), high bone mineral density (routinely measured to identify women at increased risk for osteoporosis), and biopsy-confirmed hyperplasia (especially atypical hyperplasia). High-dose radiation to the chest, typically related to a medical procedure, also increases risk. Reproductive factors that increase risk include a long menstrual history (menstrual periods that start early and/or end late in life), recent use of oral contraceptives, never having children, and having one's first child after age 30.

Risk is also increased by a personal or family history of breast cancer and inherited genetic mutations in the breast cancer susceptibility genes BRCA1 and BRCA2. Although these mutations account for approximately 5%-10% of all breast cancer cases, they are very rare in the general population (less than 1%), so widespread testing is not recommended. Some population groups, such as individuals of Ashkenazi Jewish descent, have an increased prevalence of BRCA1 and BRCA2 mutation carriers. Women with a strong family history of breast and/or ovarian cancer should be offered counseling to determine if genetic testing is appropriate. Studies suggest that prophylactic removal of the breasts and/or ovaries in BRCA1 and BRCA2 mutation carriers decreases the risk of breast cancer considerably, although not all women who choose this surgery would have developed these cancers. Women who consider these options should undergo counseling before reaching a decision. Male members of families with BRCA1 or BRCA2 mutations carriers are also at risk for these mutations and may be at increased risk for breast cancer.

Modifiable factors that are associated with a lower risk of breast cancer include breastfeeding, moderate or vigorous physical activity, and maintaining a healthy body weight. Recent studies have found that after a breast cancer diagnosis, women who are more physically active are also less likely to die from the disease than women who are inactive.

Leading Sites of New Cancer Cases and Deaths – 2009 Estimates

Estimated New Cases*		Estimated Deaths	
Male	**Female**	**Male**	**Female**
Prostate 192,280 (25%)	Breast 192,370 (27%)	Lung & bronchus 88,900 (30%)	Lung & bronchus 70,490 (26%)
Lung & bronchus 116,090 (15%)	Lung & bronchus 103,350 (14%)	Prostate 27,360 (9%)	Breast 40,170 (15%)
Colon & rectum 75,590 (10%)	Colon & rectum 71,380 (10%)	Colon & rectum 25,240 (9%)	Colon & rectum 24,680 (9%)
Urinary bladder 52,810 (7%)	Uterine corpus 42,160 (6%)	Pancreas 18,030 (6%)	Pancreas 17,210 (6%)
Melanoma of the skin 39,080 (5%)	Non-Hodgkin lymphoma 29,990 (4%)	Leukemia 12,590 (4%)	Ovary 14,600 (5%)
Non-Hodgkin lymphoma 35,990 (5%)	Melanoma of the skin 29,640 (4%)	Liver & intrahepatic bile duct 12,090 (4%)	Non-Hodgkin lymphoma 9,670 (4%)
Kidney & renal pelvis 35,430 (5%)	Thyroid 27,200 (4%)	Esophagus 11,490 (4%)	Leukemia 9,280 (3%)
Leukemia 25,630 (3%)	Kidney & renal pelvis 22,330 (3%)	Urinary bladder 10,180 (3%)	Uterine corpus 7,780 (3%)
Oral cavity & pharynx 25,240 (3%)	Ovary 21,550 (3%)	Non-Hodgkin lymphoma 9,830 (3%)	Liver & intrahepatic bile duct 6,070 (2%)
Pancreas 21,050 (3%)	Pancreas 21,420 (3%)	Kidney & renal pelvis 8,160 (3%)	Brain & other nervous system 5,590 (2%)
All sites 766,130 (100%)	All sites 713,220 (100%)	All sites 292,540 (100%)	All sites 269,800 (100%)

*Excludes basal and squamous cell skin cancers and in situ carcinoma except urinary bladder.

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Two medications, tamoxifen and raloxifene, have been approved to reduce breast cancer risk in women at high risk. Although both drugs are equally effective in reducing the risk of invasive breast cancer in postmenopausal women, only tamoxifen protects against in situ cancer. However, raloxifene appears to have a lower risk of certain side effects, such as uterine cancer and blood clots. Chemoprevention using these drugs is also routinely used to prevent second breast cancers.

There is currently no evidence that certain environmental exposures promoted by some groups as causing breast cancer (exposure to polluted water or air, exhaust fumes, personal care products containing estrogens, etc.) are associated with breast cancer risk.

Early detection: Mammography can detect breast cancer at an early stage, when treatment is more effective and a cure is more likely. Numerous studies have shown that early detection saves lives and increases treatment options. Steady declines in breast cancer mortality among women since 1990 have been attributed to a combination of early detection and improvements in treatment. Mammography is highly accurate, but like most medical tests, it is not perfect. On average, mammography will detect about 80%-90% of breast cancers in women without symptoms. All suspicious abnormalities should be biopsied for a definitive diagnosis. Several recent studies have shown that magnetic resonance imaging (MRI) is more sensitive than mammography in detecting tumors in women with an inherited susceptibility to breast cancer. Annual screening using MRI in addition to mammography is recommended for certain women at high lifetime risk of the disease. (For more information see Saslow et al. *CA Cancer J Clin* 2007; 57:75-89.) Concerted efforts should be made to improve access to health care and to encourage all women to receive regular mammograms according to guidelines.

Treatment: Taking into account tumor size, stage, and other characteristics, as well as patient preference, treatment may involve lumpectomy (surgical removal of the tumor with clear margins) or mastectomy (surgical removal of the breast). Removal of some of the axillary (underarm) lymph nodes is also recommended to obtain accurate information on stage of disease. Treatment may also involve radiation therapy, chemotherapy (before or after surgery), hormone therapy (tamoxifen, raloxifene, aromatase inhibitors), or targeted biologic therapy. Women with early-stage disease whose cancer tests positive for estrogen receptors benefit from treatment with hormone therapy for 5 years following diagnosis; recent studies suggest that risk of breast cancer recurrence is

further reduced when hormone therapy is followed by treatment with an aromatase inhibitor. For women whose cancer tests positive for HER2/neu, approved targeted therapies include trastuzumab (Herceptin) and lapatinib (Tykerb). The US Food and Drug Administration (FDA) recently granted approval for the use of bevacizumab (Avastin) for advanced breast cancer. Avastin slows tumor growth in women whose cancer has metastasized by blocking growth of new vessels that increase blood supply to the tumor, but has not been shown to increase overall survival.

Numerous studies have shown that long-term survival rates after lumpectomy plus radiation therapy are similar to survival rates after mastectomy for women whose cancer has not spread to the skin, chest wall, or distant organs. Similarly, a technique called sentinel lymph node biopsy is also as effective and is less damaging than full axillary node dissection in determining whether the tumor has spread beyond the breast in women with early-stage disease. The sentinel lymph node is the first lymph node(s) to which cancer is likely to spread from the primary tumor. Sentinel lymph nodes are identified by injecting a radioactive substance or dye near the tumor, which is then carried by the lymph system to the nodes draining the tumor site. The lymph nodes draining the tumor site are removed and examined under a microscope to determine if cancer cells are present. If cancer is found in any of the sentinel lymph nodes, additional (regional) lymph nodes in the area are removed. Sentinel lymph node biopsy allows fewer lymph nodes to be removed, so there is a lower risk for side effects, such as lymphedema, a swelling of the arm that can be painful and disabling. Not all surgeons are experienced enough with sentinel lymph node biopsies to perform them successfully. Women who elect to have sentinel lymph node biopsy should have their breast cancer surgery performed by a medical care team that is experienced with the technique. For women undergoing mastectomy, significant advances in reconstruction techniques provide several options for breast reconstruction, including the timing of the procedure (i.e., during mastectomy or in the time period following the procedure).

It is recommended that all patients with ductal carcinoma in situ (DCIS) be treated to avoid the development of invasive cancer. Although the exact percentage of mammographically detected DCIS cases that would progress to invasive breast cancer without treatment is unknown, analysis of data from mammography screening trials suggests that the majority of these cases will progress. Treatment options for DCIS include lumpectomy with radiation therapy or mastectomy; either of these options may be followed by treatment with tamoxifen. Removal of axillary lymph nodes is not generally needed.

Survival: The 5-year relative survival for female breast cancer patients has improved from 63% in the early 1960s to 89% today. The survival rate for women diagnosed with localized breast cancer (malignant cancer that has not spread to lymph nodes or other locations outside the breast) is 98%. If the cancer has spread to nearby (regional stage) or distant (distant stage) lymph nodes or organs, the 5-year survival is 84% or 27%, respectively. Survival continues to decline after 5 years; for all stages combined, rates are 81% and 74% at 10 and 15 years after diagnosis. Caution should be used when interpreting long-term survival rates since they represent patients who were diagnosed and treated many (5-22) years ago. Improvements in diagnosis and treatment may result in a better outlook for more recently diagnosed patients.

For more information about breast cancer, please see the American Cancer Society's *Breast Cancer Facts & Figures 2007-2008* (8610.07), available online at cancer.org.

Childhood Cancer

New cases: An estimated 10,730 new cases are expected to occur among children aged 0 to 14 years in 2009. Childhood cancers are rare, representing less than 1% of all new cancer diagnoses.

Deaths: An estimated 1,380 deaths are expected to occur among children aged 0 to 14 years in 2009, about one-third of these from leukemia. Although uncommon, cancer is the second leading cause of death in children, exceeded only by accidents. Mortality rates for childhood cancer have declined by 50% since 1975. The substantial progress in pediatric cancer survival rates is attributable largely to improved treatments and the high proportion of patients participating in clinical trials.

Early detection: Early symptoms are usually nonspecific. Parents should ensure that children have regular medical checkups and should be alert to any unusual symptoms that persist. These include an unusual mass or swelling; unexplained paleness or loss of energy; sudden tendency to bruise; a persistent, localized pain; prolonged, unexplained fever or illness; frequent headaches, often with vomiting; sudden eye or vision changes; and excessive, rapid weight loss.

According to the International Classification of Childhood Cancer, childhood cancers include:

- Leukemia (32.7% of all childhood cancers), which may be recognized by bone and joint pain, weakness, bleeding, and fever
- Brain and other nervous system (20.7%), which in early stages may cause headaches, nausea, vomiting, blurred or double vision, dizziness, and difficulty in walking or handling objects
- Neuroblastoma (6.9%), a cancer of the sympathetic nervous system that usually appears as a swelling in the abdomen
- Wilms tumor (4.8%), a kidney cancer that may be recognized by a swelling or lump in the abdomen
- Non-Hodgkin lymphoma (4.3%) and Hodgkin lymphoma (3.6%), which affect lymph nodes but may spread to bone marrow and other organs, and may cause swelling of lymph nodes in the neck, armpit, or groin; weakness; and fever
- Rhabdomyosarcoma (3.5%), a soft tissue sarcoma that can occur in the head and neck, genitourinary area, trunk, and extremities, and may cause pain and/or a mass or swelling
- Retinoblastoma (2.7%), an eye cancer that usually occurs in children younger than 4 years
- Osteosarcoma (2.7%), a bone cancer that often has no initial pain or symptoms until local swelling begins
- Ewing sarcoma (1.4%), another type of cancer that usually arises in bone, and most often occurs in adolescents

Treatment: Childhood cancers can be treated by a combination of therapies (surgery, radiation, and chemotherapy) chosen based on the type and stage of cancer. Treatment is coordinated by a team of experts, including pediatric oncologists, pediatric nurses, social workers, psychologists, and others who assist children and their families. Because these cancers are uncommon, outcomes are more successful when treatment is managed by a cancer center. If the patient is eligible, placement in a clinical trial should also be considered.

Survival: For all childhood cancers combined, 5-year relative survival has improved markedly over the past 30 years, from less than 50% before the 1970s to 80% today, due to new and improved treatments. Rates vary considerably, however, depending on cancer type. For the most recent time period (1996-2004), 5-year survival for neuroblastoma is 70%; bone and joint, 71%; brain and other nervous system, 74%; leukemia, 82%; non-Hodgkin lymphoma, 86%; Wilms tumor, 92%; and Hodgkin lymphoma, 96%. Survivors of childhood cancer may experience treatment-related side effects. Late treatment effects include organ malfunction, secondary cancers, and cognitive impairments. The Children's Oncology Group (COG) has developed long-term follow-up guidelines for screening and management of late effects in survivors of childhood cancer. For more on childhood cancer management, see the COG Web site at: survivorshipguidelines.org.

Colon and Rectum

New cases: An estimated 106,100 cases of colon and 40,870 cases of rectal cancer are expected to occur in 2009. Colorectal cancer is the third most common cancer in both men and women. Colorectal cancer incidence rates have been decreasing for most of the past two decades (from 66.3 cases per 100,000 population in 1985 to 46.4 in 2005). The decline accelerated from 1998-2005 (2.8% per year in men and 2.2% per year in women), in part because of increases in screening that allow the detection and removal of colorectal polyps before they progress to cancer.

Deaths: An estimated 49,920 deaths from colorectal cancer are expected to occur in 2009, accounting for almost 9% of all cancer deaths. Mortality rates for colorectal cancer have declined in both men and women over the past two decades, with a steeper decline since 2002 (4.3% per year from 2002 to 2005 in both men and women, compared to 2.0% per year from 1990 to 2002 in men and 1.8% per year from 1984 to 2002 in women). This decrease reflects declining incidence rates and improvements in early detection and treatment.

Signs and symptoms: Early stage colorectal cancer does not usually have symptoms; therefore, screening is necessary to detect colorectal cancer in its early stages. Advanced disease may cause rectal bleeding, blood in the stool, a change in bowel habits, and cramping pain in the lower abdomen. In some cases, blood loss from the cancer leads to anemia (low red blood cells), causing symptoms such as weakness and excessive fatigue.

Risk factors: The risk of colorectal cancer increases with age; 91% of cases are diagnosed in individuals aged 50 and older. Several modifiable factors are associated with increased risk of colorectal cancer. Among these are obesity, physical inactivity, a diet high in red or processed meat, heavy alcohol consumption, and possibly smoking and inadequate intake of fruits and vegetables. Studies indicate that compared to healthy-weight individuals, men and women who are overweight are more likely to

develop and die from colorectal cancer. Consumption of milk and calcium appears to decrease risk. Studies suggest that regular use of nonsteroidal anti-inflammatory drugs, such as aspirin, and menopausal hormone therapy may also reduce colorectal cancer risk. However, these drugs are not currently recommended for the prevention of colorectal cancer because they can have other serious adverse health effects.

Colorectal cancer risk is also increased by certain inherited genetic mutations [familial adenomatous polyposis (FAP) and hereditary non-polyposis colorectal cancer (HNPCC), also known as Lynch syndrome], a personal or family history of colorectal cancer and/or polyps, or a personal history of chronic inflammatory bowel disease. Studies have also found an association between diabetes and colorectal cancer.

Early detection: Beginning at age 50, men and women who are at average risk for developing colorectal cancer should begin screening. Screening can result in the detection and removal of colorectal polyps before they become cancerous, as well as the detection of cancer that is at an early stage. Thus, screening reduces mortality both by decreasing the incidence of cancer and by detecting a higher proportion of cancers at early, more treatable stages. The American Cancer Society collaborated with several other organizations to release updated colorectal cancer screening guidelines in March 2008. These new joint guidelines emphasize cancer prevention and draw a distinction between colorectal screening tests that primarily detect cancer and those that can detect both cancer and precancerous polyps. There are a number of recommended screening options that vary by the extent of bowel preparation, as well as test performance, limitations, time interval, and cost. For detailed information on colorectal cancer screening options, please see *Colorectal Cancer Facts & Figures 2008-2010* on cancer.org. (See page 68 for the American Cancer Society's screening guidelines for colorectal cancer.)

Treatment: Surgery is the most common treatment for colorectal cancer. For cancers that have not spread, surgical removal may be curative. A permanent colostomy (creation of an abdominal opening for elimination of body wastes) is rarely needed for colon cancer and is infrequently required for rectal cancer. Chemotherapy alone, or in combination with radiation (for rectal cancer), is given before or after surgery to most patients whose cancer has penetrated the bowel wall deeply or spread to lymph nodes.

Adjuvant chemotherapy (anticancer drugs in addition to surgery or radiation) for colon cancer is equally effective and can be no more toxic in otherwise healthy patients aged 70 and older than in younger patients. Oxaliplatin, in combination with 5-fluorouracil (5-FU) and followed by leucovorin (LV), may be used to treat persons with metastatic carcinoma of the colon or rectum. Three targeted monoclonal antibody therapies are approved by the FDA to treat metastatic colorectal cancer: bevacizumab (Avastin) blocks the growth of blood vessels to the tumor and cetuximab (Erbitux) and panitumumab (Vectibix) both block the effects of hormone-like factors that promote cancer cell growth.

Survival: The 1- and 5-year relative survival for persons with colorectal cancer is 83% and 64%, respectively. Survival continues to decline beyond 5 years to 58% at 10 years after diagnosis. When colorectal cancers are detected at an early, localized stage, the 5-year survival is 90%; however, only 40% of colorectal cancers are diagnosed at this stage, mostly due to underuse of screening. After the cancer has spread regionally to involve adjacent organs or lymph nodes, the 5-year survival drops to 68%. For persons with distant metastases, 5-year survival is 11%.

Leukemia

New cases: An estimated 44,790 new cases are expected in 2009, with slightly more cases of chronic (20,540) than acute (18,570) disease. Leukemia is diagnosed 10 times more often in adults than in children. Acute lymphocytic leukemia (ALL) accounts for approximately 70% of the leukemia cases among children ages 0 to 19 years. In adults, the most common types are acute myeloid leukemia (AML) and chronic lymphocytic leukemia (CLL). The incidence of AML increased by an average of 2.2% per year from 1988-2000, but decreased sharply by 3.2% per year from 2000-2005. In contrast, the incidence of CLL has remained relatively stable since 1975.

Deaths: An estimated 21,870 deaths are expected to occur in 2009. Death rates in males and females combined have decreased by about 1.5% per year since 2000.

Signs and symptoms: Symptoms may include fatigue, paleness, weight loss, repeated infections, fever, bruising easily, and nosebleeds or other hemorrhages. In children, these signs can appear suddenly. Chronic leukemia can progress slowly with few symptoms.

Risk factors: Exposure to ionizing radiation increases risk of several types of leukemia. Medical radiation, such as that used in cancer treatment, is a substantial source

Probability of Developing Invasive Cancers (%) Over Selected Age Intervals by Sex, US, 2003-2005*

		Birth to 39	40 to 59	60 to 69	70 and Older	Birth to Death
All sites†	Male	1.42 (1 in 70)	8.44 (1 in 12)	15.71 (1 in 6)	37.74 (1 in 3)	43.89 (1 in 2)
	Female	2.07 (1 in 48)	8.97 (1 in 11)	10.23 (1 in 10)	26.17 (1 in 4)	37.35 (1 in 3)
Urinary bladder‡	Male	0.02 (1 in 4,448)	0.41 (1 in 246)	0.96 (1 in 104)	3.57 (1 in 28)	3.74 (1 in 27)
	Female	0.01 (1 in 10,185)	0.12 (1 in 810)	0.26 (1 in 378)	1.01 (1 in 99)	1.18 (1 in 84)
Breast	Female	0.48 (1 in 208)	3.79 (1 in 26)	3.41 (1 in 29)	6.44 (1 in 16)	12.03 (1 in 8)
Colon & rectum	Male	0.08 (1 in 1,296)	0.92 (1 in 109)	1.55 (1 in 65)	4.63 (1 in 22)	5.51 (1 in 18)
	Female	0.07 (1 in 1,343)	0.72 (1 in 138)	1.10 (1 in 91)	4.16 (1 in 24)	5.10 (1 in 20)
Leukemia	Male	0.16 (1 in 611)	0.22 (1 in 463)	0.35 (1 in 289)	1.17 (1 in 85)	1.50 (1 in 67)
	Female	0.12 (1 in 835)	0.14 (1 in 693)	0.20 (1 in 496)	0.77 (1 in 130)	1.07 (1 in 94)
Lung & bronchus	Male	0.03 (1 in 3,398)	0.99 (1 in 101)	2.43 (1 in 41)	6.70 (1 in 18)	7.78 (1 in 13)
	Female	0.03 (1 in 2,997)	0.81 (1 in 124)	1.78 (1 in 56)	4.70 (1 in 21)	6.22 (1 in 16)
Melanoma of the skin§	Male	0.16 (1 in 645)	0.64 (1 in 157)	0.70 (1 in 143)	1.67 (1 in 60)	2.56 (1 in 39)
	Female	0.27 (1 in 370)	0.53 (1 in 189)	0.35 (1 in 282)	0.76 (1 in 131)	1.73 (1 in 58)
Non-Hodgkin lymphoma	Male	0.13 (1 in 763)	0.45 (1 in 225)	0.58 (1 in 171)	1.66 (1 in 60)	2.23 (1 in 45)
	Female	0.08 (1 in 1,191)	0.32 (1 in 316)	0.45 (1 in 223)	1.36 (1 in 73)	1.90 (1 in 53)
Prostate	Male	0.01 (1 in 10,002)	2.43 (1 in 41)	6.42 (1 in 16)	12.49 (1 in 8)	15.78 (1 in 6)
Uterine cervix	Female	0.15 (1 in 651)	0.27 (1 in 368)	0.13 (1 in 761)	0.19 (1 in 530)	0.69 (1 in 145)
Uterine corpus	Female	0.07 (1 in 1,499)	0.72 (1 in 140)	0.81 (1 in 123)	1.22 (1 in 82)	2.48 (1 in 40)

* For people free of cancer at beginning of age interval.

† All sites excludes basal and squamous cell skin cancers and in situ cancers except urinary bladder.

‡ Includes invasive and in situ cancer cases.

§ Statistic is for whites only.

Source: DevCan: Probability of Developing or Dying of Cancer Software, Version 6.3.0. Statistical Research and Applications Branch, National Cancer Institute, 2008. srab.cancer.gov/devcan.

American Cancer Society, Surveillance and Health Policy Research, 2009

of radiation exposure. Leukemia may also occur as a side effect of chemotherapy. Children with Down syndrome and certain other genetic abnormalities have higher incidence rates of leukemia. Family history is one of the strongest risk factors for CLL. Cigarette smoking and exposure to certain chemicals such as benzene, a component in gasoline and cigarette smoke, are risk factors for myeloid leukemia. Infection with human T-cell leukemia virus type I (HTLV-I) can cause a rare type of CLL called adult T-cell leukemia/lymphoma. The prevalence of HTLV-I infection is geographically localized and is most common in southern Japan and the Caribbean; infected individuals in the US tend to be descendants or immigrants from endemic regions.

Early detection: Because symptoms often resemble those of other, less serious conditions, leukemia can be difficult to diagnose early. When a physician does suspect leukemia, diagnosis can be made using blood tests and a bone marrow biopsy.

Treatment: Chemotherapy is the most effective method of treating leukemia. Various anticancer drugs are used, either in combination or as single agents. Imatinib mesylate (Gleevec) is a highly specific drug used for the treatment of chronic myeloid (or myelogenous) leukemia (CML), which will be diagnosed in about 5,050 people in 2009. Studies have found that two related drugs, nilotinib (Tasigna) and dasatinib (Sprycel), are often effective when imatinib stops working. Imatinib is also sometimes used to treat ALL. Gemtuzumab ozogamicin (Mylotarg) is a targeted drug approved for treatment in older AML patients whose cancer has relapsed or who are not able to receive other chemotherapy. Antibiotics and transfusions of blood components are used as supportive treatments. Under appropriate conditions, bone marrow transplantation may be useful in treating certain types of leukemia.

Survival: Survival in leukemia varies by type, ranging from a 5-year relative survival of 22% for people with AML to 76% for people with CLL. Advances in treatment have resulted in a dramatic improvement in survival for people with ALL, from a 5-year relative survival rate of 42% in 1975-1977 to 66% in 1996-2004. Survival rates for children with ALL have increased from 58% to 88% over the same time period.

Lung and Bronchus

New cases: An estimated 219,440 new cases of lung cancer are expected in 2009, accounting for about 15% of cancer diagnoses. The incidence rate is declining significantly in men, from a high of 102.1 cases per 100,000 in 1984 to 73.2 in 2005. In women, the rate is approaching a plateau after a long period of increase. Lung cancer is classified clinically as small cell (14%) or non-small cell (85%) for the purposes of treatment.

Deaths: Lung cancer accounts for the most cancer-related deaths in both men and women. An estimated 159,390 deaths, accounting for about 28% of all cancer deaths, are expected to occur in 2009. Since 1987, more women have died each year from lung cancer than from breast cancer. Death rates among men decreased by 1.3% per year from 1990 to 1994 and by 2.0% per year from 1994 to 2005. Female lung cancer death rates have been stable since 2003 after continuously increasing for several decades. These trends in lung cancer mortality reflect historical differences in cigarette smoking between men and women and the decrease in smoking rates over the past 40 years.

Signs and symptoms: Symptoms may include persistent cough, sputum streaked with blood, chest pain, voice change, and recurrent pneumonia or bronchitis.

Risk factors: Cigarette smoking is by far the most important risk factor for lung cancer. Risk increases with quantity and duration of cigarette consumption. Other risk factors include occupational or environmental exposure to secondhand smoke, radon, asbestos (particularly among smokers), certain metals (chromium, cadmium, arsenic), some organic chemicals, radiation, air pollution, and a history of tuberculosis. Genetic susceptibility plays a contributing role in the development of lung cancer, especially in those who develop the disease at a younger age.

Early detection: Screening for early lung cancer detection has not yet been proven to reduce mortality. Detection by chest x-ray, analysis of cells in sputum, and fiber-optic examination of the bronchial passages has shown limited effectiveness in reducing lung cancer deaths. Newer tests, such as low-dose spiral computed tomography (CT) scans and molecular markers in sputum, have produced promising results in detecting lung cancers at earlier, more operable stages in high-risk patients, but have not yet been shown to reduce lung cancer deaths. In addition, there are considerable risks associated with lung biopsy and surgery that must be considered when evaluating the risks and benefits of screening. The National Lung Screening Trial is a clinical trial to assess whether screening individuals at high risk for lung cancer with spiral CT or standard chest x-ray can prevent lung cancer deaths. The study, launched in 2002, represents a collaboration of the National Cancer Institute and the American College of Radiology Imaging Network. The American Cancer Society contributed to the recruitment of subjects for the trial. Results from the study are expected by 2010-2011.

