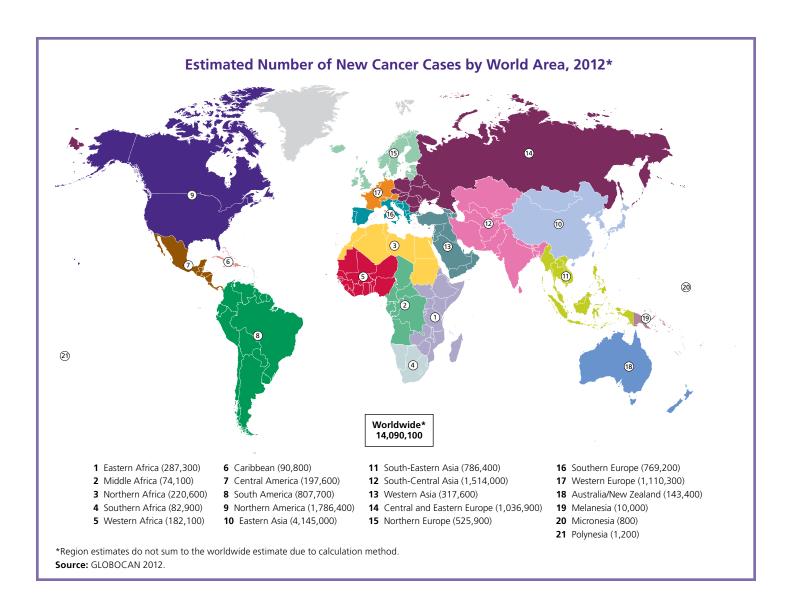
Global Cancer Facts & Figures 3rd Edition



Special Section: Female Breast Cancer see page 37



Contents

Basic Cancer Facts	1
What Is Cancer?	
How Many New Cancer Cases and Deaths Occurred in 2012 Worldwide?	1
What Factors Contribute to Geographic Variation in Cancer Occurrence?	<u>3</u>
Can Cancer Be Prevented?	6
Who Is at Risk of Developing Cancer?	
What Percentage of People Will Survive Cancer?	7
How Is Cancer Staged?	8
What Are the Costs of Cancer?	8
Interventions for Cancer Prevention and Control	8
Selected Cancers	12
Breast (see Special Section on page 37)	12
Childhood Cancer	12
Colon and Rectum	14
Esophagus	16
Liver	18
Lung and Bronchus	21
Non-Hodgkin Lymphoma	24
Prostate	26
Stomach	28
Urinary Bladder	32
Uterine Cervix	34
Special Section: Global Breast Cancer	37
The Global Fight against Cancer	52
Sources of Statistics	53
References	57

This publication would not have been possible without the contributions of the International Agency for Research on Cancer and its work in producing GLOBOCAN 2012 (globocan.iarc.fr) alongside the work of cancer registrars worldwide.

For more information, contact:

Lindsey Torre, MSPH Rebecca Siegel, MPH Ahmedin Jemal, DVM, PhD Surveillance & Health Services Research Program



International Agency for Research on Cancer



Corporate Center: American Cancer Society, Inc. 250 Williams Street, NW, Atlanta, GA 30303-1002 404-320-3333

©2015, American Cancer Society, Inc.
All rights reserved, including the right to reproduce
this publication or portions thereof in any form.

For written permission, address the Legal department of the American Cancer Society, 250 Williams Street, NW, Atlanta, GA 30303-1002.

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.

Suggested citation: American Cancer Society. *Global Cancer Facts & Figures* 3rd Edition. Atlanta: American Cancer Society; 2015.

Basic Cancer Facts

What Is Cancer?

Cancer is a group of diseases characterized by the uncontrolled growth and spread of abnormal cells. If the spread is not controlled, it can result in death. Cancer is caused by external factors, such as tobacco, infectious organisms, and an unhealthy diet, and internal factors, such as inherited genetic mutations, hormones, and immune conditions. These factors may act together or in sequence to cause cancer. Ten or more years often pass between exposure to external factors and detectable cancer. Treatments include surgery, radiation, chemotherapy, hormone therapy, immune therapy, and targeted therapy (drugs that interfere with cancer cell growth by targeting specific molecules).

Worldwide, one in seven deaths is due to cancer; cancer causes more deaths than AIDS, tuberculosis, and malaria combined. When countries are grouped according to income, cancer is the second leading cause of death in high-income countries (following cardiovascular diseases) and the third leading cause of death in low- and middle-income countries (following cardiovascular diseases and infectious and parasitic diseases) (Table 1).

How Many New Cancer Cases and Deaths Occurred in 2012 Worldwide?

According to estimates from the International Agency for Research on Cancer (IARC), there were 14.1 million new cancer cases in 2012 worldwide, of which 8 million occurred in economically developing countries, which contain about 82% of the world's population. (Figure 1, page 2). These estimates do not include non-melanoma skin cancers, which are not tracked in cancer registries. The corresponding estimates for total cancer deaths in 2012 were 8.2 million (about 22,000 cancer deaths a day) - 2.9 million in economically developed countries, and 5.3 million in economically developing countries (Figure 1, page 2).

By 2030, the global burden is expected to grow to 21.7 million new cancer cases and 13 million cancer deaths simply due to the growth and aging of the population.1 However, the estimated future cancer burden will probably be considerably larger due to the adoption of lifestyles that are known to increase cancer risk, such as smoking, poor diet, physical inactivity, and fewer pregnancies, in economically developing countries. Cancers related to these factors, such as lung, breast, and colorectal cancers, are already on the rise in economically