Treatment: Treatment options are determined by the type (small cell or non-small cell) and stage of cancer and include surgery, radiation therapy, chemotherapy, and targeted biological therapies such as bevacizumab (Avastin) and erlotinib (Tarceva). For localized cancers, surgery is usually the treatment of choice. Recent pooled analyses confirm that survival for all patients with early stage, non-small cell lung cancer is improved by giving chemotherapy after surgery. Because the disease has usually spread by the time it is discovered, radiation therapy and chemotherapy are often used, sometimes in combination with surgery. Chemotherapy alone or combined with radiation is the usual treatment of choice for small cell lung cancer; on this regimen, a large percentage of patients experience remission, which may be prolonged.

Survival: The 1-year relative survival for lung cancer increased from 35% in 1975-1979 to 41% in 2001-2004, largely due to improvements in surgical techniques and combined therapies. However, the 5-year survival rate for all stages combined is only 15%. The 5-year survival rate is 50% for cases detected when the disease is still localized, but only 16% of lung cancers are diagnosed at this early stage.

Lymphoma

New cases: An estimated 74,490 new cases of lymphoma will occur in 2009, including 8,510 cases of Hodgkin lymphoma and 65,980 cases of non-Hodgkin lymphoma (NHL). Since the early 1970s, incidence rates for NHL have nearly doubled. Although some of this increase is due to AIDS-related NHL, for the most part the rise is unexplained. NHL incidence has increased by 0.4% per year since 1991 in men and by 1.2% per year since 1990 in women. Over the past 30 years, incidence rates for Hodgkin lymphoma have decreased in men (0.6% per year), but slightly increased in women (0.4 % per year).

Deaths: An estimated 20,790 deaths from lymphoma will occur in 2009 (Hodgkin lymphoma, 1,290; non-Hodgkin lymphoma, 19,500). Death rates for Hodgkin lymphoma have been decreasing in both men and women for more

than three decades. Death rates for NHL have decreased in the past decade (by 3.0% per year since 1997 in men and by 3.7% per year since 1998 in women) after increasing for most of the previous two decades.

Signs and symptoms: Symptoms may include swollen lymph nodes, itching, night sweats, fatigue, unexplained weight loss, and intermittent fever.

Risk factors: In most cases, the cause is unknown, even though various risk factors associated with severely reduced immune function have been identified. Non-Hodgkin lymphoma risk is elevated in persons with organ transplants who receive immune suppressants to prevent transplant rejection, in people with severe autoimmune conditions, and in people infected with human immunodeficiency virus (HIV), human T-cell leukemia virus type I (HTLV-I), and probably hepatitis C virus (HCV). Epstein-Barr virus (EBV) causes Burkitt lymphoma and some non-Hodgkin lymphomas. *H. pylori* infection increases the risk of gastric lymphoma. A family history of lymphoma and certain common genetic variations in immune response genes are associated with higher risk. Occupational exposures to herbicides, chlorinated organic compounds, and certain other chemicals are also associated with an increased risk.

Treatment: Hodgkin lymphoma is usually treated with chemotherapy and/or radiotherapy, depending on stage and cell-type of the disease. Non-Hodgkin lymphoma patients are usually treated with chemotherapy; radiation, alone or in combination with chemotherapy, is used less often. Highly specific monoclonal antibodies, such as rituximab (Rituxan) and alemtuzumab (Campath), directed at lymphoma cells are used for initial treatment and recurrence of some types of non-Hodgkin lymphoma, as are antibodies linked to a radioactive atom, such as ibritumomab tiuxetan (Zevalin) and iodine I 131 tositumomab (Bexxar). High-dose chemotherapy with stem cell transplantation and low-dose chemotherapy with stem cell transplantation (called non-myeloablative) are options if non-Hodgkin lymphoma persists or recurs after standard treatment.

Survival: Survival varies widely by cell type and stage of disease. The 1-year relative survival for Hodgkin and non-Hodgkin lymphoma is 92% and 80%, respectively; the 5-year survival is 85% and 65%. Ten years after diagnosis, survival for Hodgkin and non-Hodgkin lymphoma declines to 81% and 54%, respectively.

Oral Cavity and Pharynx

New cases: An estimated 35,720 new cases of cancer of the oral cavity are expected in 2009. Incidence rates are more than twice as high in men as in women. Incidence has been declining in men since 1975 and in women since 1980.

Deaths: An estimated 7,600 deaths from oral cavity and pharynx cancer are expected in 2009. Death rates have decreased by more than 2% per year since 1980 in men and since 1990 in women.

Signs and symptoms: Symptoms may include a sore in the throat or mouth that bleeds easily and does not heal, a lump or thickening, ear pain, a neck mass, coughing up blood, and a red or white patch that persists. Difficulties in chewing, swallowing, or moving the tongue or jaws are often late symptoms.

Risk factors: Known risk factors include all forms of smoked and smokeless tobacco products and excessive consumption of alcohol. Many studies have reported a synergism between smoking and alcohol use, resulting in more than a 30-fold increased risk in individuals who both smoke and drink heavily. HPV infection is associated with certain types of oropharyngeal cancer.

Early detection: Cancer can affect any part of the oral cavity, including the lip, tongue, mouth, and throat. Dentists and primary care physicians can detect premalignant abnormalities and cancer at an early stage, when they are most curable.

Treatment: Radiation therapy and surgery, separately or in combination, are standard treatments. In advanced disease, chemotherapy is added to surgery and/or radiation. Targeted therapy with cetuximab (Erbitux) may be combined with radiation in initial treatment or used alone to treat recurrent cancer.

Survival: For all stages combined, about 83% of persons with oral cavity and pharynx cancer survive 1 year after diagnosis. The 5-year and 10-year relative survival rates are 60% and 49%, respectively.

Ovary

New cases: An estimated 21,550 new cases of ovarian cancer are expected in the US in 2009. Ovarian cancer accounts for about 3% of all cancers among women and ranks second among gynecologic cancers, following cancer of the uterine corpus. During 2001-2005, ovarian cancer incidence declined at a rate of 2.4% per year.

Five-year Relative Survival Rates* (%) by Stage at Diagnosis, 1996-2004

Site	All Stages	Local	Regional	Distant	Site	All Stages	Local	Regional	Distant
Breast (female)	88.7	98.1	83.8	27.1	Ovary	45.5	92.7	71.1	30.6
Colon & rectum	64.4	89.7	68.4	10.8	Pancreas	5.1	20.0	8.2	1.8
Esophagus	15.8	34.4	17.1	2.8	Prostate§	98.9	100.0	—	31.7
Kidney†	66.5	89.9	61.3	9.9	Stomach	24.7	60.7	24.8	3.7
Larynx	62.5	80.9	50.2	23.4	Testis	95.5	99.3	95.7	71.1
Liver‡	11.7	23.8	7.7	2.9	Thyroid	96.9	99.7	96.9	57.8
Lung & bronchus	15.2	49.5	20.6	2.8	Urinary bladder	79.8	92.5	44.7	6.1
Melanoma of the skin	91.2	98.7	65.1	15.5	Uterine cervix	71.2	91.7	55.9	16.6
Oral cavity & pharynx	59.7	82.2	52.7	28.4	Uterine corpus	82.9	95.5	67.5	23.6

*Rates are adjusted for normal life expectancy and are based on cases diagnosed in the SEER 17 areas from 1996-2004, followed through 2005.
†Includes renal pelvis. ‡Includes intrahepatic bile duct. §The rate for local stage represents local and regional stages combined.

Local: an invasive malignant cancer confined entirely to the organ of origin. **Regional:** a malignant cancer that 1) has extended beyond the limits of the organ of origin directly into surrounding organs or tissues; 2) involves regional lymph nodes by way of lymphatic system; or 3) has both regional extension and involvement of regional lymph nodes. **Distant:** a malignant cancer that has spread to parts of the body remote from the primary tumor either by direct extension or by discontinuous metastasis to distant organs, tissues, or via the lymphatic system to distant lymph nodes.

Source: Ries LAG, Melbert D, Krapcho M, et al. (eds). *SEER Cancer Statistics Review, 1975-2005*, National Cancer Institute, Bethesda, MD, seer.cancer.gov/csr/1975_2005/, 2008.

American Cancer Society, Surveillance and Health Policy Research, 2009

Deaths: An estimated 14,600 deaths are expected in 2009. Ovarian cancer causes more deaths than any other cancer of the female reproductive system. Death rates for ovarian cancer have been stable since 1998.

Signs and symptoms: The most common sign is enlargement of the abdomen, which is caused by accumulation of fluid. Early ovarian cancer usually has no obvious symptoms. However, recent studies indicate that some women may experience persistent, nonspecific symptoms, such as bloating, pelvic or abdominal pain, difficulty eating or feeling full quickly, or urinary urgency or frequency. Women who experience such symptoms daily for more than a few weeks should seek prompt medical evaluation. Abnormal vaginal bleeding is rarely a symptom of ovarian cancer.

Risk factors: Risk for ovarian cancer increases with age. Pregnancy and the long-term use of oral contraceptives reduce the risk of developing ovarian cancer. Tubal ligation and hysterectomy appear to decrease risk for most women. The use of estrogen alone as postmenopausal hormone therapy has been shown to increase risk in several large studies. Heavier body weight may be associated with increased risk of ovarian cancer. Women who have had breast cancer or who have a family history of breast or ovarian cancer are at increased risk. Inherited mutations in BRCA1 or BRCA2 genes increase risk. Studies suggest that preventive surgery to remove the ovaries and fallopian tubes can decrease the risk of ovarian cancers in women with BRCA1 and BRCA2 mutations. Another genetic syndrome, hereditary nonpolyposis colon cancer, has also been associated with endometrial and ovarian cancer. Ovarian cancer incidence rates are highest in Western industrialized countries.

Early detection: There is currently no sufficiently accurate screening test proven to be effective in the early detection of ovarian cancer. Pelvic examination only occasionally detects ovarian cancer, generally when the disease is advanced. However, the combination of a thorough pelvic exam, transvaginal ultrasound, and a blood test for the tumor marker CA125 may be offered to women who are at high risk of ovarian cancer and to women who have persistent, unexplained symptoms. For women at average risk, transvaginal ultrasound and testing for the tumor marker CA125 may help in diagnosis but are not used for routine screening.

Treatment: Treatment options include surgery, chemotherapy, and occasionally radiation therapy. Surgery usually involves removal of one or both ovaries, fallopian tubes (salpingoophorectomy), and the uterus (hysterectomy). In younger women with very early stage tumors who wish to have children, only the involved ovary and fallopian tube may be removed. In more advanced disease, surgically removing all abdominal metastases enhances the effect of chemotherapy and helps improve survival. For women with stage III ovarian cancer that has been optimally debulked (removal of as much of the cancerous tissue as possible), studies have shown that chemotherapy administered both intravenously and directly into the abdomen improves survival. Studies have found that women who are treated by a gynecologic oncologist have more successful outcomes.

Trends in 5-year Relative Survival Rates* (%) by Race and Year of Diagnosis, US, 1975-2004

Site	All races			White			African American		
	1975-77	1984-86	1996-2004	1975-77	1984-86	1996-2004	1975-77	1984-86	1996-2004
All sites	50	54	66†	51	55	68†	40	41	58†
Brain	24	29	35†	23	28	34†	27	33	39†
Breast (female)	75	79	89†	76	80	91†	62	65	78†
Colon	52	59	65†	52	60	66†	46	50	55†
Esophagus	5	10	17†	6	11	18†	3	8	11†
Hodgkin lymphoma	74	79	86†	74	80	87†	71	75	80†
Kidney	51	56	67†	51	56	67†	50	54	66†
Larynx	67	66	64†	67	68	66	59	53	50
Leukemia	35	42	51†	36	43	52†	34	34	42
Liver#	4	6	11†	4	6	10†	2	5	8†
Lung & bronchus	13	13	16†	13	14	16†	11	11	13†
Melanoma of the skin	82	87	92†	82	87	92†	60‡	70§	78
Myeloma	26	29	35†	25	27	35†	31	32	33
Non-Hodgkin lymphoma	48	53	65†	48	54	66†	49	48	58
Oral cavity	53	55	60†	55	57	62†	36	36	42†
Ovary	37	40	46†	37	39	45†	43	41	38
Pancreas	3	3	5†	3	3	5†	2	5	5†
Prostate	69	76	99†	70	77	99†	61	66	96†
Rectum	49	57	67†	49	58	67†	45	46	59†
Stomach	16	18	25†	15	18	23†	16	20	25†
Testis	83	93	96†	83	93	96†	82‡	87‡	87
Thyroid	93	94	97†	93	94	97†	91	90	95
Urinary bladder	74	78	81†	75	79	82†	51	61	66†
Uterine cervix	70	68	73†	71	70	74†	65	58	65
Uterine corpus	88	84	84†	89	85	86†	61	58	61

*Survival rates are adjusted for normal life expectancy and are based on cases diagnosed in the SEER 9 areas from 1975-1977, 1984-1986, and 1996-2004, and followed through 2005. †The difference in rates between 1975-1977 and 1996-2004 is statistically significant ($p < 0.05$). ‡The standard error of the survival rate is between 5 and 10 percentage points. §The standard error of the survival rate is greater than 10 percentage points. #Includes intrahepatic bile duct.

Source: Ries LAG, Melbert D, Krapcho M, et al (eds.). *SEER Cancer Statistics Review, 1975-2005*, National Cancer Institute, Bethesda, MD, seer.cancer.gov/csr/1975_2005/, 2008.

American Cancer Society, Surveillance and Health Policy Research, 2009

Survival: Relative survival varies by age; women younger than 65 are about twice as likely to survive 5 years (57%) following diagnosis as women 65 and older (29%). Overall, the 1- and 5-year relative survival of ovarian cancer patients is 75% and 46%, respectively. If diagnosed at the localized stage, the 5-year survival rate is 93%; however, only 19% of all cases are detected at this stage, usually fortuitously during another medical procedure. The majority of cases (67%) are diagnosed at distant stage. For women with regional and distant disease, 5-year survival rates are 71% and 31%, respectively. The 10-year relative survival rate for all stages combined is 39%.

Pancreas

New cases: An estimated 42,470 new cases of pancreatic cancer are expected to occur in the US in 2009. Incidence rates of pancreatic cancer have been stable in men since 1993 and have been increasing in women by 0.6% per year since 1994.

Deaths: An estimated 35,240 deaths are expected to occur in 2009. The death rate for pancreatic cancer has been stable since 2003 in men, but has been increasing by 0.1% per year since 1984 in women.

Signs and symptoms: Cancer of the pancreas often develops without early symptoms. Symptoms may include weight loss, discomfort in the abdomen, and occasionally glucose intolerance (high blood glucose levels). Tumors that develop near the common bile duct may cause a blockage that leads to jaundice (yellowing of the skin and eyes due to pigment accumulation). Sometimes this symptom allows the tumor to be diagnosed at an early stage.

Risk factors: Tobacco smoking increases the risk of pancreatic cancer; incidence rates are more than twice as high for cigarette smokers as for nonsmokers. Risk also appears to increase with obesity, chronic pancreatitis, diabetes, cirrhosis, and possibly use of smokeless tobacco.

Pancreatic cancer rates are slightly higher in men than in women. A family history of pancreatic cancer also increases risk. Though evidence is still accumulating, consumption of red meat may increase risk and physical activity may decrease risk.

Early detection: At present, there is no method for the early detection of pancreatic cancer. The disease is usually asymptomatic; only about 7% of cases are diagnosed at an early stage. Research is under way to identify better methods of early detection.

Treatment: Surgery, radiation therapy, and chemotherapy are treatment options that may extend survival and/or relieve symptoms in many patients, but seldom produce a cure. The targeted anticancer drug erlotinib (Tarceva) blocks tumor cell growth and has demonstrated a minimal improvement in pancreatic cancer survival. It has been approved by the FDA for the treatment of advanced pancreatic cancer. Clinical trials with several new agents, combined with radiation and surgery, may offer improved survival and should be considered as a treatment option.

Survival: For all stages combined, the 1- and 5-year relative survival rates are 24% and 5%, respectively. Even for those people diagnosed with local disease, the 5-year survival is only 20%.

Prostate

New cases: An estimated 192,280 new cases of prostate cancer will occur in the US during 2009. Prostate cancer is the most frequently diagnosed cancer in men. For reasons that remain unclear, incidence rates are significantly higher in African Americans than in whites. Incidence rates for prostate cancer have changed substantially over the past 20 years, in large part reflecting changes in prostate cancer screening with the prostate-specific antigen (PSA) blood test. After increasing from 1988 to 1992, declining from 1992 to 1995, and again increasing from 1995 to 2001, rates have been decreasing since 2001 by 4.4% per year.

Deaths: With an estimated 27,360 deaths in 2009, prostate cancer is the second-leading cause of cancer death in men. Although death rates have decreased more rapidly among African American than among white men since the early 1990s, rates in African Americans remain more than twice as high as those in whites.

Signs and symptoms: Early prostate cancer usually has no symptoms. With more advanced disease, individuals may experience weak or interrupted urine flow; inability to urinate or difficulty starting or stopping the urine flow; the need to urinate frequently, especially at night; blood in the urine; or pain or burning with urination. Advanced prostate cancer commonly spreads to the bones, which can cause pain in the hips, spine, ribs, or other areas. Many of these symptoms are more likely to be caused by conditions other than prostate cancer, however.

Risk factors: The only well-established risk factors for prostate cancer are age, race/ethnicity, and family history of the disease. About 63% of all prostate cancer cases are diagnosed in men aged 65 and older. African American men and Jamaican men of African descent have the highest prostate cancer incidence rates in the world. The disease is common in North America and northwestern Europe, but less common in Asia and South America. Recent genetic studies suggest that strong familial predisposition may be responsible for 5%-10% of prostate cancers. International studies suggest that a diet high in animal fat may also be a risk factor. Because lycopene (an antioxidant vitamin found in red and pink foods, such as tomato products) may reduce prostate cancer risk, men should consume a variety of fruits and vegetables daily. There is some evidence that the risk of dying from prostate cancer may increase with obesity.

The chemoprevention of prostate cancer is an active area of research. Two drugs of interest, finasteride and dutasteride, reduce the amount of male hormone (testosterone) produced by the body and are already used to treat the symptoms of an enlarged prostate. In the Prostate Cancer Prevention Trial, men who received finasteride had a 25% lower risk of developing prostate cancer than men who did not take the drug. Side effects from finasteride in this study included erectile dysfunction, loss of libido, and breast enlargement. Dutasteride is currently being evaluated in the Reduction by Dutasteride of Prostate Cancer Events (REDUCE) trial. Recently published results from the Selenium and Vitamin E Cancer Prevention Trial (SELECT) showed that, in contrast to previous findings, vitamin E and selenium do not appear to protect against prostate cancer.

Early detection: At this time, there are insufficient data to recommend for or against routine testing for early prostate cancer detection. The American Cancer Society recommends that health care providers discuss the potential benefits and limitations of prostate cancer early detection testing with men and offer the PSA blood test (which detects a protein made by the prostate called prostate-specific antigen) and the digital rectal examination annually, beginning at age 50, to men who are at average risk of prostate cancer, do not have any major medical problems, and have a life expectancy of at least 10 years.

Men at high risk of developing prostate cancer (African Americans or men with a close relative diagnosed with prostate cancer before age 65) should have this discussion with their health care professional beginning at age 45. Men at even higher risk (because they have several close relatives diagnosed with prostate cancer at an early age) should have this discussion with their provider at age 40. All men should be given information about the benefits and limitations of testing so they can make informed decisions. Two large clinical trials designed to determine the efficacy of PSA testing are under way in the US and Europe. See page 68 for the American Cancer Society's screening guidelines for the early detection of prostate cancer.

Treatment: Treatment options vary depending on age, stage and grade of the cancer, and other medical conditions, and should be discussed with the individual's physician. The grade assigned to the tumor, typically called the Gleason score, indicates the aggressiveness of the cancer and ranges from 2 (nonaggressive) to 10 (very aggressive). Surgery, external beam radiation, or radioactive seed implants (brachytherapy) may be used to treat early stage disease; hormonal therapy may be added in some cases. Careful observation ("watchful waiting") rather than immediate treatment may be appropriate for some men with less aggressive tumors, especially men who are older or who have other health problems. Hormonal therapy, chemotherapy, radiation, or a combination of these treatments is used to treat more advanced disease. Hormone treatment may control advanced prostate cancer for long periods by shrinking the size or limiting the growth of the cancer, thus helping to relieve pain and other symptoms.

Survival: More than 90% of all prostate cancers are discovered in the local and regional stages; the 5-year relative survival rate for patients whose tumors are diagnosed at these stages approaches 100%. Over the past 25 years, the 5-year survival rate for all stages combined has increased from 69% to almost 99%. According to the most recent data, relative 10-year survival is 93% and 15-year survival is 79%. The dramatic improvements in survival, particularly at 5 years, are partly attributable to earlier diagnosis and improvements in treatment.

Skin

New cases: Substantially more than 1 million unreported cases of basal cell or squamous cell cancers occur annually. Most, but not all, of these forms of skin cancer are highly curable. The most common serious form of skin cancer is melanoma, which is expected to be diagnosed in about 68,720 persons in 2009. Melanoma is primarily a disease of whites; rates are more than 10 times higher in whites than in African Americans. Melanoma incidence rates have been increasing for at least 30 years. In the most recent time period, rapid increases have occurred among young white women (3.8% annual increase since 1995 in those aged 15 to 34 years) and older white men (8.8% annual increase since 2003 in those 65 and older).

Deaths: An estimated 11,590 deaths (8,650 from melanoma and 2,940 from other nonepithelial skin cancers) will occur in 2009. The death rate for melanoma has been decreasing rapidly in whites younger than 50 by 3.0% per year since 1991 in men and by 2.2% per year since 1985 in women. In contrast, in those 50 and older death rates have been increasing by 3.2% per year since 2002 in men and have been stable since 1989 in women.

Signs and symptoms: Important warning signs of melanoma include changes in size, shape, or color of a skin lesion or the appearance of a new growth on the skin. Changes that occur over a few days are generally innocuous, but changes that progress over a month or more should be evaluated by a doctor. Basal cell carcinomas may appear as growths that are flat, firm, pale areas or as small, raised, pink or red, translucent, shiny areas that may bleed following minor injury. Squamous cell cancer may appear as growing lumps, often with a rough surface, or as flat, reddish patches that grow slowly. Another sign of basal and squamous cell skin cancers is a sore that doesn't heal.

Risk factors: Risk factors vary for different types of skin cancer. For melanoma, major risk factors include a personal or family history of melanoma and the presence of atypical or numerous moles (greater than 50). Other risk factors for all types of skin cancer include sun sensitivity (sunburning easily, difficulty tanning, natural blond or red hair color); a history of excessive sun exposure, including sunburns; use of tanning booths; diseases that suppress the immune system; a past history of basal cell or squamous cell skin cancers; and occupational exposure to coal tar, pitch, creosote, arsenic compounds, or radiation.

Prevention: Protect your skin from intense sun exposure with sunscreen that has a sun protection factor (SPF) of 30 or higher and clothing, and avoid sunbathing. Wear sunglasses to protect the skin around the eyes. Children in particular should be protected from the sun because severe sunburns in childhood may greatly increase risk of melanoma in later life. Avoid tanning beds and sun lamps, which provide an additional source of UV radiation.

Early detection: The best way to detect skin cancer early is to recognize changes in skin growths or the appearance of new growths. Adults should thoroughly examine their skin on a regular basis. New or unusual lesions or a progressive change in a lesion's appearance (size, shape, or color, etc.) should be evaluated promptly by a physician. Melanomas often start as small, mole-like growths that increase in size and may change color. A simple ABCD rule outlines the warning signals of the most common type of melanoma: **A** is for asymmetry (one half of the mole does not match the other half); **B** is for border irregularity (the edges are ragged, notched, or blurred); **C** is for color (the pigmentation is not uniform, with variable degrees of tan, brown, or black); **D** is for diameter greater than 6 millimeters (about the size of a pencil eraser). Other types of melanoma may not have these signs, so be alert for any new or changing skin growths.

Treatment: Removal and microscopic examination of all suspicious skin lesions are essential. Early stage basal and squamous cell cancers can be removed in most cases by one of several methods: surgical excision, electrodessication and curettage (tissue destruction by electric current and removal by scraping with a curette), or cryosurgery (tissue destruction by freezing). Radiation therapy and certain topical medications may be used in some cases. For malignant melanoma, the primary growth and surrounding normal tissue are removed and sometimes a sentinel lymph node is biopsied to determine stage. More extensive lymph node surgery may be needed if lymph node metastases are present. Melanomas with deep invasion or that have spread to lymph nodes may be treated with surgery, immunotherapy, chemotherapy, or radiation therapy. Advanced cases of melanoma are treated with palliative surgery, immunotherapy, and/or chemotherapy, and sometimes radiation therapy.

Survival: Most basal and squamous cell cancers can be cured if the cancer is detected and treated early. Melanoma is also highly curable if detected in its earliest stages and treated properly. However, melanoma is more likely than other skin tumors to spread to other parts of the body. The 5- and 10-year relative survival rates for persons with melanoma are 91% and 90%, respectively. For localized melanoma, the 5-year survival rate is 99%; 5-year survival rates for regional and distant stage diseases are 65% and 16%, respectively. About 80% of melanomas are diagnosed at a localized stage.

Urinary Bladder

New cases: An estimated 70,980 new cases of bladder cancer are expected to occur in 2009. Over the past two decades, bladder cancer incidence rates have been stable among men but have been increasing slightly among women by 0.2% per year. Bladder cancer incidence is nearly four times higher in men than in women and more than two times higher in white men than in African American men.

Deaths: An estimated 14,330 deaths will occur in 2009. Mortality rates have recently stabilized in men after decreasing for most of the past three decades; rates have been declining in women since 1975.

Signs and symptoms: Symptoms may include blood in the urine and increased frequency of urination.

Risk factors: Smoking is the most important risk factor for bladder cancer. Smokers' risk of bladder cancer is twice that of nonsmokers. Smoking is estimated to cause about 48% of bladder cancer deaths among men and 28% among women. Workers in the dye, rubber, or leather industries and people who live in communities with high levels of arsenic in the drinking water also have increased risk. Drinking more fluids and eating more vegetables may lower the risk of bladder cancer.

Early detection: Bladder cancer is diagnosed by examination of cells in the urine under a microscope and examination of the bladder wall with a cystoscope, a slender tube fitted with a lens and light that can be inserted through the urethra. These tests are not recommended for screening people at average risk but are used for people at increased risk due to occupational exposure, or for follow-up after bladder cancer treatment to detect recurrent or new tumors.

Treatment: Surgery, alone or in combination with other treatments, is used in more than 90% of cases. Superficial, localized cancers may also be treated by administering immunotherapy or chemotherapy directly into the bladder. Chemotherapy alone or with radiation before cystectomy (bladder removal) has improved treatment results.

Survival: For all stages combined, the 5-year relative survival rate is 80%. Survival declines to 76% at 10 years and 72% at 15 years after diagnosis. When diagnosed at a localized stage, the 5-year survival is 93%; 75% of cancers are detected at this early stage. For regional and distant stages, 5-year survival is 45% and 6%, respectively.

Uterine Cervix

New cases: An estimated 11,270 cases of invasive cervical cancer are expected to be diagnosed in 2009. Incidence rates have decreased over most of the past several decades in both white and African American women. As Pap screening has become more common, preinvasive lesions of the cervix are detected far more frequently than invasive cancer.

Deaths: An estimated 4,070 deaths from cervical cancer are expected in 2009. Mortality rates have declined steadily over the past several decades due to prevention and early detection as a result of screening.

Signs and symptoms: Symptoms usually do not appear until abnormal cervical cells become cancerous and invade nearby tissue. When this happens, the most common symptom is abnormal vaginal bleeding. Bleeding may start and stop between regular menstrual periods, or it may occur after sexual intercourse, douching, or a pelvic exam. Menstrual bleeding may last longer and be heavier than usual. Bleeding after menopause or increased vaginal discharge may also be symptoms.

Risk factors: The primary cause of cervical cancer is infection with certain types of human papillomavirus (HPV). Women who begin having sex at an early age or who have many sexual partners are at increased risk for HPV infection and cervical cancer. However, a woman may be infected with HPV even if she has had only one sexual partner. Importantly, HPV infections are common in healthy women and only rarely result in cervical cancer. Persistence of HPV infection and progression to cancer may be influenced by many factors, such as immunosuppression, high parity (number of childbirths), and cigarette smoking. Long-term use of oral contraceptives is also associated with increased risk of cervical cancer.

Prevention: The FDA has approved Gardasil, the first vaccine developed to prevent the most common HPV infections that cause cervical cancer, for use in females aged 9 to 26 years. Clinical trials in males are currently under way. Another vaccine (Cervarix) has been approved for use in many countries and is currently awaiting FDA approval. For information on the American Cancer Society HPV vaccine guidelines, please see Saslow D, et al. *CA: A Cancer Journal for Clinicians*. Jan 2007;57: 7-28.

Early detection: The Pap test is a simple procedure in which a small sample of cells is collected from the cervix and examined under a microscope. Pap tests are effective but not perfect. Their results sometimes appear normal even when a woman has abnormal cells of the cervix, and likewise, sometimes appear abnormal when there are no abnormal lesions on the cervix. DNA tests to detect HPV strains associated with cervical cancer may be used in conjunction with the Pap test, particularly when results are equivocal. Fortunately, most cervical precancers develop slowly, so nearly all cases can be prevented if a woman is screened regularly. See page 68 for the American Cancer Society's screening guidelines for the early detection of cervical cancer.

Treatment: Preinvasive lesions may be treated by electrocoagulation (the destruction of tissue through intense heat by electric current), cryotherapy (the destruction of cells by extreme cold), laser ablation, or local surgery. Invasive cervical cancers are generally treated with surgery, radiation, or both, and with chemotherapy in selected cases.

Survival: One- and 5-year relative survival rates for cervical cancer patients are 88% and 71%, respectively. The 5-year survival rate for patients diagnosed with localized cervical cancer is 92%. Cervical cancer is diagnosed at an early stage more often in whites (52%) than in African Americans (44%) and in women younger than 50 (62%) than in women 50 and older (37%).

Uterine Corpus (Endometrium)

New cases: An estimated 42,160 cases of cancer of the uterine corpus (body of the uterus) are expected to be diagnosed in 2009. These usually occur in the endometrium (lining of the uterus). Incidence rates of endometrial cancer have been decreasing by about 0.5% per year since 1997 after increasing in the previous decade.

Deaths: An estimated 7,780 deaths are expected in 2009. Death rates from cancer of the uterine corpus have been stable since 1991 after decreasing an average of 1.6% per year from 1975 through 1991.

Signs and symptoms: Abnormal uterine bleeding or spotting is a frequent early sign. Pain during urination, intercourse, or in the pelvic area is also a symptom.

Risk factors: Estrogen is a strong risk factor for endometrial cancer, especially when not combined with progestin. Factors that increase estrogen exposure include menopausal estrogen therapy (without use of progestin) and being overweight/obese. In addition, risk is increased slightly by tamoxifen use, early menarche (onset of menstruation), late menopause, never having children, and a history of polycystic ovary syndrome. Progestin plus estrogen therapy (called menopausal hormone therapy, or MHT) does not appear to increase risk. Research has not implicated estrogen exposures in the development of other types of uterine corpus cancer that are more aggressive and have a poorer prognosis. Other risk factors for uterine corpus cancer include infertility and Lynch syndrome, also known as hereditary nonpolyposis colon cancer (HNPCC). Pregnancy and the use of oral contraceptives provide protection against endometrial cancer.

Early detection: There is no standard or routine screening test for endometrial cancer. Most endometrial cancer is diagnosed at an early stage because of postmenopausal bleeding. Women are encouraged to report any unexpected bleeding or spotting to their physicians. For women with hereditary non-polyposis colon cancer (HNPCC) or at risk for the disease, experts suggest annual screening for endometrial cancer with endometrial biopsy and/or transvaginal ultrasound beginning at age 35.

Treatment: Uterine corpus cancers are usually treated with surgery, radiation, hormones, and/or chemotherapy, depending on the stage of disease.

Survival: The 1- and 5-year relative survival rates for uterine corpus cancer are 92% and 83%, respectively. The 5-year survival rate is 96%, 68%, or 24%, if the cancer is diagnosed at a local, regional, or distant stage, respectively. Relative survival in whites exceeds that for African Americans by more than 10 percentage points at every stage of diagnosis.

Special Section
Multiple Primary Cancers

Introduction

In the past three decades, the development of screening tests that prevent and detect some cancers at an early, more treatable stage, and treatment advances have increased the 5-year relative survival rate for all cancers combined from 50% in 1975-1977 to 66% in 1996-2004. The National Cancer Institute (NCI) estimates that there are more than 11 million cancer survivors in the US, more than 3 times the number in 1970. As the survivor population grows, it is increasingly important to address the unique needs of cancer survivors for medical surveillance, continuity of care, and information about how their cancer and its treatment may affect their future health. In addition to concerns about cancer recurrence, survivors also worry about their risk of developing a new cancer.

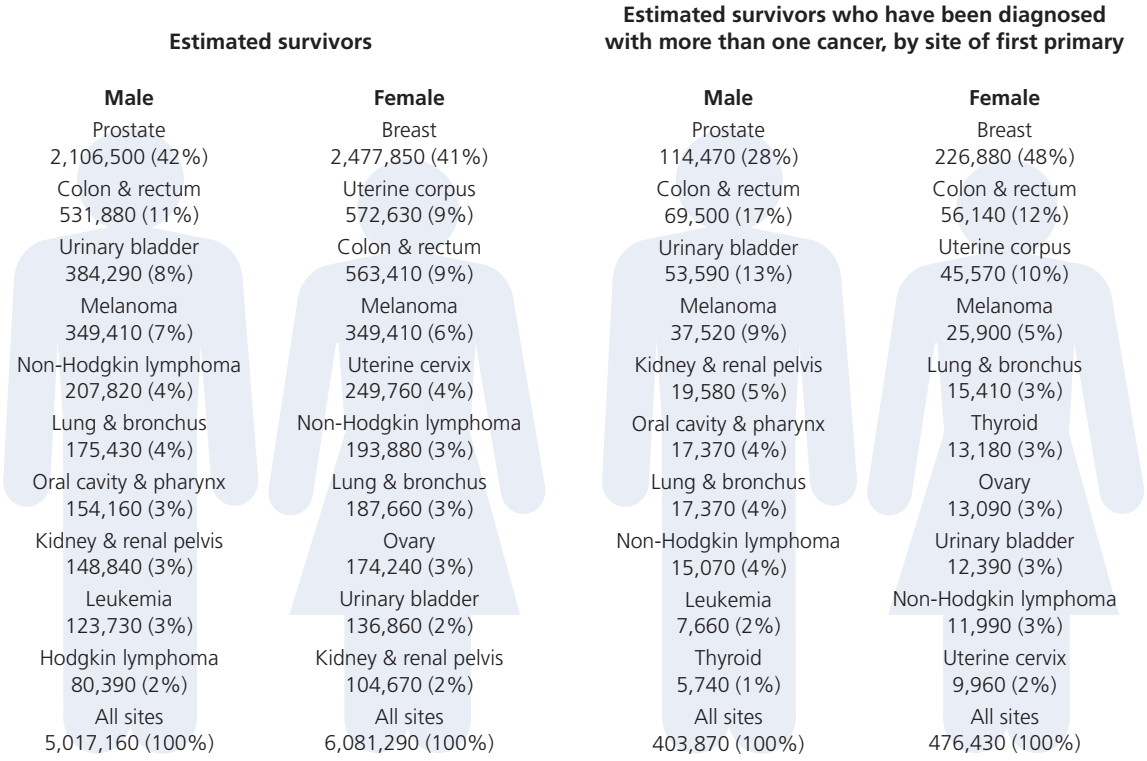
Approximately 880,300 of the 11 million cancer survivors living in the US as of January 1, 2005, had been diagnosed with more than one cancer. Most of these second or more cancers would be expected to occur even if cancer survivors had the same risk of cancer as the general population. The overall risk of cancer increases with age; for example, it is estimated that only 1% of 30-year-olds with no history of cancer will develop cancer in the next 10 years, compared to 18% of 70 year olds.[1] Although cancer survivors as a group have a small (14%) increased lifetime risk of developing new cancers compared with the general population, some subgroups of patients have a much higher risk. The risk of developing subsequent cancers varies by the type of first cancer diagnosed (referred to as the first primary site), age at first diagnosis, environmental exposures, genetic factors, treatment, and other factors. The purpose of this Special Section is to provide information about the burden and risks of multiple primary cancers, which will be useful to cancer survivors in understanding their risks and to health care providers in discussing risks of developing additional cancers with their patients.

This Special Section is organized into several broad topics. First, it provides background information about how clinicians and cancer registries define multiple primary cancers and descriptive statistics about the frequency and risk of subsequent cancers by primary site. It then describes the major factors that cause increased and decreased risk of multiple cancers, including family cancer syndromes and genetic susceptibility factors, shared-risk factors, and effects of treatment of a previous primary cancer. Next, it provides more detail on patterns of subsequent cancers for selected cancer sites (female breast cancer, colon and rectum, tobacco-related cancer, lymphomas, and melanoma) and childhood cancers. The final section describes American Cancer Society programs and resources for cancer survivors, including those who are at increased risk or have been diagnosed with more than one cancer.

How are multiple primaries defined?

- A cancer of a different site and histologic (microscopic composition of cells and/or tissue) type than the original cancer is considered a separate primary.
- Cancers of different histologic types in the same site are considered separate primaries regardless of whether they are diagnosed at the same or different times.
- A new cancer of the same site or with the same histology as an earlier one is considered the same primary cancer if diagnosed within 2 months or a separate primary cancer if diagnosed after 2 months, unless the medical record specifically states that it is recurrent or metastatic disease.
- If an organ is paired, each member of the pair is generally considered to be a separate site.
- Important exceptions to these general rules include most histological types of cancer in the prostate and urinary bladder, for which multiple tumors are reported as a single primary with the date of the first invasive lesion.
- A different set of rules is used to determine multiple primaries of the lymphatic and hematopoeitic (the production of blood cells) systems.

Figure 1. Estimated Number of Cancer Survivors* Alive as of January 1, 2005, and the Number Diagnosed with More than One Primary Site by Site of First Primary



* Rounded to the nearest 10.

Source: Angela Mariotto, Statistics, Research, and Evaluations Branch, Surveillance, Epidemiology, and End Results (SEER) Program, 17 SEER Registries, 1973-2005, Division of Cancer Control and Population Sciences, National Cancer Institute, 2008.

What Distinguishes a Recurrence from a Second Primary Cancer?

When a tumor is determined to be cancer, this indicates that cells within the tumor have developed the ability to invade into surrounding tissues and to move to remote sites (metastasize) where they can grow and invade. Even after treatment of the original cancer appears to have been effective, cancer cells may persist in the body and eventually grow to the point where they are detected either at or near the site of the original cancer or at a remote site. When this occurs, it is called a recurrence or a metastasis. By definition, a second (or multiple) primary cancer is the occurrence of a new cancer that is biologically distinct from the original primary cancer.[2] The determination of whether a new cancer is a separate primary or a recurrence or a metastasis from the original cancer is important clinically because it influences staging procedures, prognosis, and treatment. This determination usually involves a combination of pathological, clinical and, in some cases, additional laboratory studies. The distinction is easy when pathological information shows that the cancers being compared have different histological features that show that they have originated from distinct types of cells. Clinicians may also use information about typical patterns of recurrence and common sites of metastases for the first cancer. When the answer is not clear cut, molecular and cellular tools may be used to analyze the DNA of cells from the original and the new tumor to determine if they have a common origin, similar to taking a molecular fingerprint of the cancer. Tumor registries rely on the information in the medical record to determine whether a cancer is a recurrence or metastasis of a previously treated cancer, or a new cancer. In addition, cancer registries use coding rules to count multiple primary cancers in a consistent way. The coding rules consider the cancer site of origin, date of diagnosis, his-

Measures of risk for a subsequent cancer diagnosis among cancer survivors

Observed-to-Expected Ratio (O/E)

The observed number of cancers in a population of cancer survivors divided by the number of cancers expected. The number of cancers expected is calculated using cancer rates from the general population and person-years-at-risk (PYAR) of the survivor population under study. PYAR is counted from the date 2 months after the diagnosis of the first cancer (to exclude multiple primaries diagnosed at the same time) until the date of last known vital status or death, and allocated by age, sex, race, and calendar year. All second and later (third, fourth, etc.) cancer diagnoses are included.

Estimated absolute risk (EAR) per 10,000 PYAR

The EAR is calculated by subtracting the expected number of cancer cases from the observed number, dividing by the PYAR, and multiplying by 10,000 [((O-E)/PYAR) x 10,000]. The EAR represents the number of excess cancers per 10,000 PYAR (for example, a population of 10,000 cancer survivors followed for 1 year or 1,000 cancer survivors followed 10 years).

tology, behavior (i.e. in situ or malignant), and laterality of paired organs. Multiple primary cancers can either be diagnosed at the same time (synchronous) or at different times (metachronous); coding rules exclude cancers diagnosed within two months of the primary cancer, which are considered to be synchronous cancers, from the multiple primary counts. The coding rules used in this article are those used by the Surveillance, Epidemiology, and End Results (SEER) registries.[3]

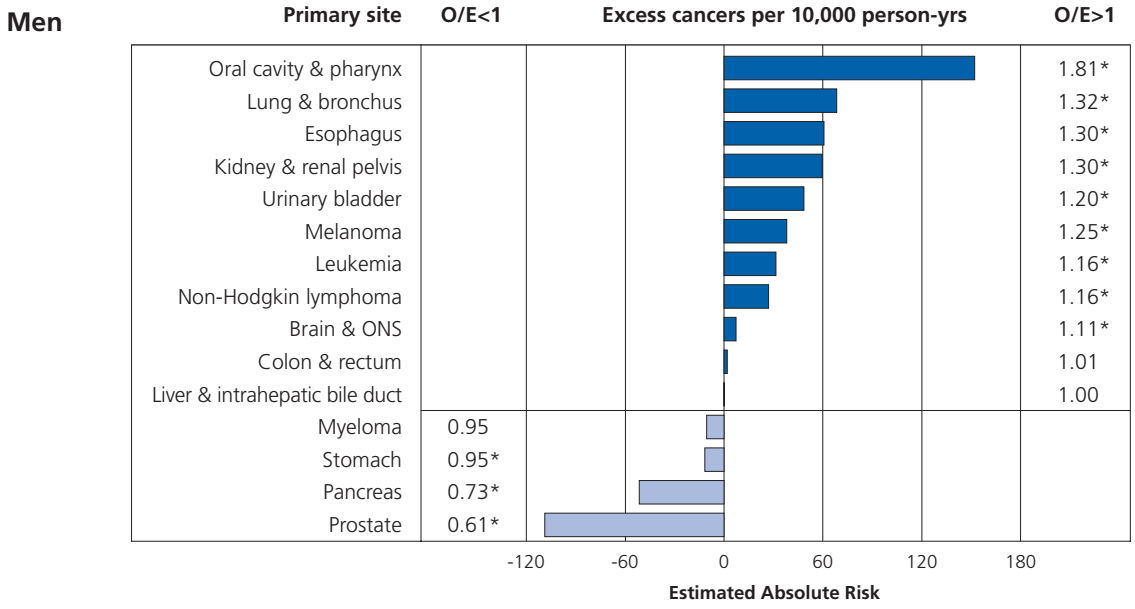
Population-based cancer registries are an important resource for studying multiple primary cancers. Registries collect information about each cancer patient in such a way that subsequent primary cancers diagnosed in the same person can be identified. The earliest studies of multiple primaries were done by cancer registries in Connecticut and Denmark.[4] More recently, the SEER Program published a monograph on new malignancies among cancer survivors based on data from the 9 original SEER registries during the 28-year period 1973-2000. The SEER Monograph, with data updated to 2005 (using SEER*Stat software version 6.4.4), is the primary resource for statistics used in this report and will be referred to throughout as the SEER Multiple Primary Study; the monograph can be accessed at http://seer.cancer.gov/publications.[5] The categories of primary and secondary cancer sites are provided in Appendix 2.A and 2.B of the monograph. In some cases, the categories reported for primary and secondary sites differ; for example, the category "acute myeloid leukemia" is used for primary sites and "acute non-lymphocytic leukemia," which includes acute myeloid leukemia and several other categories, is used for secondary sites. More information on the methods used and limitations of the study are provided in the Sources of Statistics section, from pages 17-19.

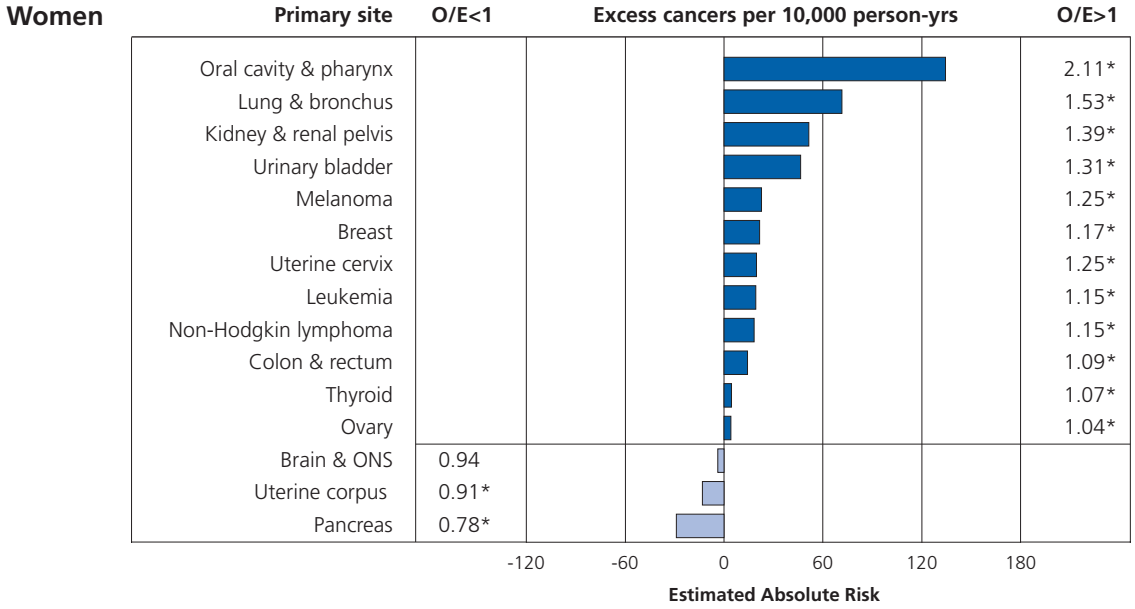
How Common Are Multiple Primary Cancers?

An estimated 880,300 cancer survivors who have been diagnosed with more than one cancer were living in the US as of January 1, 2005.[6] Among men who have been diagnosed with more than one cancer, the 10 most common primary sites are prostate, colon and rectum, urinary bladder, melanoma, kidney and renal pelvis, oral cavity and pharynx, lung and bronchus, non-Hodgkin lymphoma, leukemia, and thyroid (Figure 1). Among women who have been diagnosed with more than one cancer, the 10 most common primary sites are breast, colon and rectum, uterine corpus, melanoma, lung and bronchus, thyroid, ovary, urinary bladder, non-Hodgkin lymphoma, and uterine cervix (Figure 1). These rankings generally reflect high incidence and survival rates for the first primary cancer rather than unusually high risks for a subsequent cancer. For example, the large number of prostate cancer survivors who have been diagnosed with a multiple cancer reflects the fact that prostate cancer is the most commonly diagnosed cancer in men and has a 5-year relative survival rate of more than 99%, not that prostate cancer survivors have an increased risk of developing additional cancers. (See "What causes decreased risk of developing another cancer?" on page 30.)

The Observed-to-Expected Ratios (O/Es) and Estimated Absolute Risks (EARs) for subsequent cancers for the 15 most common primary cancer sites in men and women are shown in Figure 2. For both men and women, the highest O/Es and EARs are observed for cancers related to tobacco, including cancer of the oral cavity and pharynx, lung and bronchus, esophagus (men only), kidney and renal pelvis, and urinary bladder. Among men, primary sites associated with modest increased risks of subsequent cancer include melanoma, leukemia,

Figure 2. Estimated Absolute Risk (EAR) per 10,000 Person-Years and Observed-to-Expected Ratios (O/E) for Subsequent Cancers by Primary Site, Men and Women Ages 20 and Older, 1973-2005





Source: Surveillance, Epidemiology, and End Results (SEER) Program, 17 SEER Registries, 1973-2005, Division of Cancer Control and Population Sciences, National Cancer Institute, 2008.

Note: Top 15 sites are based on Jemal A, Thun MJ, Ries LAG, et al. Annual report to the nation on the status of cancer, 1975-2005, featuring trends in lung cancer, tobacco use, and tobacco control. *J Natl Cancer Institute* 2008;100(23):1672-1694.

Table 1. Observed-to-Expected Ratio and Estimated Absolute Risk of Developing Subsequent Primary Cancer by Age at Initial Cancer Diagnosis, SEER 1973-2005

Age at initial diagnosis	Male and female			Male			Female		
	Observed	O/E	EAR	Observed	O/E	EAR	Observed	O/E	EAR
All Ages	**258,997**	**1.14***	**21**	**140,888**	**1.12***	**22**	**118,109**	**1.17***	**21**
0-17	585	5.63*	17	266	5.69*	15	319	5.59*	19
18-29	2,171	2.41*	21	880	2.83*	21	1,291	2.19*	20
30-39	7,394	2.00*	33	2,315	2.22*	34	5,079	1.92*	33
40-49	20,501	1.51*	36	6,958	1.68*	48	13,543	1.44*	30
50-59	48,737	1.23*	29	23,097	1.28*	40	25,640	1.19*	22
60-69	85,461	1.12*	22	49,908	1.10*	22	35,553	1.14*	22
70-79	72,119	1.03*	8	45,015	1.02*	5	27,104	1.06*	12
80+	22,029	0.95*	-11	12,449	0.95*	-14	9,580	0.96*	-9

Note: Excludes the first 2 months after initial cancer diagnosis. Subsequent cancers exlcude non-melanoma skin and subsequent prostate cancers following an initial prostate cancer.

O/E = observed-to-expected ratio; EAR = excess absoute risk per 10,000 person years at risk (PYAR).

* $p<0.05$

and non-Hodgkin lymphoma; sites with no significant increase or decrease in risk include colon and rectum, liver and intrahepatic bile duct, and myeloma; and those with significantly decreased risk include stomach, pancreas, and prostate cancer. Among women, primary sites with modest increased risks include melanoma, breast, uterine cervix, leukemia, non-Hodgkin lymphoma, colon and rectum, thyroid, and ovary. Women who have had a primary brain cancer do not have significantly increased or decreased risk, and those who have a history of uterine cancer (including uterus not otherwise specified) or pancreatic cancer have a significantly decreased risk of subsequent cancer. Reasons that risk for second or more cancers differ by primary site are discussed below.

In addition to primary site, age at initial diagnosis is strongly associated with relative risk of developing a subsequent cancer (Table 1). Individuals diagnosed with cancer at ages 0 to 17 years have a substantially increased risk of developing subsequent cancers (O/E=5.63), with O/E ratios declining for patients diagnosed with their first cancer in each subsequent age interval (Table 1). Elevated O/Es for subsequent cancers among individuals diagnosed with cancer at younger ages are primarily related to genetic susceptibility and effects of radiation and chemotherapy treatment. Although the O/Es for subsequent cancers are highest for those diagnosed at ages 0 to 17 years, the absolute risks are not. The EAR for male and female patients diagnosed under age 18, 17 per 10,000 PYAR, is considerably lower than the EARs for middle-aged adults, which peak among men and women diagnosed at age 40 to 49 years (EAR = 36 per 10,000 PYAR) (Table 1). Persons diagnosed at age 80 and older have a significantly decreased O/E of subsequent cancer, likely reflecting in part underreporting of second cancers among elderly patients.

What Causes Excess Risk of Developing Another Cancer?

Cancers arise through a multistage process involving initiation, promotion, malignant transformation, and tumor progression. The critical initiating events often involve damage to DNA (the genetic material of the cell) that is not repaired before the cell divides, resulting in heritable mutations (permanent changes in the DNA) that are passed on to daughter cells. Mutations in critical areas of genes that regulate cell growth, cell death, or DNA repair may result in the selective growth of damaged cell lines and accumulation of further genetic damage. Factors that increase cell turnover, such as some hormones, can increase the proliferation of cells and the likelihood of malignant transformation even if they are not themselves mutagenic. In general, many mistakes in the DNA must accumulate for a cancer to develop. Factors associated with increased risk of developing more than one primary cancer have been grouped into three broad categories: familial cancer syndromes and other genetic susceptibility factors, common exposures (e.g. tobacco), and carcinogenic effects of cancer treatment. [7,8]

Familial Cancer Syndromes and Genetic Susceptibility Factors

About 1-2% of all cancers are associated with hereditary cancer syndromes; these syndromes are associated with very high lifetime probabilities of developing certain cancers.[7] Individuals with hereditary cancer syndromes have a heritable mutation in every cell, which may have been inherited from a parent or arisen early in development. Even in people with inherited syndromes, the development of cancer still depends on acquiring additional mutations. Many of these syndromes are autosomal dominant, which means there is a 50% chance that someone carrying the gene will pass it to their child. Retinoblastoma, a rare childhood cancer in the retina of the eye, is an example of an autosomal dominant hereditary cancer that is associated with a specific gene mutation in about 35% of all cases. Children born with this mutation have a very high probability of developing one or more retinoblastomas, as well as several other cancers, and are more susceptible to the adverse effects of radiation.[9]

Additional hereditary syndromes are associated with increased risk of developing multiple primary cancers.[9] Familial adenomatous polyposis (FAP) and hereditary nonpolyposis colorectal cancer (HNPCC) are two genetic syndromes that confer a high risk of colorectal cancer at an early age and at multiple sites within the colon and rectum. (See section on colon and rectal cancer on page 32.) Individuals with HNPCC are also predisposed to endometrial and ovarian cancers. Inherited mutations in the cancer susceptibility genes BRCA1 and BRCA2 are associated with early-onset breast and ovarian cancers and increased risk of second primaries of the breast, ovary, and other sites. (See section on breast cancer on page 30.) Heritable cancer syndromes should be suspected when several generations of a family are diagnosed with certain cancers at a relatively young age, or when several individuals in a family develop multiple primary cancers. When a heritable cancer syndrome is suspected, genetic counseling should be discussed because this may identify mutations in known cancer susceptibility genes.

Shared Risk Factors

Tobacco and alcohol use

Individuals may be at increased risk of developing multiple primary cancers due to exposure to risk factors that are associated with several cancers. As noted previously, individuals with tobacco-related cancer have very high O/Es for developing additional tobacco-related cancers. Tobacco smoke contains numerous carcinogens and prolonged exposure may result in a phenomenon called "field cancerization" in which there are multiple patches of transformed cells in the respiratory and urinary tract, some of which evolve to second (or more) cancers. Alcohol consumption has been associated with increased risk of a number of cancers, including oral cavity and pharynx, esophagus, liver, colon, larynx, and female breast. For some cancers, the risks associated with excessive alcohol consumption and tobacco use are much higher than for either exposure alone. It is estimated that alcohol consumption combined with tobacco use account for 75-85% of cancers of the oral cavity, pharynx, larynx, and esophagus in the US.[9]

Hormonal factors

Individuals may be at increased risk of developing multiple primary cancers due to hormonal factors that are associated with several cancers. Hormonal factors play an important role in the development of female breast cancer and several cancers of the female reproductive system. Studies of multiple primary cancers have found similar increases in relative risks for breast, ovarian, and uterine corpus cancers.[7, 9] This may result from common hormonal risk factors related to menstrual and pregnancy history and use of hormonal medications, as well as genetic susceptibility factors that increase risk for several cancers.

Immune deficiency and infection

Immunodeficiency syndromes, either acquired or inherited, are associated with an increased risk of non-Hodgkin lymphoma and some other cancers. Patients receiving immunosuppressive therapy after kidney transplants are at increased risk of non-Hodgkin lymphoma, Kaposi sarcoma, and squamous cell cancer on sun-exposed areas of their skin.[7] Suppression of the immune system may predispose a patient to other forms of skin cancer, including malignant melanoma. Patients with human immunodeficiency virus (HIV)-related immunodeficiency are at increased risk of non-Hodgkin lymphoma, Kaposi sarcoma, and cervical and anal cancer. Although case reports document multiple cancers in HIV-infected individuals, the relative risk for multiple primary tumors in patients with HIV-related immunodeficiency is unknown.

Human papillomavirus (HPV) infections are the main cause of cancer of the uterine cervix and have been implicated in other cancers of the anogenital tract (vulva, vagina, perineum, anus, and penis) for which there is evidence for mutually increased risk. There is growing

evidence to support a causal role for HPV, especially HPV-16, in oropharyngeal cancers.[10] HPV infections are relatively more aggressive and persistent in individuals with compromised immune systems.[7]

Effects of treatment of a previous primary cancer

Some of the treatments for cancer can damage normal cells and result in short-term and long-term side effects, including an increased risk of subsequent cancer years or decades later. The benefits of treatment of the first cancer are large compared to the risks of developing a second cancer.[11] The second cancers associated with radiation therapy include acute leukemia, chronic myelogenous leukemia, breast, lung, thyroid, and non-melanoma skin cancers.[12] Second cancers of the bone and connective (soft) tissues occur within or adjacent to the irradiated area among patients treated with high-dose radiation. Dose and type of radiation, the intrinsic susceptibility of exposed tissues, and patient characteristics influence the risk for radiation-associated cancers. The risk is generally higher when developing tissue is exposed at a young age. Improvement in radiotherapy techniques over time has allowed the damage to normal tissue to be minimized while delivering an effective dose to the cancer. Both radiotherapy and chemotherapy can cause treatment-related leukemia (most commonly acute non-lymphocytic leukemia). Chemotherapy drugs associated with increased risk of acute myeloid leukemia include some alkylating agents, topoisomerase II inhibitors, and anthracyclines. The carcinogenic potential of some chemotherapeutic drugs may be enhanced when administered in conjunction with ionizing radiation. Research has resulted in the development of chemotherapy agents that are equally or more effective in treating cancer while having less short-term and long-term toxicity to patients, including lower risk of second cancers.[13]

What Causes Decreased Risk of Developing Another Cancer?

Adult patients diagnosed with cancers that have low 5-year survival rates, such as pancreatic cancer, appear to be at decreased risk for second cancers. This may result in part from the exclusion of other cancers diagnosed within the first two months of the first, short interval of follow-up, and lack of differentiation of metastatic lesions from new primary tumors in terminally ill patients. Decreased risks for some cancers may be influenced by treatment and coding rules; this typically applies primarily to subsequent cancers of the same site. When a cancer is treated by removing an organ, the patient is no longer at risk for second tumors of that site. For example, many women with cancer of the uterine corpus are treated with hysterectomy and thus are not at risk for subsequent cancer of the uterine cervix or corpus. Some men with prostate cancer have their prostate surgically removed; in addition, coding rules specify that when second or more prostate cancers of the most common histological type (adenocarcinomas) are detected they are not considered a separate primary. When overall risk of subsequent cancer is thought to be influenced by treatment or coding rules for cancers of the same primary site, it is useful to examine the O/E ratio for cancers excluding the primary site. For the cancers mentioned above, the O/E calculated before and after excluding cancers of the same primary site goes from 0.91* to 0.96 for uterine corpus and 0.61* to 0.91* for prostate cancer. In contrast, the decreased risk of subsequent cancers after stomach cancer does not change after exclusion of the primary site (O/E in men and women combined changes from 0.91* to 0.92*); this may in part reflect the uniqueness of the primary risk factor for this cancer (*Helicobacter pylori* infection), which is not strongly associated with any other cancer. In addition, reduced rates of subsequent cancer may result from caloric restriction after stomach cancer treatment; reduced cancer mortality rates have been observed in long-term follow-up of patients with gastric bypass surgery.[14]

Multiple Primary Cancers Associated with Selected Primary Sites

Female breast cancer

Invasive breast cancer is the most frequently diagnosed non-skin cancer among women in the US and has a 5-year relative survival rate of 89%. The SEER multiple primary study found an O/E of 1.17 for all subsequent cancers among women diagnosed with a first primary breast cancer during 1973-2005 (Table 2).[15] New primary cancers of the breast account for nearly 40% of all cancers diagnosed among female breast cancer survivors, followed by cancer of the lung, uterine corpus, ovary, and acute non-lymphocytic leukemia. There is a strong relationship between younger age at diagnosis of the primary breast cancer and risk of a subsequent cancer (Table 2). Women diagnosed with early-onset breast cancer (age < 40) had almost a 3-fold increased risk of any subsequent cancer, with a 4.5-fold increased risk of subsequent breast cancer. In contrast, women diagnosed at age 70 and older had no excess risk of any subsequent cancer, and only a small (1.2-fold) increased risk of subsequent breast cancer. Genetic

Table 2. Observed-to-Expected Ratio for Developing Subsequent Primary Cancer after Female Breast Cancer by Age at Diagnosis of First Primary, SEER 1973-2005

Subsequent site	Birth to 39 (N=27,633)	40 to 49 (N=70,941)	50-69 (N=180,355)	70 and older (N=120,028)	All ages (N=398,957)	Observed number	Expected number	EAR
Breast	4.54*	1.98*	1.42*	1.20*	1.55*	18,523	11,932	19.64
Lung & bronchus	1.79*	1.24*	0.99	0.77*	0.96*	5,478	5,684	-0.61
Uterine corpus	1.77*	1.25*	1.32*	1.65*	1.40*	3,552	2,538	3.02
Ovary	4.67*	1.82*	1.16*	0.98	1.29*	1,815	1,408	1.21
ANLL	6.33*	3.31*	1.89*	1.03	1.74*	616	354	0.78
All subsequent cancers†	2.87*	1.49*	1.15*	0.99	1.17*	48,934	41,689	21.59

Note: Excludes the first 2 months after initial cancer diagnosis. Site definitions are based on Appendix 2a and 2b from Curtis RE, Freeman DM, Ron E, et al., (eds.) *New malignancies among cancer survivors: SEER cancer registries, 1973-2000*. Bethesda, MD: National Cancer Institute, NIH Publ. No. 05-5302; 2006.

EAR = excess absoute risk per 10,000 person years at risk (PYAR); ANLL = acute non-lymphocytic leukemia.

* $p<0.05$

† All subsequent cancers excludes non-melanoma skin cancer.

predisposition, notably mutations in BRCA1 and BRCA 2 genes, contribute to the excess risk of subsequent cancer among women with early-onset breast cancer. [7]

In addition to genetic predisposition, breast cancer survivors may be at increased risk of developing subsequent cancers of the breast and ovary associated with hormonal and reproductive risk factors, such as nulliparity (not having a child) and a long menstrual history (menstrual periods that start early and/or end late in life), as well as the adverse effects of treatment.[16] Patients receiving tamoxifen therapy for estrogen receptor positive breast cancer have a substantially decreased risk of recurrence and of developing a second primary breast cancer, but have an increased risk of developing cancer of the uterus.[16] The increased risk of acute non-lymphocytic leukemia (ANLL) among breast cancer survivors is thought to be related to some chemotherapy treatments, with radiation possibly adding to the risk.

Although the overall risk of lung cancer is lower for breast cancer survivors than the general population, an elevated O/E has been observed for women treated with radiotherapy after mastectomy.[5] While no significant excess risk has been reported among women receiving lower-dose radiation treatment after lumpectomy, women receiving this therapy may not have been followed long enough to detect such a risk if it was present. Radiation treatment may also be related to increased risk of several less common cancers among breast cancer survivors, including esophagus, bone, and soft tissue. Other relatively uncommon cancers that occur more frequently in breast cancer survivors are malignant melanoma, thyroid cancer, and salivary gland cancer. In contrast to some studies, the SEER study did not find significantly increased risk for colon cancer among breast cancer survivors.[15]

Recommendations exist for identification of women with primary breast cancer who have hereditary syndromes that increase the risk of developing multiple primaries. Women with predisposing mutations that increase the risk of breast and ovarian cancer may choose to undergo prophylactic bilateral mastectomy (removal of both breasts) or contralateral prophylactic mastectomy (removal of unaffected breast) after diagnosis of a primary breast cancer. Removal of the ovaries and fallopian tubes may also be considered because this reduces risk of subsequent invasive breast cancer by 50% and nearly eliminates the risk of ovarian cancer.[17] Both the American Society for Clinical Oncology (ASCO) and the National Comprehensive Cancer Network (NCCN) have published guidelines for follow-up of women after treatment for breast cancer.[18, 19] These guidelines recommend that all women who have had a diagnosis of breast cancer undergo regular physician visits, including history and physical examination and annual diagnostic mammography. Recent American Cancer Society guidelines recommend magnetic resonance imaging (MRI) in addition to screening mammography for women who have a high lifetime risk of breast cancer, including those with BRCA1 and BRCA2 mutations.[20] MRI is not recommended for women with a personal history of breast cancer, whose absolute lifetime risk of subsequent breast cancer is estimated to be 10%, because there is little data to support the benefits.[20]

Table 3. Observed-to-Expected Ratio for Developing Subsequent Primary Cancer after Cancer of the Colon, Rectum, and Rectosigmoid Junction by Age at Diagnosis of First Primary, SEER 1973-2005

Primary colon cancer

Subsequent site	Birth to 39 (N=4,614)	40 to 59 (N=41,397)	60-69 (N=54,664)	70 and older (N=112,500)	All ages (N=213,175)	Observed number	Expected number	EAR
Colon	12.46*	2.42*	1.67*	1.31*	1.57*	4,487	2,867	12.56
Rectum & rectosigmoid junction	12.24*	2.05*	1.23*	1.17*	1.36*	1,272	937	2.60
Uterine corpus	7.10*	1.54*	1.04	1.12	1.23*	697	567	1.01
Ovary	4.26*	1.42*	1.09	0.76*	1.01	340	338	0.01
ANLL	3.17	0.53*	1.10	1.02	0.99	238	241	-0.02
All subsequent cancers†	2.77*	1.22*	1.06*	1.00	1.06*	27,344	25,752	12.34

Primary cancer of the rectum or rectosigmoid junction

Subsequent site	Birth to 39 (N=2,361)	40 to 59 (N=23,731)	60-69 (N=26,210)	70 and older (N=39,380)	All ages (N=91,682)	Observed number	Expected number	EAR
Colon	7.45*	2.05*	1.40*	1.28*	1.45*	1,621	1,115	9.13
Rectum & rectosigmoid junction	7.57*	1.09	0.59*	0.92	0.86*	335	390	-1.00
Uterine corpus	4.28*	1.27*	1.06	0.84	1.07	227	213	0.26
Ovary	–	0.87	0.86	0.54*	0.72*	88	122	-0.61
ANLL	5.09	0.86	0.87	1.09	0.99	96	97	-0.02
All subsequent cancers†	2.14*	1.10*	0.98	0.94*	0.99	10,591	10,661	-1.27

Note: Excludes the first 2 months after initial diagnosis. Site definitions are based on Appendix 2a and 2b from Curtis RE, Freeman DM, Ron E, et al., (eds.) *New malignancies among cancer survivors: SEER cancer registries, 1973-2000*. Bethesda, MD: National Cancer Institute, NIH Publ. No. 05-5302; 2006.

EAR = excess absoute risk per 10,000 person years at risk (PYAR); ANLL = acute non-lymphocytic leukemia.

* p<0.05

† All subsequent cancers excludes non-melanoma skin cancer.

Colon and rectum

Cancers of the colon and rectum are the third most common cancer in men and women in the US, with a 5-year relative survival rate of 64%. The SEER multiple primary study found that most common second cancers among colon cancer survivors are new cancers of the colon and rectum.[21] Among colon cancer survivors, the O/E for subsequent primary colon cancer is 1.57 and for rectal cancer is 1.36 (Table 3). The O/E for all subsequent cancers is highest for colon cancer patients diagnosed with their initial cancer under age 40 (O/E = 2.77) and declines with age, with no overall increased risk among patients diagnosed at age 70 and older. Among patients diagnosed with colon cancer before age 40, the O/E is 12.46 for subsequent colon cancer, 12.24 for subsequent rectal cancer, 7.10 for cancer of the uterine corpus, 4.26 for ovarian cancer, and 3.17 for acute non-lymphocytic leukemia (Table 3).

Much of this increased risk for subsequent cancers among colorectal cancer patients diagnosed at an early age is related to two genetic susceptibility syndromes associated with early onset colon cancer mentioned previously: FAP and HNPCC, also known as Lynch syndrome. Both of these syndromes are inherited diseases in which carrier parents have a 50:50 chance of passing the mutation to each child.[22] FAP is due to an inherited defect that leads to the appearance of numerous (> 100) polyps throughout the large bowel, and usually becomes evident in the second decade of life. If untreated, patients typically develop colorectal cancer at a mean age of 39 years. FAP is responsible for < 1% of colon cancers. The risk of multiple

colon cancers is so high that the recommended treatment is removal of the entire colon at an early age in anyone identified with this syndrome. FAP is also associated with increased risk of cancer of the stomach, small intestine, thyroid, pancreas, and brain. HNPCC is characterized by early onset of predominantly right-sided colon cancer and the tendency to develop multiple cancers. Affected individuals generally develop only a few polyps, and these generally occur at a later age than in patients with FAP.[22] HNPCC families are defined by the occurrence of colorectal cancer in three relatives, one of whom is a first-degree relative of the other two, diagnosis of at least one of the colorectal cancers before age 50, involvement of at least two generations, and exclusion of FAP. HNPCC occurs as a result of mutations in genes that repair errors in DNA and is associated with approximately 3-6% of colorectal cancers in the US.[22] Affected individuals can now be identified using molecular approaches rather than relying exclusively on family history. HNPCC also predisposes to early-onset cancers of the small intestine, stomach, bile ducts, uterine corpus, ovary, renal pelvis, ureter, and brain.[21] Patients can be monitored with colonoscopy and do not require removal of the colon since the risk of colon cancer is less than in patients with FAP. Recommendations are available for identification, genetic screening and counseling, and colorectal cancer screening for individuals who may be at high risk of colorectal cancer because of recognized genetic syndromes, and for those whose family history indicates high risk without one of the identified factors.[23]

Risks of developing subsequent cancers among patients who have a history of rectal cancer are lower than those among patients with a history of colon cancer. Although rectal cancer survivors are not at increased risk of developing subsequent cancers of all types combined, they do have an elevated O/E for subsequent colon cancer (O/E=1.45), particularly if the first cancer is diagnosed at younger ages (Table 3).

In addition to the hereditary syndromes, survivors of colorectal cancer may be at increased risk of developing subsequent cancers because of common risk factors, including treatment with chemotherapy or radiation, diet, obesity, physical inactivity, and hormonal/reproductive factors. Since the overwhelming majority of subsequent cancers among colorectal cancer survivors occur in the colon and rectum, medical surveillance for these patients has the potential to detect recurrence and to detect new colorectal adenomas or cancers.[24] Colonoscopy is recommended one year after curative surgery for colon and rectal cancer; if that examination is normal, another colonoscopy is recommended at 3 years, and if that is normal, the next examination is at 5 years. In addition, since rectal cancer patients have a higher probability of local recurrence than colon cancer patients, surveillance sigmoidoscopy or endoscopic ultrasonography is recommended at 3- to 6-month intervals for the first 2 to 3 years after treatment.[24]

Tobacco-related cancer

Patients with primary cancers of sites related to tobacco use have an increased risk of developing subsequent cancers at tobacco-related sites. The SEER multiple primary study found that the O/Es for subsequent cancer among individuals with tobacco-related primary cancers are higher in women than in men (Table 4).[25, 26, 27] This difference is likely due to the fact that a much higher proportion of men than women in the general population are current or former smokers, and thus the rates of smoking-related cancers used to calculate the expected number of cancers are higher.[26] Among patients with primary lung cancer, subsequent lung cancers constitute almost a third of new primary cancers, with increases in risk being highest (greater than 3-fold) among patients surviving 5 or more years after initial diagnosis. Elevated O/Es among lung cancer survivors have also been observed for cancer of the oral cavity and pharynx, larynx, esophagus, bladder and renal pelvis, and ureter in men and women, and uterine cervix in women, as well as some other less common cancers. The risks of subsequent cancers of the lung and oral cavity are especially high among lung cancer survivors who continue to smoke cigarettes. Some data suggest that smoking cessation following lung cancer lowers the risk of new smoking-related cancers.[26]

Male survivors of laryngeal cancer have a relative risk of 1.62 for developing a subsequent cancer. The subsequent tumors associated with laryngeal cancer include lung, oral cavity and pharynx, and esophagus and likely result from joint exposure to tobacco and alcohol. The SEER study also found increased risk of subsequent cancers of adjacent sites among patients whose laryngeal cancer was treated with radiation.[26] Survivors of cancers of the oral cavity and pharynx have more than a 2-fold excess risk of developing a subsequent cancer, with especially high relative risks of subsequent cancers of the oral cavity and pharynx, esophagus, and larynx (Table 4). Tobacco and/or alcohol consumption probably account for much of the increased risk. Squamous cell carcinoma of the esophagus is strongly related to tobacco smoking and is also associated with alcohol abuse and low fruit and

Table 4. Observed-to-Expected Ratio for Developing Subsequent Tobacco-related Cancer after Selected Tobacco-related First Primary Cancers, SEER 1973-2005

Females

First primary cancer	Subsequent primary cancer: Lung	Oral cavity & pharynx	Larynx	Esophagus	Bladder	Kidney parenchyma	Renal pelvis & ureter	Uterine cervix	All subsequent cancers†
Lung & bronchus	3.81*	2.61*	5.03*	3.63*	1.92*	1.83*	1.71*	0.9	1.53*
Oral cavity & pharynx	4.59*	39.85*	12.88*	23.90*	1.32	1.02	0.88	1.47	2.47*
Larynx	7.01*	13.49*	7.22*	13.03*	1.64*	2.01*	1.16	1.56	2.38*
Esophagus‡	2.46*	28.74*	7.25*	5.50*	1.39	2.38	5.02	3.11	1.78*
Bladder	2.17*	1.00	2.04*	1.07	2.43*	1.64*	18.13*	0.75	1.31*
Kidney parenchyma§	1.17*	0.90	0.78	0.59	2.45*	5.50*	0.99	1.31	1.18
Renal pelvis & ureter	2.75*	1.73	3.33	1.10	47.90*	0.45	16.38*	0.36	2.96*
Uterine cervix	2.35*	1.76*	2.98*	1.66*	2.59*	1.11	3.01*	0.61*	1.25*

Males

First primary cancer	Subsequent primary cancer: Lung	Oral cavity & pharynx	Larynx	Esophagus	Bladder	Kidney parenchyma	Renal pelvis & ureter	All subsequent cancers†
Lung & bronchus	2.06*	2.26*	2.73*	2.29*	1.50*	1.58*	1.40*	1.32*
Oral cavity & pharynx	3.82*	18.31*	5.64*	12.50*	1.13	1.13	1.10	2.36*
Larynx	3.39*	5.27*	1.73*	3.63*	1.31*	1.27*	1.34	1.62*
Esophagus‡	2.05*	12.85*	4.41*	0.76	1.09	0.37	0.84	1.67*
Bladder	1.58*	0.92	1.31*	1.00	0.89*	1.44*	11.00*	1.20*
Kidney parenchyma§	0.97	0.69*	0.80	0.73	1.51*	3.98*	1.29	1.17*
Renal pelvis & ureter	1.85*	0.84	1.13	1.26	15.81*	1.05	18.37*	2.44*

Note: Excludes the first 2 months after initial cancer diagnosis. Site definitions are based on Appendix 2a and 2b from Curtis RE, Freeman DM, Ron E, et al., (eds.) *New malignancies among cancer survivors: SEER cancer registries, 1973-2000*. Bethesda, MD: National Cancer Institute, NIH Publ. No. 05-5302; 2006.

EAR = excess absoute risk per 10,000 person years at risk (PYAR); ANLL = acute non-lymphocytic leukemia.

* $p<0.05$

† All subsequent cancers excludes non-melanoma skin cancer.

‡ Squamous cell carcinoma of the esophagus.

§ Site definition includes age ≥ 20 years.

vegetable intake.[28] Patients with primary squamous cell carcinomas of the esophagus have a large excess risk for subsequent cancers of the oral cavity and pharynx, and of the larynx. Although HPV infection is the primary cause of cancer of the uterine cervix, increased risks of cervical cancer among smokers have been observed in many studies. HPV infection likely explains elevated risks of some anogenital cancers following oral and pharyngeal cancers and reciprocal excesses of oral cancer following cancers of the anus, cervix, vulva, and penis (data not shown).[25]

Patients with primary cancers of the bladder have a very high (>10-fold) excess risk of developing subsequent cancers of the renal pelvis and ureter with reciprocally elevated large excess risks of bladder cancer among patients with primary cancer of the renal pelvis and ureter (Table 4). Although transitional cell carcinomas of the bladder and

Table 5.Observed-to-Expected Ratio for Developing Subsequent Primary Cancer after Hodgkin and Non-Hodgkin Lymphoma by Age at Diagnosis of First Primary, SEER 1973-2005

Hodgkin lymphoma

Second primary site	Birth to 19 (N=3,026)	20 to 39 (N=10,272)	40-59 (N=4,365)	60 and older (N=3,352)	All ages (N=21,015)	Observed number	Expected number	EAR
Lung & bronchus	10.16*	5.07*	3.47*	1.78*	3.03*	365	120	11.34
Female breast	17.00*	2.99*	1.36*	1.04	2.50*	307	123	8.54
Non-Hodgkin lymphoma	7.49*	6.54*	6.83*	3.78*	5.86*	225	38	8.66
ANLL	31.86*	19.86*	18.16*	6.57*	15.24*	121	8	5.24
All subsequent cancers†	7.80*	2.87*	2.11*	1.28*	2.20*	2,013	917	50.85

Non-Hodgkin lymphoma

Second primary site	Birth to 19 (N=2,236)	20 to 39 (N=9,683)	40-59 (N=27,862)	60 and older (N=54,641)	All ages (N=94,422)	Observed number	Expected number	EAR
Lung & bronchus	–	2.37*	1.59*	1.18*	1.30*	1,449	1,115	6.52
Hodgkin lymphoma	4.13	5.65*	7.94*	3.85*	5.35*	99	18	1.57
ANLL	23.94*	12.13*	5.51*	2.38*	3.34*	212	63	2.90
Melanoma	2.08	1.61	1.42*	1.42*	1.44*	293	204	1.74
Kaposi sarcoma	–	15.31*	16.89*	2.34*	11.25*	119	11	2.12
All subsequent cancers†	4.55*	2.14*	1.34*	1.05*	1.16*	8,408	7,262	22.42

Note: Excludes the first 2 months after initial cancer diagnosis. Site definitions are based on Appendix 2a and 2b from Curtis RE, Freeman DM, Ron E, et al., (eds.) *New malignancies among cancer survivors: SEER cancer registries, 1973-2000*. Bethesda, MD: National Cancer Institute, NIH Publ. No. 05-5302; 2006.

EAR = excess absoute risk per 10,000 person years at risk (PYAR); ANLL = acute non-lymphocytic leukemia.

* $p<0.05$

† All subsequent cancers excludes non-melanoma skin cancer.

renal pelvis and ureter are known to be strongly related to tobacco smoking, a more modest (1.6 to 2.8-fold) excess risk is observed for subsequent lung cancers among survivors of cancers of the bladder and renal pelvis and ureter.

Primary prevention (tobacco avoidance) and tobacco cessation in smokers is the main strategy to reduce the burden of primary and secondary cancers related to tobacco. The high rates of subsequent primary cancers among patients who have been treated for head and neck and lung cancers led to attempts at chemoprevention. For example, several clinical trials have involved high doses of vitamin A in response to an earlier clinical trial that found that high doses of 13-cis-retinoic acid (vitamin A) were effective in reversing oral premalignant lesions (leukoplakia).[29] A subsequent phase II clinical trial in which patients were treated with 13-cis-retinoic acid, interferon alpha and alpha-tocopherol, and alpha had promising results but the phase III randomized trial was canceled because of persistent low recruitment.[30] An NCI trial of supplementation with high doses of vitamin A to prevent recurrence and second cancers among patients with early stage non-small cell lung cancer found no evidence of benefit in the population overall, but did find potential benefit for the subgroup of patients who were nonsmokers. Other chemopreventive agents have been tested with little or no evidence of benefit, but this remains an active area of research.[31]

Medical surveillance recommendations for lung cancer survivors focus on detection of recurrence and second primary lung cancers and include imaging studies (chest x-ray or CT) every 4-6 months in the first 2 years following diagnosis and then annually.[32] Surveillance for recurrence and subsequent primary tumors after primary tumors of the head and neck generally includes clinical examination, flexible fiberoptic nasopharyngeal endoscopy, and chest x-ray. [33]

Lymphomas

Lymphomas represent a family of tumors that arise from cells that are found in lymph nodes and other lymphoid tissues. There are many different forms of lymphoma that have different levels of aggressiveness and different treatments. Lymphomas are broadly classified as Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL) based on the appearance of a specific cancer cell type called the Reed-Sternberg cell found in HL. Subsequent cancers among survivors of HL have been well-studied because of the high survival rate for the disease, the relatively young age at diagnosis, and the resultant long life expectancy. HL was also one of the earliest cancers for which effective treatments with radiotherapy and chemotherapy were developed. As a result, the 5-year relative survival rate increased from 74 % in 1975-1977 to 86% in 1996-2004. The SEER study found an O/E of 2.20 for all subsequent cancers among patients treated for HL (Table 5).[34] Survivors of HL had a substantially increased risk of lung cancer (O/E=3.03), which has been related in a dose-dependent fashion to both chemotherapy and radiation therapy. The risk of lung cancer was higher among HL survivors who smoked, compared to those who did not smoke. Substantially elevated relative and absolute risks were also observed among HL survivors for subsequent cancers of the female breast, non-Hodgkin lymphoma, and acute non-lymphocytic leukemia (Table 5). The risk of breast cancer among women treated with radiotherapy for HL increases with higher radiation doses to the breast, and occurs primarily among women treated for HL as young adults. Females ages 10 to 30 years who have been treated for HL with radiation therapy to the chest are included in high-risk groups for whom the American Cancer Society recommends MRI screening as an adjunct to mammography for breast cancer screening.[20] The increased risk of breast cancer among HL survivors treated with radiation therapy is moderated among women who also received alkylating agent chemotherapy, likely the result of treatment-related ovarian failure. The high O/E for acute non-lymphocytic leukemia (ANLL) (O/E=15.24) among HL survivors was first observed among patients treated in the 1970s and is thought to be related to the alkylating agent chemotherapy regimens used at the time.[34] An increased risk for NHL is also observed among HL survivors (Table 5); it is not known whether the increased risk is associated with therapy or other factors.[35]

NHL represents a broader range of diseases than HL. Risk factors and treatments for NHL can differ substantially, and the relative risk for subsequent cancers also depends on the specific type of NHL and the treatment used. As a group, survivors of NHL also have an increased O/E for developing subsequent cancers, but this risk is lower than for HL survivors (O/E=1.16). NHL survivors as a group also have increased risk for Kaposi sarcoma (O/E=11.25), HL (O/E=5.35), ANLL (O/E=3.34), melanoma (O/E=1.44), and cancer of the lung and bronchus (O/E=1.30). Some forms of NHL are increased in patients who are infected with HIV, and HIV also increases risk of Kaposi sarcoma.[34]

Melanoma

Ultraviolet radiation from the sun is associated with several types of skin cancer, including malignant melanoma. Although the incidence of basal and squamous cell skin cancer is not tracked by cancer registries in the US, many patients develop multiple skin cancers, commonly in sun-exposed areas. In the SEER study, the O/E for subsequent primary cancer among multiple melanoma survivors was 1.26, due primarily to excess risk of subsequent melanomas (O/E=8.63).[36] About 10% of patients who had a subsequent melanoma had 3 or more primary melanomas. In addition to ultraviolet radiation exposure, host susceptibility factors likely account for the increased risk of subsequent melanomas. The risk of multiple primary melanomas is greater among patients with a family history of melanoma or atypical moles. It is recommended that patients who have been treated for a malignant melanoma receive lifelong annual dermatologic follow-up and perform self-examinations. More intensive dermatologic surveillance may be recommended for patients who have had multiple melanomas, positive family history, or a history of atypical moles.[37]

Childhood cancer

Progress in treatment of childhood cancer has produced increasing numbers of childhood cancer survivors who are living into adulthood. Currently, more than 80% of children and adolescents with cancer survive 5 or more years after diagnosis. Unfortunately, the childhood cancer experience predisposes long-term survivors to a variety of long-term health problems, including increased risk of subsequent primary cancers.[38]

The SEER study found an O/E of 5.58 for subsequent cancer among childhood cancer survivors diagnosed at age 0 to 17 years (Table 6).[12] The highest O/Es were observed among patients initially diagnosed with Hodgkin lymphoma (O/E=9.21), primitive neuroectodermal tumors of the brain and central nervous system (O/E= 13.54),

Table 6. Observed-to-Expected Ratio for Subsequent Primary Cancer (All Sites Combined) Following Childhood Cancer (Aged 0-17 Years) by Type of First Cancer, SEER 1973-2005

First Primary Cancer	Male and female			Male			Female		
	Observed	O/E	EAR	Observed	O/E	EAR	Observed	O/E	EAR
All Cancers	**587**	**5.58***	**17**	**266**	**5.62***	**15**	**321**	**5.55***	**19**
Leukemia	84	4.64*	9	39	4.18*	8	45	5.12*	11
Acute lymphocytic	65	4.39*	9	32	4.09*	8	33	4.73*	10
Acute non-lymphocytic	10	5.34*	13	3	3.88	7	7	6.36*	17
Hodgkin lymphoma	149	9.21*	47	42	6.22*	24	107	11.36*	72
Non-Hodgkin lymphoma	25	5.49*	17	17	5.80*	17	8	4.92*	16
Brain & CNS	98	6.19*	17	60	7.65*	20	38	4.75*	14
Ependymoma	7	7.63*	18	6	12.69*	28	1	2.25	4
Astrocytoma	39	3.90*	10	25	5.12*	13	14	2.74*	7
PNET, brain & CNS	29	13.54*	34	17	15.09*	33	12	11.83*	34
Neuroblastoma	15	4.63*	8	6	3.64*	5	9	5.65*	10
Retinoblastoma	27	14.89*	28	15	17.16*	32	12	12.78*	24
Wilms tumor	21	5.20*	10	11	6.19*	11	10	4.42*	8
Bone & joints	44	7.16*	27	17	6.25*	20	27	7.89*	36
Osteosarcoma	23	6.30*	25	9	5.96*	19	14	6.54*	31
Ewing sarcoma	19	11.03*	39	8	9.62*	31	11	12.34*	49
Soft-tissue incl. heart	41	4.85*	15	17	4.23*	11	24	5.41*	20
Rhabdomyosarcoma	18	6.73*	18	9	5.97*	14	9	7.73*	23
Fibrosarcoma†	10	3.37*	11	2	1.6	2	8	4.65*	18
Other soft-tissue	13	4.70*	17	6	4.81*	15	7	4.62*	19
Germ-cell tumors	25	3.21*	10	14	4.16*	13	11	2.49*	8
Carcinomas/epithelial‡	41	2.64*	10	19	4.61*	18	22	1.93*	6
Other Codes§	20	5.52*	14	12	5.87*	14	8	5.06*	15

First primary cancer categorized using the International Classification of Childhood Cancer; O/E=observed to expected ratio; EAR= excess absoute risk per 10,000; CNS=central nervous system; PNET=primitive neuroectodermal tumor.

* p<0.05

† Also includes neurofibrosarcoma.

‡ Includes adrenocortical carcinoma, thyroid carcinoma, nasopharyngeal carcinoma, malignant melanoma, skin carcinoma other than melanoma, and other or unspecified carcinoma.

§ Includes Burkitt lymphoma, unspecified lymphoma, miscellaneous lymphoreticular cancers, other tumors of sympathetic nervous system, non-CNS PNET, renal carcinoma, hepatoblastoma, hepatic carcinoma, and other or unspecified cancers.

retinoblastoma (O/E=14.89), and Ewing sarcoma (O/E=11.03) (Table 6). Survivors of acute lymphocytic leukemia, the most common cancer in childhood, had a O/E of 4.39; most of this excess is due to subsequent cancers of the salivary glands, brain/central nervous system, bone, and thyroid gland. Cranial radiation given to prevent or treat CNS involvement may be associated with these excesses.[39] The most common types of second cancers occurring among childhood cancer survivors are cancers of the female breast, brain/central nervous system, bone, thyroid gland and soft tissue, as well as melanoma and acute non-lymphocytic leukemia (ANLL).[39] Secondary ANLL commonly develops in association with alkylating agent or topoisomerase II therapy; radiation exposure has also been linked to secondary leukemias, but risks are much lower. Radiation therapy contributes to excess risks for the solid tumors; data on the influence of chemotherapy as a contributor to subsequent solid tumors are more limited. Treatment for these tumors has been modified over the years to maximize efficacy and to minimize long-term risks, including secondary cancer. Secondary breast cancer is most strongly associated with radiation therapy to the chest for women treated between the ages of 10 and 30 years. Breast cancer incidence rates among women with such exposure starts to rise about 8 years after radiation treatment and continues to be elevated for more than 25 years. American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography recommend annual MRI screening for women who received radiation therapy to the chest between the

ages of 10 and 30 years. For most women at high risk, the guidelines recommend screening with MRI and mammography beginning at age 30 and continuing for as long as the woman is in good health.[20]

Follow-up care for survivors of childhood cancers includes surveillance for recurrence of the original cancer or the development of a new cancer, assessing psychosocial needs, monitoring growth and maturation, counseling regarding preventive health, and testing for specific risk factors and late effects. The Children's Oncology (COG) group has published "Long Term Follow-up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers," which provides detailed information on late effects associated with childhood cancer and its treatment, identifies those at highest risk, and makes specific recommendations for periodic evaluations and health counseling. Since some late effects may not become apparent until adolescence or adulthood, models are available for coordinating care as the child transitions from active treatment and monitoring to longer-term follow-up, young adulthood, and adulthood. Some of the elements of survivorship plans developed in the context of childhood cancer may also be of value for adult patients.

Treatment Summaries and Survivorship Care Plans

It is important that patients diagnosed with cancer have information about their diagnosis, details of their treatment, and a recommended follow-up plan.[40] This plan should include information about recommended cancer screening, surveillance for recurrence, the schedule on which tests and examinations should be performed, information about possible late- and long-term effects of treatment and their symptoms, and possible signs of recurrence and second tumors. In addition to recommendations that are specific to their primary cancer, age at initial diagnosis, and potential risks related to treatment, it is important that cancer survivors follow the recommendations for cancer prevention and early detection in the general population, including tobacco avoidance or cessation, physical activity, nutrition and diet, healthy weight, and recommendations for cancer screening. [41]

American Cancer Society

Intramural Research

As noted previously, the number of people with a personal history of cancer living in the US has continued to rise, and is expected to double by the year 2030 to more than 20 million.[42] In response to the need to identify the quality-of-life concerns of this growing population, the American Cancer Society's intramural Behavioral Research Center designed and implemented a program of research known collectively as the Studies of Cancer Survivors (SCS).[43] The SCS are two large-scale, population-based, national studies of cancer survivors' quality of life: SCS-I and SCS-II. SCS-I enrolled more than 6,000 1-year survivors of 10 common cancers and is following this group for up to 10 years. In order to learn about the experience of longer-term survivors, SCS-II enrolled approximately 10,000 cancer survivors at either 3, 6, or 11 years following diagnosis. Because health behaviors impact the risk for subsequent cancers, one focus of research is lifestyle choices and behavior changes among survivors after their cancer diagnosis. One SCS-II study found that survivors demonstrated good compliance with the American Cancer Society recommendation to avoid tobacco products (82.6%–91.6%), but showed relatively poor compliance with the guidelines in the areas of physical activity (29.6%–47.3%) and consumption of fruits and vegetables (14.8%–19.1%).[44] Greater compliance with the recommendations was associated with a better quality of life among the survivors in this study. Future analyses planned for the SCS data include investigations of the prevalence, predictors, and impact of fear of cancer recurrence and patterns in the use of complementary and alternative medicine.

Extramural Research

The American Cancer Society's extramural grants program has supported research related to multiple primary cancers at various academic institutions across the country. Focus areas of recent research have included:

- The chemoprevention of secondary cancers in the head and neck
- Reducing the side effects of chemopreventive drugs, such as tamoxifen
- Expanding the knowledge about cancer susceptibility syndromes, such as Li-Fraumeni syndrome and familial adenomatous polyposis (FAP)
- Further understanding the excess cancer risk in childhood cancer survivors

Advocacy

The American Cancer Society Cancer Action Network℠ (ACS CAN), the nonprofit, nonpartisan advocacy affiliate of the American Cancer Society, supports evidence-based

policy and legislative solutions designed to eliminate cancer as a major health problem. ACS CAN has been an active participant in the development and dissemination of several Institute of Medicine reports that make policy and practice recommendations for addressing the barriers to survivorship care planning, coordination of care, and monitoring of late- and/or long-term post-treatment side effects in survivors. The health policy recommendations in these IOM reports form the backbone for federal bills ACS CAN supports through its advocacy work to promote prevention and care planning for patients as well as follow-up care for survivors. ACS CAN works to encourage elected officials and candidates to make cancer a top national priority. ACS CAN gives ordinary people extraordinary power to fight cancer with the training and tools they need to make their voices heard. For more information, visit acscan.org.

Programs

In order to better serve our constituents – particularly newly diagnosed patients and their caregivers, the American Cancer Society offers an integrated network of programs and services through the Cancer Resource Network. The network can provide constituents with information, day-to-day help, and emotional support they need to get well. These programs and services can be accessed through the Society's National Cancer Information Center, Division service centers, the cancer.org Web site, Patient Navigator Program and Cancer Resource Center sites, Employer Initiative, and by health care provider referrals. Using these services, constituents have access to not only the American Cancer Society's programs, but also other national, state, and local resources through the Society's Cancer Resource Connection, a repository of other organizations' programs and services.

The Society's Web site, cancer.org, offers information, online decision-making tools, and other resources to aid in patient care management, and also provides information on the prevention and early detection of cancer, as well as opportunities for community involvement. Staffed by volunteers and patient navigators (trained health professionals), Cancer Resource Centers are located in selected hospitals across the country. These services help the patient and caregiver navigate the various systems and overcome barriers to their care by improving access to information, services, programs, and referral to community resources.

The American Cancer Society's programs assist those touched by cancer – from newly diagnosed, in treatment, and through survivorship – with a wide array of offerings. The Hope Lodge® program can provide people who must travel to their treatment temporary lodging. The Society can also assist those trying to find a clinical trial, or access to health insurance specialists and legal guidance. Help is available with local transportation needs to treatment facilities through the Road to Recovery® program. For those individuals dealing with the physical impact of their treatment, products and services are available that improve appearance and self-esteem through the Look Good...Feel Better® and *"tlc"*™ programs. To assist in addressing the emotional support needs for breast cancer and prostate cancer patients and their family members, Reach to Recovery® and Man to Man® programs, along with the Cancer Survivors Network®, provide peer-to-peer support and education to improve the quality of life in group, individual, face-to-face, phone, or online settings.

Data Sources

The observed-to-expected ratio (O/E) and estimated absolute risk (EAR) are calculated using a cohort study approach in which individuals with a specific first cancer are followed over time to examine the risk of developing a subsequent primary cancer. Person-years-at-risk (PYAR) of developing a subsequent cancer are counted from the date two months after the diagnosis of the first cancer (to exclude multiple primaries diagnosed at the same time) until the date of last known vital status or death, and allocated by age, sex, race, and calendar year. The number of expected cancers is calculated for each PYAR stratum using cancer incidence rates from the referent (SEER) population, and then summed over all strata. The O/E is calculated by dividing the observed number of cancers by the expected number; statistical significance and confidence intervals are calculated using standard methods.[45] The O/E is used to identify increased or decreased risks of developing another cancer. The EAR is obtained by subtracting the expected number of cancer cases from the observed number of cancer cases, dividing by the PYAR, and multiplying by 10,000 to yield the number of excess cancers per 10,000 PYAR. The EAR is a useful measure of the impact of the subsequent cancer in a population of cancer patients. Statistical methods have also been developed to estimate the total number of cancer survivors in the US by primary site and the number who have been diagnosed with more than one cancer.[46]

Certain methodological limitations should be considered when interpreting data on multiple primaries from population-based registries and other population groups. Cancer patients are often under closer medical surveillance than the general population, which could lead to earlier detection of asymptomatic cancers that would not have been clinically evident for several years, or possibly not detected during the patient's lifetime. Apparent reduced risk of subsequent cancers may occur when surgery removes one or more organs from risk (such as removal of the uterus and ovaries for gynecologic cancer) or when multiple primary tumors of the same organ are considered single primaries (such as multiple cancers in the prostate and urinary bladder). Another limitation of studies in geographically defined areas, such as the SEER registries, is that subsequent cancers are not recorded for patients who migrate from their original geographic areas. This leads to under-ascertainment of cancer cases and conservative (negatively biased) estimates of cancer risk, which may be stronger for younger patients and those from more mobile populations.[47]

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Cancer Disparities

An overarching objective of the American Cancer Society's 2015 challenge goals is to eliminate disparities in the cancer burden among different segments of the US population. The causes of health disparities are complex and interrelated, but likely arise from socioeconomic disparities in work, wealth, income, education, housing and overall standard of living; economic and social barriers to high-quality cancer prevention, early detection, and treatment services; and the impact of racial and ethnic discrimination on all of these factors. Recent immigrants may also have other risk factors related to their country of origin, as well as language and cultural barriers. Biologic or inherited differences associated with race are thought to make a minor contribution to the disparate cancer burden between different racial/ethnic groups.

Racial and Ethnic Minorities

African Americans: African Americans are more likely to develop and die from cancer than any other racial or ethnic group. The death rate for cancer among African American males is 36% higher than among white males; for African American females, it is 17% higher than among white females. African Americans have higher incidence and mortality rates than whites for each of the cancer sites listed on page 43 with the exception of cancers of the breast (incidence) and lung (incidence and morality) in women and kidney (mortality) in both men and women.

Hispanics: Hispanics have lower incidence rates for all cancers combined and for most common types of cancer compared to whites, but have higher rates of cancers associated with infection, such as uterine cervix, liver, and stomach. For example, incidence rates of liver cancer are almost twice as high in Hispanic men and women as in whites.

Asian Americans and Pacific Islanders: Similar to Hispanics, Asian Americans and Pacific Islanders have lower incidence rates than whites for the most common cancer sites but have a higher incidence of many of the cancers related to infection. As shown in the table on page 43, they have the highest incidence rates for liver and stomach cancers of all racial and ethnic groups in both men and women, and among the highest death rates for these cancer sites. For more information on cancers related to infection, see *Cancer Facts & Figures 2005* (5008.05), Special Section, available online at cancer.org.

American Indians and Alaska Natives: Mortality rates for kidney cancer in American Indian and Alaska Native men and women are higher than in any other racial or ethnic population. Cancer rates for American Indians and Alaska Natives are based on a linkage of cancer registry data and the Indian Health Service patient database.

In addition to the variation in cancer burden between different racial and ethnic groups, significant disparities exist within subpopulations. For example, among Asian Americans, incidence rates for cervical cancer are almost three times as high in Vietnamese women as in Chinese and Japanese women, partly because the Vietnamese, in general, immigrated more recently, are poorer, and have less access to cervical cancer screening.

Racial and ethnic minorities face many obstacles to receiving health care services related to cancer prevention, early detection, and high-quality treatment. These include low income; inadequate health insurance; geographic, cultural, and language barriers; and racial bias. Poverty influences both the prevalence of underlying risk factors for cancer (such as tobacco use and obesity) and access to health care services. Nearly 1 in 4 (24%) African Americans, and 21% of Hispanics/Latinos live below the poverty line, compared to 10% of whites. Moreover, data from the 2007 National Health Interview Survey indicate that 19% of African Americans and 34% of Hispanics/Latinos were uninsured for at least part of the previous year, while only 14% of whites similarly lacked health insurance. Low-income and uninsured people in particular are more likely to be diagnosed with cancer at later stages of disease, receive substandard clinical care and services, and die from cancer. Consequently, the 5-year relative survival rate for all cancers combined is lower for African Americans (58%) than for whites (68%).

Racial and ethnic minorities tend to receive lower quality health care than whites even when insurance status, income, age, and severity of conditions are comparable. Social inequalities, including racial discrimination, communication barriers, and provider assumptions, can affect interactions between patient and physician and contribute to miscommunication or delivery of substandard care. Opportunities to reduce disparities exist across the entire cancer continuum, from primary prevention to palliative care.

Not all cancer disparities among population groups result from inequities in health care. Cancer risks and rates may also be influenced by cultural and/or inherited factors that decrease or increase risk. For example, in cultures where early marriage is encouraged, women may have

Cancer Incidence and Mortality Rates* by Site, Race, and Ethnicity, US, 2001-2005

Incidence	White	African American	Asian American and Pacific Islander	American Indian and Alaska Native†	Hispanic/ Latino‡§
All sites					
Male	551.4	651.5	354.0	336.6	419.4
Female	423.6	398.9	287.8	296.4	317.8
Breast (female)	130.6	117.5	89.6	75.0	90.1
Colon & rectum					
Male	58.9	71.2	48.0	46.0	47.3
Female	43.2	54.5	35.4	41.2	32.8
Kidney & renal pelvis					
Male	18.8	21.3	9.1	19.5	17.4
Female	9.5	10.1	4.6	12.7	9.6
Liver & bile duct					
Male	8.2	13.2	21.7	14.4	15.0
Female	2.9	4.0	8.3	6.3	5.8
Lung & bronchus					
Male	79.3	107.6	53.9	54.3	44.2
Female	54.9	54.6	28.0	39.7	25.4
Prostate	156.7	248.5	93.8	73.3	138.0
Stomach					
Male	10.0	17.4	18.6	16.8	15.5
Female	4.7	8.9	10.5	7.7	9.5
Uterine cervix	8.2	10.8	8.0	6.9	13.2

Mortality	White	African American	Asian American and Pacific Islander	American Indian and Alaska Native†	Hispanic/ Latino‡¶
All sites					
Male	230.7	313.0	138.8	190.0	159.0
Female	159.2	186.7	95.9	142.0	105.2
Breast (female)	24.4	33.5	12.6	17.1	15.8
Colon & rectum					
Male	22.1	31.8	14.4	20.5	16.5
Female	15.3	22.4	10.2	14.2	10.8
Kidney & renal pelvis					
Male	6.2	6.1	2.4	9.3	5.3
Female	2.8	2.7	1.2	4.3	2.4
Liver & bile duct					
Male	6.7	10.3	15.2	10.6	11.1
Female	2.9	3.9	6.6	6.6	5.1
Lung & bronchus					
Male	71.3	93.1	37.5	50.2	35.1
Female	42.0	39.9	18.5	33.8	14.6
Prostate	24.6	59.4	11.0	21.1	20.6
Stomach					
Male	5.0	11.5	10.1	9.9	8.7
Female	2.5	5.5	5.9	5.2	4.9
Uterine cervix	2.3	4.7	2.2	3.7	3.2

*Per 100,000, age adjusted to the 2000 US standard population. †Data based on Contract Health Service Delivery Areas (CHSDA), 624 counties comprising 54% of the US American Indian/Alaska Native population. ‡Persons of Hispanic/Latino origin may be of any race. §Data unavailable from the Alaska Native Registry and Kentucky. ¶Data unavailable from Minnesota, New Hampshire, and North Dakota.

Source: Ries LAG, Melbert D, Krapcho M, et al. (eds). SEER Cancer Statistics Review, 1975-2005, National Cancer Institute, Bethesda, MD, seer.cancer.gov/csr/1975_2005/, 2008.

American Cancer Society, Surveillance and Health Policy Research, 2009

a lower risk of breast cancer because they begin having children at an earlier age, which decreases breast cancer risk. Higher rates of infection-related cancers in populations that include a large number of recent immigrants may reflect exposure in the country of origin. Individuals who maintain a primarily plant-based diet or do not use tobacco because of cultural or religious beliefs have a lower risk of many cancers. Genetic factors may also explain some differences in cancer incidence. For example, women from population groups with an increased frequency of mutations in the BRCA1 and BRCA2 genes, such as women of Ashkenazi Jewish descent, have an increased risk of breast and ovarian cancer. Genetic factors may also play a role in the elevated risk of prostate cancer among African American men and the incidence of more aggressive forms of breast cancer in African American women.

Socioeconomic Status

Factors associated with socioeconomic status (SES) contribute to substantial differences in cancer incidence and mortality within, as well as among, racial and ethnic groups. For example, cancer mortality rates (all sites combined) among both African American and non-Hispanic white men with 12 or fewer years of education are more than twice those in men with higher levels of education. (See table below.) Similarly, death rates for each of the four major cancer sites are higher in less educated African American and non-Hispanic white men and women than in those with more years of education. Although overall mortality rates for the 4 major cancer sites have decreased in the US since the early 1990s, a recent study reported that these declines have mostly been confined to more highly educated individuals. While colorectal cancer death rates among African American men with 16 or more years of education decreased by 4.8% per year between 1993-2001, rates among African American men with fewer than 12 years of education increased by 2.7% per year during the same time period. No single factor (such as education or income) fully captures all of the important characteristics that may influence the association between socioeconomic status and health, but for most cancers, the risk is inversely related to socioeconomic status, regardless of which measure is used.

Cancer Death Rates* by Educational Attainment, Race, and Sex, US, 2001

	Men		Women	
	African American	Non-Hispanic White	African American	Non-Hispanic White
All sites				
≤12 years of education	214.4	163.8	148.1	128.8
>12 years of education	90.1	73.0	103.3	73.0
RR(95% CI)	2.38 (2.33-2.43)	2.24 (2.23-2.26)	1.43 (1.41-1.46)	1.76 (1.75-1.78)
Lung				
≤12 years of education	73.2	61.0	30.8	37.1
>12 years of education	25.8	18.1	17.9	14.2
RR (95% CI)	2.84 (2.69-3.00)	3.36 (3.30-3.43)	1.72 (1.61-1.84)	2.6 (2.53-2.67)
Colorectal				
≤12 years of education	20.6	14.2	14.1	9.4
>12 years of education	11.3	7.9	10.8	5.4
RR (95% CI)	1.81 (1.63-2.02)	1.81 (1.73-1.89)	1.31 (1.18-1.45)	1.72 (1.63-1.82)
Prostate				
≤12 years of education	10.5	3.3	—	—
>12 years of education	4.8	2.2	—	—
RR (95% CI)	2.17 (1.82-2.58)	1.47 (1.34-1.62)	—	—
Breast				
≤12 years of education	—	—	36.1	25.2
>12 years of education	—	—	31.1	18.5
RR (95% CI)	—	—	1.16 (1.10-1.22)	1.36 (1.32-1.40)

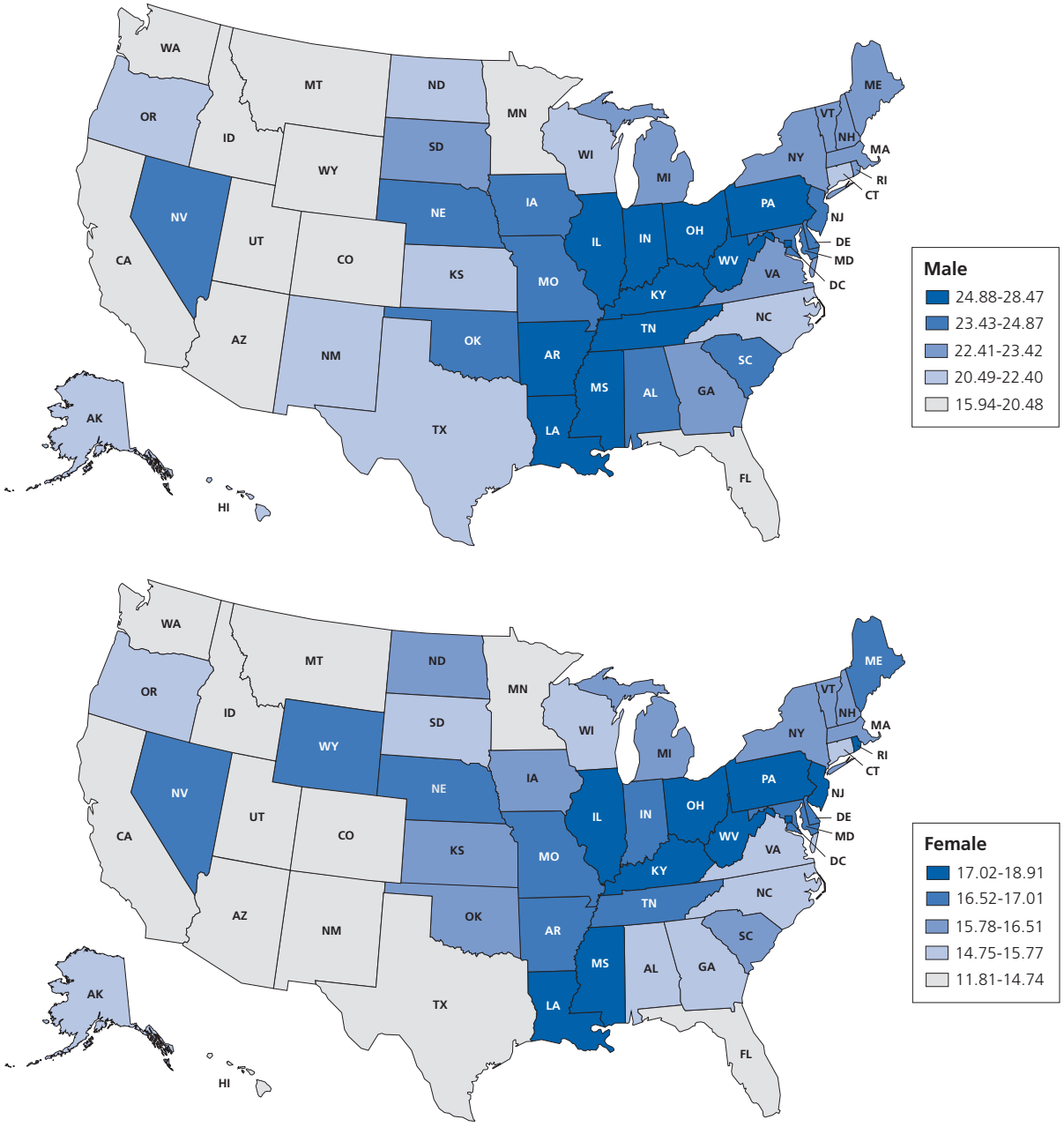
*Rates are for individuals 25-64 years at death, per 100,000, and age-adjusted to the 2000 US standard population.

RR=relative risk; CI=confidence interval; NA=not applicable.

Source: Albano JD, Ward E, Jemal A, et al. Cancer Mortality in the United States by Education Level and Race. JNCI.2007;99:1-11.

American Cancer Society, Surveillance and Health Policy Research, 2009

Geographic Patterns in Colorectal Cancer Death Rates*by State, US, 2001-2005



*Per 100,000, age adjusted to the 2000 US standard population.

Source: Surveillance, Epidemiology, and End Results (SEER) Program (seer.cancer.gov) SEER*Stat Database: Mortality – All COD, Aggregated With State, Total US (1990-2005) <Katrina/Rita Population Adjustment>, National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2008. Underlying mortality data provided by NCHS (cdc.gov/nchs).

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Socioeconomic status is highly correlated with cancer risk and outcomes across the continuum from prevention to palliative care. Persons with lower status are more likely to engage in behaviors that increase cancer risk, such as tobacco use, physical inactivity, and poor diet, in part because of marketing strategies that target these populations and in part because of environmental or community factors that provide fewer opportunities for physical activity and less access to fresh fruits and vegetables. Lower socioeconomic status is also associated

with financial, structural, and personal barriers to health care, including lack of or inadequate health insurance, reduced access to recommended preventive care and treatment services, and lower literacy rates. Individuals with no health insurance and those with Medicaid insurance are more likely to be diagnosed with advanced cancer. The later stage at diagnosis for Medicaid-insured patients likely results in part from retroactive enrollment of uninsured patients after diagnosis. For more information about the relationship between health insurance and cancer, please see *Cancer Facts & Figures 2008* (5008.08), Special Section, available online at cancer.org.

Geographic Variability

Cancer rates in the US vary widely by geographic area. The figure on page 45 depicts geographic variability in colorectal cancer mortality by state and sex in the US. Among men, there is a 1.8-fold difference between those states with the highest and lowest colorectal cancer death rates; among women the difference is 1.6-fold. These differences may be related to differences in major risk factors and access to screening and high-quality treatment, which may be affected by state legislative policies. Geographic variations may also reflect differences in population demographics.

For more information about cancer disparities, please see *Cancer Facts & Figures 2004* (5008.04), Special Section, available online at cancer.org.

Public Policy

While the causes of cancer disparities are multifaceted, several policy initiatives seek to reduce these disparities. The National Breast and Cervical Cancer Early Detection Program (NBCCEDP), run by the Centers for Disease Control and Prevention (CDC), provides low-income, uninsured women with community-based breast and cervical cancer screening services. Medical assistance and treatment for women diagnosed with cancer through the NBCCEDP are available through Medicaid. The American Cancer Society and its nonprofit, nonpartisan advocacy affiliate, the American Cancer Society Cancer Action Network℠ (ACS CAN), work to maintain and increase funding for this program.

Similarly, ACS CAN supports legislation to create a colorectal cancer screening and treatment program at the CDC that will provide medically underserved communities with access to lifesaving screenings for colorectal cancer. The program will focus on low-income, uninsured men and women, as well as those at highest risk, such as African Americans, who are more likely to die of colorectal cancer than any other racial or ethnic group. Efforts also continue to secure funding for the patient navigator demonstration program to help patients navigate through the health care system, from screening to diagnosis and treatment, with culturally and linguistically competent providers and advocates. Legislation for this program was approved in 2005 and received $2.95 million in funding in 2008; the first round of grants was awarded in September 2008. Efforts continue to secure additional funding needed to implement this important program in communities across the country.

Finally, ACS CAN seeks increased funding for the National Center on Minority Health and Health Disparities (NCMHD) at the National Institutes of Health, along with the Disparities Center at the National Cancer Institute. The NCMHD is leading efforts to determine the causes and extent of cancer and other health disparities and is developing effective interventions to reduce these disparities, as well as exploring methods to facilitate delivery of those interventions. The American Cancer Society is committed to ensuring that all individuals have access to preventive cancer screenings and treatment. Barriers that limit access to preventive services and early detection cause cancer to be diagnosed at later stages, when the options for treatment and odds of survival are decreased.

Tobacco Use

*S*moking-related diseases remain the world's most preventable cause of death. Since the first US Surgeon General's report on smoking and health in 1964, there have been more than 12 million premature deaths attributable to smoking in the US.[1] The World Health Organization estimates that there are 5.4 million smoking-related premature deaths worldwide each year. The number of smoking-attributable deaths is almost evenly divided between industrialized and developing nations, and is greater in men (80%) than in women. More men die from smoking in developing nations than in industrialized nations.[2, 3]

Health Consequences of Smoking

Half of all those who continue to smoke will die from smoking-related diseases.[4] In the US, tobacco use is responsible for nearly 1 in 5 deaths; this equaled an estimated 443,600 premature deaths each year between 2000-2004.[5, 6] In addition, an estimated 8.6 million people suffer from chronic conditions related to smoking, such as chronic bronchitis, emphysema, and cardiovascular diseases.[7]

- Smoking accounts for at least 30% of all cancer deaths and 87% of lung cancer deaths.[8, 9]
- The risk of developing lung cancer is about 23 times higher in male smokers and 13 times higher in female smokers compared to lifelong nonsmokers.[1]
- Smoking is associated with increased risk of at least 15 types of cancer: nasopharynx, nasal cavity and paranasal sinuses, lip, oral cavity, pharynx, larynx, lung, esophagus, pancreas, uterine cervix, kidney, bladder, stomach, and acute myeloid leukemia.[1]
- Smoking is a major cause of heart disease, cerebrovascular disease, chronic bronchitis, and emphysema, and is associated with gastric ulcers.[1, 9]
- The risk of lung cancer is just as high in smokers of "light" or "low-tar" yield cigarettes as in those who smoke "regular" or "full-flavored" products.[10]

Reducing Tobacco Use and Exposure

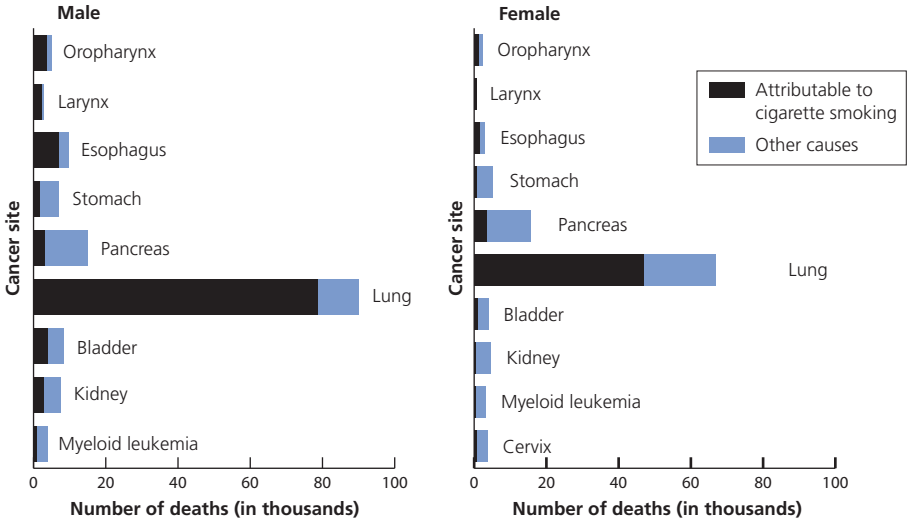
A recent US Surgeon General's report outlined the goals and components of comprehensive statewide tobacco control programs.[11] These programs seek to prevent the initiation of tobacco use among youth; promote quitting at all ages; eliminate nonsmokers' exposure to secondhand smoke; and identify and eliminate the disparities related to tobacco use and its effects among different population groups.[12] The Centers for Disease Control and Prevention (CDC) recommends funding levels for comprehensive tobacco use prevention and cessation programs for all 50 states and the District of Columbia. In 2009, 9 states allocated 50% or more of CDC recommended funding levels for tobacco control programs.[13] States that have invested in comprehensive tobacco control programs, such as California, Massachusetts, and Florida, have reduced smoking rates and saved millions of dollars in tobacco-related health care costs.[11, 14] For more information about tobacco control, please see the American Cancer Society's *Cancer Prevention & Early Detection Facts & Figures 2008*, available online at http://cancer.org/downloads/STT/CPED_2008.pdf.

Trends in Smoking

- Between 1965 and 2004, cigarette smoking among adults aged 18 and older declined by half from 42% to 21%; rates declined to 20% in 2007. An estimated 43.4 million Americans currently smoke cigarettes.[15, 16]
- Although cigarette smoking became prevalent among men before women, the gender gap narrowed in the mid-1980s and has since remained constant.[17] As of 2007, there was a 3% absolute difference in smoking prevalence between white men (23%) and women (20%), and a 9% difference between African American men (25%) and women (16%).[16]
- Smoking is most common among the least educated. While the percentage of smokers has decreased at every level of educational attainment since 1983, college graduates had the greatest decline, from 21% to 6% in 2007. By contrast, among those with a high school diploma, prevalence decreased modestly from 34% to 24% during the same time period. [15, 16]
- Annual cigarette consumption among US adults continues to decline, peaking in 1963 at 4,345 cigarettes per capita and decreasing to an estimated 1,691 in 2006 – a net reduction of 61%.[18, 19]
- Although cigarette smoking among US high school students increased significantly from 1991 to 1997 (28% to 36%), the rate declined to 20% by 2007.[20, 21]

- In 1997, nearly one-half (48%) of male high school students and more than one-third (36%) of female students reported using some form of tobacco – cigarettes, cigars, or smokeless tobacco – in the past month. The percentages declined to 30% for male students and to 21% for female students in 2007.[20, 22]

Annual Number of Cancer Deaths Attributable to Smoking by Sex and Site, US, 2000-2004



Source: Centers for Disease Control and Prevention. Smoking-attributable mortality, years of potential life lost, and productivity losses – United States, 2000-2004. *MMWR Morb Mortal Wkly Rep*. 2008;57(45):1226-1228.

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Smokeless Tobacco Products

Smokeless tobacco products include moist snuff, chewing tobacco, snus (a "spitless," low-nitrosamine, moist powder tobacco pouch), and a variety of other tobacco-containing products that are not smoked. Tobacco companies are actively promoting these products both for use in settings where smoking is prohibited and as a way to quit smoking; however, there is no evidence that these products are as effective as proven cessation therapies. Use of any smokeless tobacco product, including snus, is not considered a safe substitute for quitting. These products cause oral and pancreatic cancers, precancerous lesions of the mouth, gum recession, bone loss around the teeth, and tooth staining; they can also lead to nicotine addiction.[23]

- Smokers who use smokeless products as a supplemental source of nicotine to postpone or avoid quitting will increase rather than decrease their risk of lung cancer.
- The risk of cancer of the cheek and gums increases up to 50-fold among long-term snuff users.[23]
- According to the US Department of Agriculture, manufactured output of moist snuff has increased more than 83% in the past two decades, from 48 million pounds in 1991 to an estimated 88 million pounds in 2007.[18, 19]
- When smokeless tobacco was aggressively marketed in the US in the 1970s, use of these products increased among adolescent males, not among older smokers trying to quit.[25-27] Nationwide, 13% of male high school students were currently using chewing tobacco, snuff, or dip in 2007.[20]

Cigars

Cigar smoking has health consequences similar to those of cigarette smoking and smokeless tobacco.[28]

- Regular cigar smoking is associated with an increased risk of cancers of the lung, oral cavity, larynx, esophagus, and probably pancreas. Cigar smokers have 4 to 10 times the risk of dying from laryngeal, oral, or esophageal cancer compared to nonsmokers.[28]
- The consumption of large cigars and cigarillos increased by an estimated 124% from 1993-2007.[19, 29] An estimated 4.8 billion large cigars and cigarillos were consumed in 2007.[19] Manufactured output of small cigars increased from 1.5 billion cigars in 1997 to an estimated 5.9 billion in 2007.[19]
- In 2006, 6% of adults aged 18 and older had smoked cigars in the past month. American Indian/Alaska Natives (8%) and African Americans (8%) had the highest prevalence of past month cigar use, followed by, whites (6%), Hispanics (5%), and Asians (1%).[30]
- Smoking initiation among adolescents often begins with experimentation with cigars. In 2007, 14% of US high school students had smoked cigars, cigarillos, or little cigars at least once in the past 30 days.[20]

Smoking Cessation

In 1990, the US Surgeon General outlined the benefits of smoking cessation:[32]

- People who quit, regardless of age, live longer than people who continue to smoke.
- Smokers who quit before age 50 cut their risk of dying in the next 15 years in half, compared to those who continue to smoke.
- Quitting smoking substantially decreases the risk of lung, laryngeal, esophageal, oral, pancreatic, bladder, and cervical cancers.
- Quitting lowers the risk for other major diseases, including heart disease and stroke.

Among adults aged 18 and older in 2007, national or state data showed:[16, 33]

- An estimated 47.3 million adults were former smokers, representing 52% of persons who ever smoked.
- Among those who smoked, an estimated 13.4 million (or 40%) had stopped smoking at least one day during the preceding 12 months because they were trying to quit.[16]
- In 43 states the majority of adults (50% or more) who ever smoked have now quit smoking.[34]
- In 2007, among high school students who were current cigarette smokers, national data showed that one-half (49.7%) had tried to quit smoking cigarettes during the 12 months preceding the survey; female students (55.1%) were more likely to have made a quit attempt than male students (45.1%).[20]

Secondhand Smoke

Secondhand smoke (SHS) contains numerous human carcinogens for which there is no safe level of exposure. It is estimated that more than 126 million nonsmoking Americans are exposed to SHS in homes, vehicles, workplaces, and public places.[35] Numerous scientific consensus groups have reviewed data on the health effects of SHS.[35-40] In 2006, the US Surgeon General published a comprehensive report titled *The Health Consequences of Involuntary Exposure to Tobacco Smoke*.[35] Public policies to protect people from SHS are based on the following detrimental effects:

- SHS contains more than 4,000 substances, more than 50 of which are known or suspected to cause cancer in humans and animals, and many of which are strong irritants.[37]
- Each year, about 3,400 nonsmoking adults die of lung cancer as a result of breathing SHS.[6]
- SHS causes an estimated 46,000 deaths from heart disease in people who are not current smokers.[6]
- SHS may cause coughing, wheezing, chest tightness, and reduced lung function in adult nonsmokers.[35]
- Exposure to SHS causes an estimated 150,000 to 300,000 lower respiratory tract infections (i.e., pneumonia and bronchitis) each year in US infants and children younger than 18 months of age. These infections result in 7,500 to 15,000 hospitalizations annually.[37]
- SHS increases the number and severity of asthma attacks in about 200,000 to 1 million asthmatic children.[37]
- Some studies have reported an association between SHS exposure and breast cancer. The US Surgeon General has designated this evidence suggestive rather than conclusive.[35] In any case, women should be aware that there are many health reasons to avoid exposure to tobacco smoke.

Laws that prohibit smoking in public places and create smoke-free environments are the most effective approach to prevent exposure to and harm from SHS. An additional benefit of smoke-free policies is the modification of smoking behaviors among current smokers. Momentum to regulate public smoking began to increase in 1990 and these laws have become increasingly common and comprehensive. [41]

- Exposure to SHS among nonsmokers, as measured by detectable levels of cotinine (a metabolite of nicotine), declined from 84% in 1988-1994 to 46% in 1999-2004.[42]
- Presently in the US, more than 2,960 municipalities (as of October 2008) have passed smoke-free legislation and 37 states, the District of Columbia, and Puerto Rico have either implemented or enacted statewide smoking bans that prohibit smoking in workplaces and/or restaurants and/or bars.[43]
- Currently, approximately 69% of the US population is covered by a smoke-free policy or provision in workplaces and/or restaurants and/or bars.[43]
- Nationally, coverage of all indoor workers by smoke-free policies increased substantially from 1992-1993 (47%) to 2003 (77%).[44]

- Workplace smoking restrictions vary by occupation: in 2003, 83% of white-collar employees reported working under a smoke-free policy, compared to 75% of service workers, 63% of blue-collar workers, and 72% of food-service workers. [44,]
- In addition to providing protection against harmful exposure to secondhand smoke, there is strong evidence that smoke-free policies decrease the prevalence of both adult and youth smoking.[45]

Worldwide Tobacco Use

While the prevalence of smoking has been slowly declining in the US and many other high-income countries over the past 25 years, smoking prevalence rates have been increasing in many low- and middle-income nations, where about 85% of the world population resides.

- Developing countries consume an increasing proportion of the world's tobacco. By 2010, developing countries are projected to consume 71% of the world's tobacco. About 80% of the projected increase will occur in East Asia, particularly China.[46]
- In 2003, the number of smokers in the world was estimated at about 1.3 billion (more than 1 billion men and 250 million women). This figure is expected to rise to at least 1.7 billion (1.2 billion men and 500 million women) by 2025, with the doubling in the number of female smokers making the greatest contribution to the increase.[2, 47]
- Female smoking prevalence rates have peaked and are decreasing in a handful of economically developed countries, such as Australia, Canada, the United Kingdom, and the US. However, in most countries female smoking rates are still increasing or show no evidence of decline.[48] Female smoking rates in both developing and developed nations are expected to converge at 20%-25% by 2030.[48, 49]
- There are currently estimated to be about 5.4 million smoking-related premature deaths each year worldwide.[2, 3]
- Based on current patterns, smoking-attributable diseases will kill as many as 650 million of the world's 1.3 billion smokers alive today.[50, 51] Deaths from tobacco are projected to decline by 9% between 2002-2030 in high-income countries, but to double from 3.4 million to 6.8 million in low- and middle-income countries in the same time period.[52]
- In a series of surveys among youth aged 13 to 15 years conducted in 117 countries and territories during 2000-2007, 12% of boys and 7% of girls reported smoking cigarettes, and 12% of boys and 8% of girls reported using other tobacco products.[53] In every region of the world, the ratio of male to female smoking among youth was lower than the ratio reported among adults, reflecting a global trend of increased smoking among female youth.[54]

To curtail the tobacco pandemic, the 192 Member States of the World Health Assembly unanimously adopted the first global public health treaty, the Framework Convention on Tobacco Control (FCTC) on May 21, 2003. The treaty was ratified by a requisite of 40 countries on November 30, 2004, and subsequently entered into force as a legally binding accord for all ratifying states on February 27, 2005.[55] The FCTC features specific provisions to control both the global supply and demand for tobacco, including regulation of tobacco product contents, packaging, labeling, advertising, promotion, sponsorship, taxation, smuggling, youth access, exposure to secondhand tobacco smoke, and environmental and agricultural impacts.[56] Parties to the treaty are expected to strengthen national legislation, enact effective tobacco control policies, and cooperate internationally to reduce global tobacco consumption.[57] As of August 2008, 168 countries have signed the FCTC and 157 countries have ratified the treaty.[55]

Costs of Tobacco

The number of people who prematurely die or suffer illness from tobacco use results in substantial health-related economic costs to society. It is estimated that in the US, between 2000-2004, smoking accounted for 3.1 million years of potential life lost in men and 2.0 million years of potential life lost in women. Smoking, on average, reduces life expectancy by approximately 14 years.[6] In addition:

- Between 2000-2004, smoking, on average, resulted in more than $196 billion in annual health-related economic costs, including smoking-attributable medical economic costs and productivity losses.[58]
- Smoking-attributable health care expenditures totaled an estimated $100 billion annually between 2000-2004, up $24 billion from $75.5 billion spent during 1999-2001.[58] In 1998, smoking-related medical costs accounted for 8% of personal health care medical expenditures. This translated to $1,623 in excess medical expenditures per adult smoker in 1999.[6, 59]

- Smoking-attributable productivity losses in the US amounted to $96.8 billion annually during 2000-2004, up about $4.3 billion from the $92.5 billion lost annually during 1999-2001.[6, 58]
- Smoking-attributable costs for newborns were $366 million in 1996, or $704 per maternal smoker.[59]
- For each pack of cigarettes sold in 1999, $3.45 was spent on medical care due to smoking and $3.73 was lost in productivity, for a total cost of $7.18 per pack. [59]

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Nutrition and Physical Activity

Scientific evidence suggests that about one-third of the cancer deaths that occur in the US each year are due to nutritional and physical inactivity factors, including excess weight. For the majority of Americans who do not use tobacco, dietary choices and physical activity are the most important modifiable determinants of cancer risk.

The American Cancer Society reviews and updates its nutrition and physical activity guidelines every 5 years. The Society's most recent guidelines, published in 2006, emphasize the importance of weight control, physical activity, and dietary patterns in reducing cancer risk. Because it is clear that the social environment in which people live, work, play, and go to school is a powerful influence on diet and activity habits, the guidelines include an explicit Recommendation for Community Action to promote the availability of healthy food choices and opportunities for physical activity in schools, workplaces, and communities.

The following recommendations reflect the best nutrition and physical activity evidence available to help Americans reduce their risk not only of cancer, but also of heart disease and diabetes.

Recommendations for Individual Choices

1. Maintain a healthy weight throughout life.

- Balance caloric intake with physical activity.
- Avoid excessive weight gain throughout life.
- Achieve and maintain a healthy weight if currently overweight or obese.

In the US, overweight and obesity contribute to 14%-20% of all cancer-related mortality. Overweight and obesity are clearly associated with increased risk for developing many cancers, including cancers of the breast (in postmenopausal women), colon, endometrium, kidney, and adenocarcinoma of the esophagus. Evidence is highly suggestive that obesity also increases risk for cancers of the pancreas, gallbladder, thyroid, ovary, and cervix, as well as for myeloma, Hodgkin lymphoma, and aggressive prostate cancer. The best way to achieve a healthy body weight is to balance energy intake (food intake) with energy expenditure (metabolism and physical activity). Excess body fat can be reduced by restricting caloric intake and increasing physical activity. Caloric intake can be reduced by decreasing the size of food portions and limiting the intake of high-calorie foods (e.g., those high in fat and refined sugars, such as fried foods, cookies, cakes, candy, ice cream, and soft drinks). Such foods should be replaced with more healthy vegetables and fruits, whole grains, and beans. Although knowledge about the relationship between weight loss and cancer risk is incomplete, weight loss is associated with reduced levels of circulating hormones, some of which are associated with increased cancer risk. Recent studies exploring intentional weight loss suggest that losing weight may reduce the risk of breast cancer. Therefore, individuals who are overweight should be encouraged and supported in their efforts to reduce weight.

Because overweight in youth tends to continue throughout life, efforts to establish healthy body weight patterns should begin in childhood. The increasing prevalence of overweight and obesity in preadolescents and adolescents may increase incidence of cancer in the future.

2. Adopt a physically active lifestyle.

- Adults: Engage in at least 30 minutes of moderate to vigorous physical activity, in addition to usual activities, on 5 or more days of the week. Forty-five to 60 minutes of intentional physical activity is preferable.
- Children and adolescents: Engage in at least 60 minutes per day of moderate to vigorous physical activity at least 5 days per week.

Scientific evidence indicates that physical activity may reduce the risk of certain cancers as well as provide other important health benefits. Regular physical activity contributes to the maintenance of a healthy body weight by balancing caloric intake with energy expenditure. Other mechanisms by which physical activity may help to prevent certain cancers may involve both direct and indirect effects. For colon cancer, physical activity accelerates the movement of food through the intestine, thereby reducing the length of time that the bowel lining is exposed to potential carcinogens. For breast cancer, vigorous physical activity may decrease the exposure of breast tissue to circulating estrogen. Physical activity may also affect cancers of the colon, breast, and other sites by improving energy metabolism and reducing circulating concentrations of insulin and related growth factors. Physical activity helps to prevent type 2 diabetes, which is associated with increased risk of cancers of the colorectum, pancreas, and possibly other sites. The benefits of physical activity go far beyond reducing the risk of cancer. They include reducing the risk of heart disease, high blood pressure, diabetes, osteoporosis, falls, stress, and depression.

3. Consume a healthy diet with an emphasis on plant sources.

- Choose foods and beverages in amounts that help achieve and maintain a healthy weight.
- Eat 5 or more servings of a variety of vegetables and fruits each day.
- Choose whole grains in preference to processed (refined) grains.
- Limit consumption of processed and red meats.

There is strong scientific evidence that healthy dietary patterns, in combination with regular physical activity, are needed to maintain a healthy body weight and to reduce cancer risk. Many epidemiologic studies have shown that populations that eat diets high in vegetables and fruits and low in animal fat, meat, and/or calories have reduced risk of some of the most common cancers. The scientific study of nutrition and cancer is highly complex, and many important questions remain unanswered. It is not presently clear how single nutrients, combinations of nutrients, over-nutrition and energy imbalance, or the amount and distribution of body fat at particular stages of life affect one's risk of specific cancers. Until more is known about the specific components of diet that influence cancer risk, the best advice is to consume wholesome foods following an overall healthy dietary pattern as outlined, with special emphasis placed on controlling total caloric intake to help achieve and maintain a healthy weight.

4. If you drink alcoholic beverages, limit consumption.

People who drink alcohol should limit their intake to no more than two drinks per day for men and one drink per day for women. Alcohol consumption is an established cause of cancers of the mouth, pharynx, larynx, esophagus, liver, and breast. For each of these cancers, risk increases substantially with intake of more than two drinks per day. Regular consumption of even a few drinks per week has been associated with an increased risk of breast cancer in women. The mechanism for how alcohol can affect breast cancer is not known with certainty, but it may be due to alcohol-induced increases in circulating estrogen or other hormones in the blood, reduction of folic acid levels, or a direct effect of alcohol or its metabolites on breast tissue. Alcohol consumption combined with tobacco use increases the risk of cancers of the mouth, larynx, and esophagus far more than either drinking or smoking alone.

The American Cancer Society Recommendation for Community Action

Evidence continues to increase on the influence that social, economic, and cultural factors have on individual choices about diet and physical activity. While many Americans would like to adopt a healthy lifestyle, many encounter substantial barriers that make it difficult to follow diet and activity guidelines. Indeed, current trends toward increasing portion sizes, as well as the consumption of high-calorie convenience foods, beverages, and restaurant meals, and declining levels of physical activity are contributing to increasing rates of obesity seen in the US. Longer workdays and more households with multiple wage earners reduce the amount of time available for preparation of meals, with a resulting shift toward increased consumption of high-calorie food outside the home – frequently less nutritious than foods prepared at home. Large-portion sizes and calorie-dense foods are used extensively in marketing by restaurants, supermarkets, and food companies. Reduced leisure time, increased reliance on automobiles for transportation, and increased availability of electronic entertainment and communications media all contribute to reduced physical activity. Increasing evidence indicates associations between the built environment and obesity and physical activity levels. Poor access to sidewalks, parks, and recreation facilities is associated with greater obesity risk, while neighborhoods that facilitate walking and safe physical recreation have lower obesity prevalence.

To promote changes that address these environmental issues, the Society's nutrition and physical activity guidelines include an explicit Recommendation for Community Action. Public, private, and community organizations should work to create social and physical environments that support the adoption and maintenance of healthy nutrition and physical activity behaviors.

- Increase access to healthy foods in schools, workplaces, and communities.
- Provide safe, enjoyable, and accessible environments for physical activity in schools and for transportation and recreation in communities.

Achieving this recommendation will require multiple strategies and bold action, ranging from the implementation of community and workplace health promotion programs to policies that affect community planning, transportation, school-based physical education, and food services. The tobacco control experience has shown that policy and environmental changes at the national,

state, and local levels are critical to achieving changes in individual behavior. Measures such as clean indoor air laws and increases in cigarette excise taxes are highly effective in deterring tobacco use. To avert an epidemic of obesity-related disease, similar purposeful changes in public policy and in the community environment will be required to help individuals maintain a healthy body weight and remain physically active throughout life.

Environmental Cancer Risks

Two major classes of factors influence the incidence of cancer: hereditary factors and acquired (environmental) factors. Hereditary factors come from our parents and cannot be modified. Environmental factors are potentially modifiable. They include tobacco use, poor nutrition, physical inactivity, obesity, certain infectious agents, certain medical treatments, excessive sun exposure, and exposures to carcinogens (cancer-causing agents) that exist as pollutants in our air, food, water, and soil. Some carcinogens occur naturally and some are created or concentrated by human activity. Radon, for example, is a naturally occurring carcinogen present in soil and rock; however, occupational exposure occurs in underground mines and substantial exposures also occur in poorly ventilated basements in regions where radon soil emissions are high.

Environmental (as opposed to hereditary) factors account for an estimated 75%-80% of cancer cases and deaths in the US. Exposure to carcinogenic agents in occupational, community, and other settings is thought to account for a relatively small percentage of cancer deaths, about 4% from occupational exposures and 2% from environmental pollutants (man-made and naturally occurring). Although the estimated percentage of cancers related to occupational and environmental carcinogens is small compared to the cancer burden from tobacco smoking (30%) and the combination of nutrition, physical activity, and obesity (35%), the relationship between such agents and cancer is important for several reasons.

First, even a small percentage of cancers can represent many deaths: 6% of cancer deaths in the US each year corresponds to approximately 33,700 deaths. Second, the burden of exposure to occupational and environmental carcinogens is borne disproportionately by lower-income workers and communities, contributing to disparities in the cancer burden across the population. Third, although much is known about the relationship between occupational and environmental exposure and cancer, some important research questions remain. These include the role of exposures to certain classes of chemicals (such as hormonally active agents) during critical periods of human development and the potential for pollutants to interact with each other, as well as with genetic and acquired factors.

How Carcinogens Are Identified

The term carcinogen refers to exposures that can increase the incidence of malignant tumors (cancer). The term can apply to a single chemical such as benzene; fibrous minerals such as asbestos; metals and physical agents such as x-rays or ultraviolet light; or exposures linked to specific occupations or industries (e.g., nickel refining). Carcinogens are usually identified on the basis of epidemiological studies or by testing in animals. Studies of occupational groups (cohorts) have played an important role in understanding many chemical carcinogens – as well as radiation – because exposures are often higher among workers, who can be followed for long periods of time. Some information has also come from studies of persons exposed to carcinogens during medical treatments (such as radiation and estrogen), as well as from studies conducted among individuals who experienced large, short-term exposure to a chemical or physical agent due to an accidental or intentional release (such as survivors of the atomic bomb explosions of Hiroshima and Nagasaki).

It is more difficult to study the relationship between exposure to potentially carcinogenic substances and

cancer risk in the general population because of uncertainties about exposure and the challenge of long-term follow-up. Moreover, relying upon epidemiological information to determine cancer risk does not fulfill the public health goal of prevention since, by the time the increased risk is detected, a large number of people may have been exposed. Thus, for the past 40 years, the US and many other countries have developed methods for identifying carcinogens through animal testing using the "gold standard" of a 2-year or lifetime bioassay in rodents. This test is expensive and time-consuming, but it can provide information about potential carcinogens so that human exposure can be reduced or eliminated.

Many substances that are carcinogenic in rodent bioassays have not been adequately studied in humans, usually because an acceptable study population has not been identified. Among the substances that have proven carcinogenic in humans, all have shown positive results in animals when tested in well-conducted 2-year bioassays.[1] Moreover, between 25%-30% of established human carcinogens were first identified through animal bioassays. Since animal tests necessarily use high-dose exposures, human risk assessment usually requires extrapolation of the exposure-response relationship observed in rodent bioassays to predict effects in humans at lower doses. Typically, regulatory agencies in the US and abroad have adopted the default assumption that no threshold level (level below which there is no increase in risk) of exposure exists for carcinogenesis.

Evaluation of Carcinogens

The National Toxicology Program (NTP) plays an important role in the identification and evaluation of carcinogens in the US, and the International Agency for Research on Cancer (IARC) plays a similar role internationally. The National Toxicology Program was established in 1978 to coordinate toxicology testing programs within the federal government, including tests for carcinogenicity.

The NTP is also responsible for producing the Report on Carcinogens, an informational scientific and public health document that identifies agents, substances, mixtures, or exposure circumstances that may increase the risk of developing cancer.[2] For a list of substances listed in the *11th Report on Carcinogens* as known or reasonably anticipated to be human carcinogens, see http://ntp.niehs.nih.gov/ntp/roc/toc11.html.

The IARC is a branch of the World Health Organization that regularly convenes scientific consensus groups to evaluate potential carcinogens. After reviewing published data from laboratory, animal, and human research, these committees reach consensus about whether the evidence should be designated "sufficient," "limited," or "inadequate" to conclude that the substance is a carcinogen. For a list of substances that have been reviewed by the IARC monograph program, visit http://monographs.iarc.fr/ENG/Publications/internrep/07-001.pdf. The American Cancer Society does not have a formal program to review and evaluate carcinogens. However, information on selected topics can be found at cancer.org.

Although the relatively small risks associated with low-level exposure to carcinogens in air, food, or water are difficult to detect in epidemiological studies, scientific and regulatory bodies throughout the world have accepted the principle that it is reasonable and prudent to reduce human exposure to substances shown to be carcinogenic at higher levels of exposure. Although much public concern about the influence of man-made pesticides and industrial chemicals has focused on cancer, pollution may adversely affect the health of humans and ecosystems in many other ways. Research to understand the short- and long-term impact of environmental pollutants on a broad range of outcomes, as well as regulatory actions to reduce exposure to recognized hazards, has contributed to the protection of the public and the preservation of the environment for future generations. It is important that this progress be recognized and sustained.

For more information on environmental cancer risks, see *Cancer Facts & Figures 2007* (5008.07), Special Section, at cancer.org

References

1. Tomatis L, Melnick RL, Haseman J, et al. Alleged "misconceptions" distort perceptions of environmental cancer risks. *FASEBJ*. 2001; 15:195-203.

2. National Toxicology Program *11th Report on Carcinogens*. Research Triangle Park; 2005.

The International Fight against Cancer

The ultimate mission of the American Cancer Society is to eliminate cancer as a major health problem. Because cancer knows no boundaries, this mission extends around the world. Better prevention, early detection, and advances in treatment have helped some developed nations lower incidence and mortality rates for certain cancers, but in most parts of the world, cancer is a growing problem. It is estimated that cancer killed 7.6 million people around the world in 2007, and this figure is expected to rise to 17.5 million by 2050 simply due to the growth and aging of the population.

Today, most cancers are linked to a few controllable factors – tobacco use, poor diet, lack of exercise, and infectious diseases. Tobacco use is the most preventable cause of death worldwide. If current trends in tobacco use continue, 650 million people alive today will eventually die of tobacco-related diseases, including cancers of the lung, esophagus, and bladder. In the developed world, poor diets, inadequate physical activity, and obesity are second only to tobacco as causes of cancer.

Recognizing the growing global burden of cancer, the American Cancer Society has established international efforts that include capacity building, information delivery, and advocacy:

- American Cancer Society University, International Relay For Life®, and National Cancer Planning are three key capacity-building initiatives aimed at developing and strengthening the knowledge, skills, and resources that communities need to achieve their goals in cancer control and prevention.
- The American Cancer Society provides cancer information to millions of individuals throughout the world on its Web site, cancer.org. Information is currently available in English, Spanish, Mandarin, and several other Asian languages.
- Media outreach is conducted in priority regions worldwide and trainings and fellowships are provided for journalists from low- and middle-income countries to help raise awareness about cancer and tobacco control.

The American Cancer Society also advocates for the global fight against cancer through its collaboration with other international, cancer-related organizations around the world. A significant collaborative focus has been placed on global tobacco control through the adoption and implementation of the Framework Convention on Tobacco Control, the world's first public health treaty.

The American Cancer Society seeks to place cancer on the global agenda as a critical health issue through strategic alliances with key partners. Among its collaborators are the International Union Against Cancer; International Network for Cancer Treatment and Research; intergovernmental agencies of the United Nations, such as the World Health Organization; International Agency for Research on Cancer; and International Atomic Energy Agency. Together with these global leaders, the American Cancer Society is expanding its efforts to address the rising cancer burden throughout the world.

For more information on the global cancer burden, see the following publications available available on cancer.org:

- *Global Cancer Facts & Figures 2007*
- *The Cancer Atlas*
- *The Tobacco Atlas*

The American Cancer Society

In 1913, 10 physicians and five laypeople founded the American Society for the Control of Cancer. Its stated purpose was to disseminate knowledge about cancer symptoms, treatment, and prevention; to investigate conditions under which cancer was found; and to compile cancer statistics. Later renamed the American Cancer Society, Inc., the organization now includes more than 3 million volunteers working together to conquer cancer. Since its inception nearly a century ago, the American Cancer Society has made significant contributions to progress against cancer in the US. The Society's work to save lives by helping people stay well, by finding cures, and by fighting back has yielded remarkable strides in cancer prevention, early detection, treatment, and patient quality of life. As a result, overall cancer mortality has steadily declined since the early 1990s, and the 5-year survival rate is now 66%, up from 50% in the 1970s. Today, more than ever, our goal of eliminating cancer as a major public health threat is within reach.

How the American Cancer Society Is Organized

The American Cancer Society consists of a National Home Office with 13 chartered Divisions and a local presence in nearly every community nationwide.

The National Society

A National Assembly of volunteer representatives from each Division approves Division charters and elects a national volunteer Board of Directors. The Board of Directors sets and approves strategic goals for the Society, ensures management accountability, and provides stewardship of donated funds. The National Home Office is responsible for overall planning and coordination of the Society's programs, provides technical support and materials to Divisions and local offices, and administers the Society's research program.

American Cancer Society Divisions

The Society's 13 Divisions are responsible for program delivery and fundraising in their regions. They are governed by Division Boards of Directors composed of both medical and lay volunteers in their regions.

Local offices

More than 3,400 local offices nationwide raise funds at the community level and deliver cancer prevention, early detection, and patient service programs.

Volunteers

More than 3 million volunteers carry out the Society's work in communities across the country. These dedicated people donate their time and talents to further cancer research; educate the public about early detection and prevention; advocate for responsible cancer legislation at the local, state, and federal levels; serve cancer patients and their families; and raise funds for the fight against cancer.

How the American Cancer Society Fights Cancer

The Society has set challenge goals for 2015 to dramatically decrease cancer incidence and mortality rates while increasing the quality of life for all cancer survivors. The Society is uniquely qualified to make a difference in the fight against cancer by continuing its leadership position in supporting high-impact research; improving the quality of life for those affected by cancer; preventing and detecting cancer; and reaching more people, including the medically underserved, with the reliable cancer-related information they need.

Simply stated, the American Cancer Society saves lives by helping people stay well and get well, by finding cures, and by fighting back against cancer.

Stay Well

The American Cancer Society helps everyone stay well by preventing cancer or detecting it early, when it is most treatable.

Prevention

Primary cancer prevention means taking the necessary precautions to prevent the occurrence of cancer. The Society's prevention programs focus on preventing the use of tobacco products; educating individuals, health professionals, and policy-makers about the relationship between weight control, diet, physical activity, and cancer; reducing excessive sun exposure; and encouraging individuals to follow the Society's guidelines for preventive screenings for colorectal and cervical cancers, as well as vaccination against HPV to prevent cervical cancer.

The American Cancer Society collaborates with several national groups to implement comprehensive tobacco control programs. The Society's tobacco control efforts include:

- Reducing tobacco advertising and promotions directed at young people
- Increasing funding to support comprehensive tobacco control programs and tobacco-related research
- Reducing secondhand smoke exposure by supporting clean indoor air laws
- Providing access to cessation programs for people who wish to quit, including a science-based telephone counseling service
- Advocating for increased tobacco taxes to offset the health care costs associated with tobacco use
- Supporting global partnerships to reduce tobacco-related deaths and diseases

For the majority of Americans who do not smoke, the most important ways to reduce cancer risk are to maintain a healthy weight, be physically active on a regular basis, and eat a mostly plant-based diet that limits red and processed meats. The Society publishes *Guidelines on Nutrition and Physical Activity for Cancer Prevention* to review the accumulating scientific evidence on diet and cancer; to synthesize this evidence into clear, informative recommendations for the general public; to promote healthy individual behaviors, as well as environments that support healthy eating and physical activity habits; and, ultimately, to reduce cancer risk. These guidelines form the foundation for the Society's communication, worksite, school, advocacy, and community strategies designed to encourage and support people in making healthy lifestyle behavior changes.

In January 2007, the *American Cancer Society Guideline for Human Papillomavirus (HPV) Vaccine Use to Prevent Cervical Cancer and Its Precursors* was published. Studies show the vaccine has the potential to prevent up to 70% of the more than 11,000 invasive cervical cancers and 3,600 cervical cancer deaths in the US each year. Routine use of the HPV vaccine, coupled with continued screening according to American Cancer Society guidelines, has the potential to greatly reduce the occurrence of cervical cancer.

Early Detection

Finding cancer at its earliest, most treatable stage gives patients the greatest chance of survival. To help the public and health care providers make informed decisions about cancer screening, the American Cancer Society publishes a variety of early detection guidelines. These guidelines are assessed regularly to ensure that recommendations are based on the most current scientific evidence. The Society currently provides screening recommendations for cancers of the breast, cervix, colon and rectum, and endometrium; information and guidance on testing for early prostate cancer detection; and general recommendations for a cancer-related component of a periodic checkup to examine the thyroid, mouth, skin, lymph nodes, testicles, and ovaries.

Throughout its history, the American Cancer Society has implemented a number of aggressive public awareness campaigns targeting the public and health care professionals. Campaigns to increase usage of Pap testing and mammography have contributed to a 70% decrease in cervical cancer incidence rates since the introduction of the Pap test in the 1950s and a steady decline in breast cancer mortality rates since 1990. In the past 5 years, the Society has launched ambitious multimedia campaigns to encourage adults aged 50 and older to get tested for colorectal cancer. The Society also continues to encourage the early detection of breast cancer through public awareness and other efforts targeting poor and underserved communities.

Get Well

For more than 1.4 million cancer patients diagnosed this year and 11 million American cancer survivors, the American Cancer Society Cancer Resource Network is here to help. The Cancer Resource Network consists of free, comprehensive resources, including cancer information, programs, services, and community referrals, that the American Cancer Society offers to help patients, survivors, and caregivers manage their cancer experience and get well.

24-Hour Information from the Cancer Resource Network

The American Cancer Society is available 24 hours a day, seven days a week online at cancer.org and through our call center (1-800-227-2345). Callers are connected with a Cancer Information Specialist, who can help them locate a hospital, understand cancer and treatment options, learn what to expect and how to plan, help address insurance concerns, find financial resources, or find a local support group. We can also help those who speak a language other than English or Spanish find the assistance they need.

Information on every aspect of the cancer experience, from prevention to survivorship, is also available 24 hours a day, seven days a week, through the Society's Web site (cancer.org). The site includes an interactive cancer resource center containing in-depth information on every major cancer type. The Society also publishes a wide variety of pamphlets and books that covers a multitude of topics, from patient education, quality-of-life, and caregiving issues to healthy living. A complete list of Society books is available online at cancer.org/bookstore.

The Society publishes a variety of information sources for health care providers, including three clinical journals: *Cancer*, *Cancer Cytopathology*, and *CA: A Cancer Journal for Clinicians*. More information about free subscriptions and online access to *CA* and *Cancer Cytopathology* articles can be found at cancer.org/journals.

The American Cancer Society also collaborates with numerous community groups, nationwide health organizations, and large employers to deliver health information and encourage Americans to adopt healthy lifestyle habits through the Society's science-based worksite programs.

Treatment

The Society provides comprehensive information about all available cancer treatments 24 hours a day, seven days a week through the Society's National Cancer Information Center (1-800-227-2345) and Web site (cancer.org).

Day-to-day Help from the Cancer Resource Network

Transportation to treatment: The American Cancer Society can help cancer patients and their families find transportation to and from treatment facilities. In some areas, trained American Cancer Society volunteer drivers donate their time to take patients to and from their appointments.

***"tlc" Tender Loving Care*™:** A magazine and catalog in one, *"tlc"* offers helpful articles and a line of products made for women battling cancer to help restore their appearance and dignity with information and one-stop, private shopping for products that address special appearance-related needs, such as wigs, hairpieces, breast forms, bras, hats, turbans, swimwear, and accessories. All proceeds from product sales go back into the American Cancer Society's programs and services for patients and survivors.

Hope Lodge®: For patients whose best hope for a cure may be far from home, this nurturing, home-like environment near major cancer centers provides free housing and support for cancer patients undergoing treatment and their caregivers.

Scholarships: Fighting cancer can be an enormous financial and emotional hardship, especially on young people. In an effort to ease this burden, many American Cancer Society Divisions offer college scholarships to young cancer survivors to help them pursue higher education.

Emotional Support from the Cancer Resource Network

Reach to Recovery®: Breast cancer survivors provide one-on-one support, information, and inspiration to help individuals cope with breast cancer. Volunteer survivors are trained to respond in person or by telephone to individuals facing breast cancer diagnosis, treatment, recurrence, or recovery.

Man to Man®: This community-based education and support program offers individual and group support and information to men with prostate cancer. Man to Man also offers men the opportunity to educate their communities about prostate cancer and to advocate with lawmakers for stronger research and treatment policies.

I Can Cope®: Educational classes for adults with cancer and their loved ones are conducted in a supportive environment by doctors, nurses, social workers, and other health care professionals. Participants gain practical knowledge and skills to help them cope with the challenges of living with cancer.

Children's camps: In some areas, the Society sponsors camps for child cancer survivors. These camps are equipped to handle the special needs of children undergoing treatment and the needs of the cancer survivor.

Look Good...Feel Better®: A collaboration of the American Cancer Society, the Personal Care Products Council Foundation, and the National Cosmetology Association, Look Good…Feel Better is a free service that helps women in active cancer treatment learn beauty techniques to restore their self-image and cope with appearance-related side effects. Certified beauty professionals provide tips on makeup, skin care, nail care, and head coverings. Additional information and materials are available for men and teens.

Cancer Survivors Network℠: Created by and for cancer survivors and their families, this online community offers unique opportunities for people with cancer and their loved ones to find and connect with others like themselves. It's a welcoming, safe place for people to find hope and inspiration from others who have "been there."

Find Cures

The aim of the American Cancer Society's research program is to determine the causes of cancer and to support efforts to prevent, detect, and cure the disease. The Society is the largest source of private, nonprofit cancer research funds in the US, second only to the federal government in total dollars spent. In 2008, the Society spent an estimated $146 million on research and health professional training and has invested approximately $3.3 billion in cancer research since the program began in 1946. The Society's comprehensive research program consists of extramural grants, as well as intramural programs in epidemiology and surveillance research, behavioral research, and statistics and evaluation. Intramural research programs are led by the Society's own staff scientists.

Extramural Grants

The American Cancer Society's extramural grants program supports research in a wide range of cancer-related disciplines at about 230 US medical schools and universities. Grant applications are solicited through a nationwide competition and are subjected to a rigorous external peer review, ensuring that only the most promising research is funded. The Society usually funds investigators early in their research careers, a time when they are less likely to receive funding from the federal government. The Society's priorities focus on needs that are unmet by other funding organizations, such as the current targeted research area of cancer in the poor and medically underserved. To date, 42 Nobel Prize winners have received grant support from the Society early in their careers.

Epidemiology and Surveillance Research

For more than 60 years, the Society's intramural epidemiologic research program has evaluated trends in cancer incidence, mortality, and survival. Through this program, the Society publishes the most current statistics and trend information in *CA: A Cancer Journal for Clinicians* (caonline.amcancersoc.org), as well as a variety of *Cancer Facts & Figures* publications. These publications are the most widely cited sources for cancer statistics and are available in hard copy from Division offices or online through the Society's Web site at cancer.org. Over the years, Society researchers have conducted three large prospective studies to identify factors that cause or prevent cancer:

- Hammond-Horn Study (188,000 men followed from 1952-1955 in 9 states)
- Cancer Prevention Study I (CPS-I, 1 million people followed from 1959-1972 in 25 states)
- Cancer Prevention Study II (CPS-II, an ongoing study of 1.2 million people enrolled in 1982 in 50 states)

More than 400 scientific publications resulting from these studies have identified the contributions of lifestyle (smoking, nutrition, obesity, etc.), family history, illness, medications, and environmental exposures to various cancers. Recruitment into a new Cancer Prevention Study (CPS-3), which includes an ethnically and geographically diverse population of 500,000 adults, began in 2006 and will continue through 2011.

Additional information about the Cancer Prevention Studies, including copies of questionnaires and publication citations, is available at cancer.org.

Since 1998, the Society has collaborated with the National Cancer Institute (NCI), the Centers for Disease Control and Prevention, the National Center for Health Statistics, and the North American Association of Central Cancer Registries to produce the Annual Report to the Nation on the Status of Cancer, a peer-reviewed journal article that reports current information related to cancer rates and trends in the US. More recently, the Society has become involved in a series of studies to identify inherited susceptibility genes and gene-environmental interactions that affect cancer occurrence as part of The Cohort Consortium, an international collaboration of leading cancer research groups formed by NCI. Society scientists also monitor trends in cancer risk factor and screening prevalence and publish these results annually – along with Society recommendations, policy initiatives, and evidence-based programs – in *Cancer Prevention & Early Detection Facts & Figures*.

In addition, in 2007 the Surveillance Research department collaborated with the Department of International Affairs to publish the first edition of *Global Cancer Facts & Figures*, an international companion to *Cancer Facts & Figures*.

Behavioral Research Center

The American Cancer Society was one of the first organizations to recognize the importance of behavioral and psychosocial factors in the prevention and control of cancer and to fund extramural research in this area. In 1995, the Society established the Behavioral Research Center (BRC) as an intramural department. The BRC's research has focused on five aspects of the cancer experience: prevention, detection and screening, treatment, survivorship, and end-of-life issues. It also focuses on special populations, including minorities, the poor, rural populations, and other underserved groups. The BRC's ongoing research projects include:

- An extensive, nationwide longitudinal study of adult cancer survivors to explore physical and psychosocial adjustment, identify factors affecting quality of life (QOL), examine late effects, and assess changes over time and the long-term impacts of cancer.
- A large-scale, nationwide, cross-sectional study of cancer survivors who are two, five, and 10 years from their initial diagnosis and treatment, focusing on QOL and psychosocial functioning. This study provides immediate information on long-term survivors.
- Two studies of family caregivers that explore the impact of the family's involvement in cancer care on the quality of life of the cancer survivor and the caregiver. The first study identifies the prevalence of the family's involvement in cancer care and the unmet needs of caregivers at two and five years after diagnosis; it also examines the impact on the caregiver's quality of life and health behaviors. The second longitudinal study follows cancer patients and their caregivers from the time of diagnosis and examines the behavioral, physical, psychological, and spiritual adjustment of the patients and their family caregivers across various ethnic groups.
- Two studies of underserved populations to help reduce cancer inequalities. One study investigates patient-related, provider-related, and systemic barriers to colorectal cancer screening among patients at federally funded primary care clinics. The other examines how African Americans diagnosed with cancer have reported their symptoms in comparison with how their loved ones interpret and report the symptoms to health care providers.

The BRC is also developing research projects designed to prevent and control tobacco use and research that explores individual and community-level factors affecting health behaviors among diverse cultural, racial, and socioeconomic groups.

Statistics and Evaluation Center

In August 2005, the American Cancer Society inaugurated the Statistics and Evaluation Center (SEC), a shared resource that provides consultation to investigators in the research department, health promotion experts at the National Home Office, and mission delivery staff throughout the Society. The SEC has three main responsibilities: 1) to assist Society researchers in the design, analysis, and preparation of manuscripts for publication in peer-reviewed scientific journals; 2) to function as part of the Society team that evaluates selected mission delivery interventions; and 3) to conduct methods research on cancer-related problems for publication in peer-reviewed journals. The group provides design and analysis support for a number of Society projects, including:

- BRC quality-of-life research
- Optimization testing and deriving best practices by Society online team and e-communications
- Tobacco control and the National Cancer Information Center/Quitline®, including clinical trials design and analysis, operational improvements, and Employer Initiative activities with the Health Promotions department
- Predictive modeling for Planned Giving

The SEC researchers also engage in original research on predictive modeling for cancer control and advocacy and in developing optimal and ethical cancer study designs that minimize the required number of patients to be accrued for the study.

Fight Back

Conquering cancer is as much a matter of public policy as scientific discovery. Whether it's increasing funding for cancer research and programs, enacting laws and policies that curb tobacco use, or expanding access to quality, affordable health care, government action is constantly required. The American Cancer Society and its nonprofit, nonpartisan advocacy affiliate, the American Cancer Society Cancer Action Network℠ (ACS CAN), use applied policy analysis, direct lobbying, grassroots action, and media outreach to ensure elected officials nationwide pass laws furthering the organizations' shared mission to eliminate cancer as a major public health problem.

Created in 2001, ACS CAN is the force behind a new movement uniting and empowering cancer patients, survivors, caregivers, and their families. ACS CAN is a community-based grassroots movement that unites cancer survivors and caregivers, volunteers and staff, health care professionals, public health organizations, and other partners. ACS CAN gives ordinary people extraordinary power to fight cancer.

In recent years, the Society and ACS CAN have successfully partnered to:

- Lead the fight to enact legislation that will grant the US Food and Drug Administration the authority to regulate tobacco product manufacturing and marketing.
- Secure millions of dollars in new federal and state funding for cancer research, prevention, early detection, and education, and implement comprehensive state cancer control plans and fight efforts to cut funding.

- Build support for new legislation to create a National Cancer Fund, which would serve as a dedicated funding source to meet broad cancer research prevention, early detection, and treatment needs in a comprehensive way.
- Pass and protect laws that guarantee insurance coverage of critical cancer screenings and treatments, including clinical trials.
- Enact a new law that not only eliminated copays and deductibles for the Welcome to Medicare benefit and expanded eligibility from six months to a year, but also empowered the US Secretary of Health and Human Services to approve new Medicare preventive services without need for congressional authorization.
- Reauthorize and seek full funding for the National Breast and Cervical Cancer Early Detection Program, which helps low-income, uninsured, and medically underserved women gain access to lifesaving breast and cervical cancer screenings and offers a gateway to treatment upon diagnosis.
- Pass state laws that will help all eligible Americans get screened and treated for colon cancer.
- Advocate for legislation to create a new nationwide colorectal screening and treatment program modeled after the National Breast and Cervical Cancer Early Detection Program.
- Increase the number of states and communities covered by comprehensive smoke-free workplace laws.
- Push for higher cigarette taxes and sufficient funding for tobacco prevention and cessation programs.
- Serve as the leading public health organization in the battle to increase the federal cigarette tax and use the revenue to expand the State Children's Health Insurance Program.
- Enact and seek full funding for the federal patient navigator program, which supports health care outreach in medically underserved communities for cancer patients and others suffering from chronic diseases.
- Eliminate statutory and regulatory barriers to effective management of pain and other side effects of cancer and its treatment at the state level, and to seek passage of federal legislation that will improve pain care research, education, training, and access.
- Pursue expanded access to care through systemic change so that all Americans, regardless of income level or insurance status, have access to lifesaving prevention, early detection, and treatment opportunities.
- Pass federal legislation that will require insurance companies to continue covering college students who take medical leave for up to 12 months.
- Put federal and state lawmakers on the record in support of legislative action that helps the cancer community by having them sign the ACS CAN Congressional Cancer Promise and the American Cancer Society State Cancer Promise, respectively.
- Support legislation that allows volunteers to be reimbursed for the transportation expenses they incur helping cancer patients get to the doctor.

Some efforts in the fight against cancer are more visible than others, but each successful battle is an important contribution to what will ultimately be victory over the disease. The Society, working together with ACS CAN and its grassroots movement, is making sure the voice of the cancer community is heard in the halls of government and empowering communities everywhere to fight back.

Sources of Statistics

New cancer cases. The estimated numbers of new US cancer cases are projected using a spatio-temporal model based on incidence data from 41 states and the District of Columbia for the years 1995-2005 that met the North American Association of Central Cancer Registries' (NAACCR) high-quality data standard for incidence, which covers about 85% of the US population. This method considers geographic variations in socio-demographic and lifestyle factors, medical settings, and cancer screening behaviors as predictors of incidence, as well as accounting for expected delays in case reporting. (See "B" in Additional Information on page 66 for more detailed information.)

Incidence rates. Incidence rates are defined as the number of people per 100,000 who are diagnosed with cancer during a given time period. State incidence rates presented in this publication are published in NAACCR's publication *Cancer Incidence in North America, 2001-2005*. Incidence rates for the US by race/ethnicity were originally published in *SEER Cancer Statistics Review (CSR), 1975-2005*. Unless otherwise indicated, incidence rates in this publication are age adjusted to the 2000 US standard population to allow comparisons across populations with different age distributions. Incidence trends described in this publication are based on delay-adjusted incidence rates. Incidence rates that are not adjusted for delays in reporting may underestimate the number of cancer cases in the most recent time period. Cancer rates most affected by reporting delays are melanoma of the skin, leukemia, and prostate because these cancers are frequently diagnosed in non-hospital settings. The trends in cancer incidence rates reported in this publication were first published in the 2008 Annual Report to the Nation on the Status of Cancer. (See "D" in Additional Information on page 68 for full reference.) This is different from previous years when trends were reported based on the SEER Cancer Statistics Review.

Cancer deaths. The estimated numbers of US cancer deaths are calculated by fitting the numbers of cancer deaths for 1969-2006 to a statistical model that forecasts the numbers of deaths expected to occur in 2009. The estimated numbers of cancer deaths for each state are calculated similarly, using state-level data. For both US and state estimates, data on the numbers of deaths are obtained from the National Center for Health Statistics (NCHS) at the Centers for Disease Control and Prevention.

Mortality rates. Mortality rates or death rates are defined as the number of people per 100,000 dying of a disease during a given year. In this publication, mortality rates are based on counts of cancer deaths compiled by NCHS for 1930-2005 and population data from the US Census Bureau. Unless otherwise indicated, death rates in this publication are age adjusted to the 2000 US standard population to allow comparisons across populations with different age distributions. These rates should be compared only to other statistics that are age adjusted to the US 2000 standard population. The trends in cancer mortality rates reported in this publication were first published in the 2008 Annual Report to the Nation on the Status of Cancer. (See "D" in Additional Information on page 66 for full reference.) This is different from previous years when trends were reported based on the SEER Cancer Statistics Review.

Important note about estimated cancer cases and deaths for the current year. The estimated numbers of new cancer cases and deaths in the current year are model-based and may produce numbers that vary considerably from year to year, particularly for less common cancers and for smaller states. For this reason, we discourage the use of our estimates to track year-to-year changes in cancer occurrence or deaths. Incidence and mortality rates reported by SEER and NCHS are more informative statistics to use when tracking cancer incidence and mortality trends for the US. Rates from state cancer registries are useful for tracking local trends.

Survival. Unless otherwise specified, 5-year relative survival rates are presented in this report for cancer patients diagnosed between 1996-2004, followed through 2005. Relative survival rates are used to adjust for normal life expectancy (and events such as death from heart disease, accidents, and diseases of old age). Relative survival is calculated by dividing the percentage of observed 5-year survival for cancer patients by the 5-year survival expected for people in the general population who are similar to the patient group with respect to age, sex, race, and calendar year of observation. Five-year survival statistics presented in this publication were originally published in *CSR 1975-2005*. In addition to 5-year survival rates, 1-year, 10-year, and 15-year survival rates are presented for selected cancer sites. These survival statistics are generated using the NCI SEER 17 database and SEER*Stat software version 6.3.5. (See "G" in Additional Information on page 66.) One-year survival rates are based on cancer patients diagnosed between 2001-2004, 10-year survival rates are based on diagnoses between 1992-2004, and 15-year survival rates are based on diagnoses between 1987-2004. All patients were followed through 2005.

Probability of developing cancer. Probabilities of developing cancer are calculated using DevCan (Probability of Developing Cancer software), developed by the National Cancer Institute. These probabilities reflect the average experience of people in the US and do not take into account individual behaviors and risk factors. For example, the estimate of 1 man in 13 developing lung cancer in a lifetime underestimates the risk for smokers and overestimates risk for nonsmokers.

Additional information. More information on the methods used to generate the statistics for this report can be found in the following publications:

A. For information on data collection methods used by the North American Association of Central Cancer Registries: Wu XC, McLaughlin CC, Lake A, et al. (eds). *Cancer in North America, 2001-2005. Volume One: Incidence*. Springfield, IL: North American Association of Central Cancer Registries, Inc. May 2008. Available at naaccr.org/filesystem/pdf/CINA2008.v1.incidence.pdf.

B. For information on the methods used to estimate the numbers of new cancer cases: Pickle L, Hao Y, Jemal A, et al. *CA Cancer J Clin*. 2007;57:30-42.

C. For information on data collection methods used by the SEER program: Ries LAG, Melbert D, Krapcho M, et al. (eds). *SEER Cancer Statistics Review, 1975-2005*. National Cancer Institute. Bethesda, MD, 2008. Available at: seer.cancer.gov/csr/1975_2005/.

D. For information on cancer incidence trends reported herein: Jemal A, Thun MJ, Ries LAG, et al. *J Natl Cancer Institute*. 2008;100:1672-1694.

E. For information on data collection and processing methods used by NCHS: cdc.gov/nchs/deaths.htm. Accessed October 15, 2008.

F. For information on the methods used to estimate the number of cancer deaths: Tiwari, et al. *CA Cancer J Clin*. 2004; 54:30-40.

G. For information on the methods used to calculate relative survival rates: software – Surveillance Research Program, National Cancer Institute SEER*Stat software (seer.cancer.gov/seerstat) version 6.4.4; database – Surveillance, Epidemiology, and End Results (SEER) Program (seer.cancer.gov) SEER*Stat Database: Incidence – SEER 17 Regs Limited-Use, Nov 2007 Sub (1973-2005 varying) – Linked to County Attributes – Total US, 1969-2005 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2008, based on the November 2007 submission.

H. For information on the methods used to calculate the probability of developing cancer: DevCan 6.3.0. Probability of developing or dying of cancer. Statistical Research and Applications Branch, NCI, 2008. Available at: srab.cancer.gov/devcan/.

Factors That Influence Cancer Rates

Age Adjustment to the Year 2000 Standard

Epidemiologists use a statistical method called "age adjustment" to compare groups of people with different age compositions. This is especially important when examining cancer rates, since cancer is generally a disease of older people. For example, without adjusting for age, it would be inaccurate to compare the cancer rates of Florida, which has a large elderly population, to that of Alaska, which has a younger population. Without adjusting for age, it would appear that the cancer rates in Florida are much higher than Alaska. However, once the ages are adjusted, it appears their rates are similar.

Since the publication of *Cancer Facts & Figures 2003*, the American Cancer Society has used the Year 2000 Standard for age adjustment. This is a change from statistics previously published by the Society. Prior to 2003, most age-adjusted rates were standardized to the 1970 census, although some were based on the 1980 census or even the 1940 census. This change has also been adopted by federal agencies that publish statistics. The new age standard applies to data from calendar year 1999 forward. The change also requires a recalculation of age-adjusted rates for previous years to allow valid comparisons between current and past years.

The purpose of shifting to the Year 2000 Standard is to more accurately reflect contemporary incidence and mortality rates, given the aging of the US population. On average, Americans are living longer because of the decline in infectious and cardiovascular diseases. Greater longevity allows more people to reach the age when cancer and other chronic diseases become more common. Using the Year 2000 Standard in age adjustment instead of the 1970 or 1940 standards allows age-adjusted rates to be closer to the actual, unadjusted rate in the population.

The effect of changing to the Year 2000 Standard will vary from cancer to cancer, depending on the age at which a particular cancer usually occurs. For all cancers combined, the average annual age-adjusted incidence rate for 2000-2004 will increase approximately 20% when adjusted to the Year 2000, compared to the Year 1970 Standard. For cancers that occur mostly at older ages, such as colon cancer, the Year 2000 Standard will increase incidence by up to 25%, whereas for cancers such as acute lymphocytic leukemia, the new standard will decrease the incidence by about 7%. These changes are caused by the increased representation of older ages (for all cancers combined and colon cancer) or by the decreased representation of younger ages (for acute lymphocytic leukemia) in the Year 2000 Standard, compared to the Year 1970 Standard.

It is important to note that in no case will the actual number of cases/deaths or age-specific rates change, only the age-standardized rates that are weighted to the different age distribution.

Change in Population Estimates

Cancer rates are also affected by changes in population estimates, which are the basis for calculating rates for new cancer cases and deaths. The US Census Bureau updates and revises population estimates every year. The Bureau calculates "intercensal" estimates after a new census is completed – for example, using information from both the 1990 and 2000 censuses, the Bureau obtains better estimates for the 1990s. These revisions are based on the most recent census information and on the best available demographic data reflecting components of population change (e.g., births, deaths, net internal migration, and net international immigration). Thus, it is customary to recalculate cancer rates based on the revised population estimates. In less populated areas, such as rural counties, or in adjacent urban and suburban areas where there is substantial migration of residents from a more populous urban area to a less populous suburban one between censuses, a change in the population estimates can affect the county rate by as much as 20%. This is in contrast to large counties, where a small change in a large population estimate will not affect rates nearly as much. More information about the influence of change in population count on US cancer rates is available on the National Cancer Institute Web site (cancer.gov/newscenter/pressreleases/Census2000).

Screening Guidelines for the Early Detection of Cancer in Average-risk Asymptomatic People

Cancer Site	Population	Test or Procedure	Frequency
Breast	Women, age 20+	Breast self-examination	Beginning in their early 20s, women should be told about the benefits and limitations of breast self-examination (BSE). The importance of prompt reporting of any new breast symptoms to a health professional should be emphasized. Women who choose to do BSE should receive instruction and have their technique reviewed on the occasion of a periodic health examination. It is acceptable for women to choose not to do BSE or to do BSE irregularly.
		Clinical breast examination	For women in their 20s and 30s, it is recommended that clinical breast examination (CBE) be part of a periodic health examination, preferably at least every three years. Asymptomatic women aged 40 and over should continue to receive a clinical breast examination as part of a periodic health examination, preferably annually.
		Mammography	Begin annual mammography at age 40.*
Colorectal†	Men and women, age 50+	Fecal occult blood test (FOBT)‡ with at least 50% test sensitivity for cancer, or fecal immunochemical test (FIT) with at least 50% test sensitivity for cancer, or	Annual, starting at age 50
		Stool DNA test	Interval uncertain, starting at age 50
		Flexible sigmoidoscopy, or	Every five years, starting at age 50
		Fecal occult blood test (FOBT)‡ and flexible sigmoidoscopy,§ or	Annual FOBT (or or fecal immunochemical test (FIT)) and flexible sigmoidoscopy every five years, starting at age 50
		Double-contrast barium enema (DCBE), or	Every five years, starting at age 50
		Colonoscopy	Every 10 years, starting at age 50
		CT colonography	Every five years, starting at age 50
Prostate	Men, age 50+	Digital rectal examination (DRE) and prostate-specific antigen test (PSA)	Health care providers should discuss the potential benefits and limitations of prostate cancer early detection testing with men and offer the PSA blood test and the digital rectal examination annually, beginning at age 50, to men who are at average risk of prostate cancer, and who have a life expectancy of at least 10 years.¶
Cervix	Women, age 18+	Pap test	Cervical cancer screening should begin approximately three years after a woman begins having vaginal intercourse, but no later than 21 years of age. Screening should be done every year with conventional Pap tests or every two years using liquid-based Pap tests. At or after age 30, women who have had three normal test results in a row may get screened every two to three years with cervical cytology (either conventional or liquid-based Pap test) alone, or every three years with an HPV DNA test plus cervical cytology. Women 70 years of age and older who have had three or more normal Pap tests and no abnormal Pap tests in the past 10 years and women who have had a total hysterectomy may choose to stop cervical cancer screening.
Endometrial	Women, at menopause	At the time of menopause, women at average risk should be informed about risks and symptoms of endometrial cancer and strongly encouraged to report any unexpected bleeding or spotting to their physicians.	
Cancer-related checkup	Men and women, age 20+	On the occasion of a periodic health examination, the cancer-related checkup should include examination for cancers of the thyroid, testicles, ovaries, lymph nodes, oral cavity, and skin, as well as health counseling about tobacco, sun exposure, diet and nutrition, risk factors, sexual practices, and environmental and occupational exposures.	

* Beginning at age 40, annual clinical breast examination should be performed prior to mammography.

† Individuals with a personal or family history of colorectal cancer or adenomas, inflammatory bowel disease, or high-risk genetic syndromes should continue to follow the most recent recommendations for individuals at increased or high risk.

‡ FOBT as it is sometimes done in physicians' offices, with the single stool sample collected on a fingertip during a digital rectal examination, is not an adequatre substitute for the recommended at-home procedure of collecting two samples from three consecutive specimens. Toilet bowl FOBT tests also are not recommended. In comparison with guaiac-based tests for the detection of occult blood, immunochemical tests are more patient-friendly, and are likely to be equal or better in sensitivity and specificity. There is no justification for repeating FOBT in response to an initial positive finding.

§ Flexible sigmoidoscopy, together with FOBT, is preferred, compared to FOBT or flexible sigmoidoscopy alone.

¶ Information should be provided to men about the benefits and limitations of testing so that an informed decision about testing can be made with the clinician's assistance.

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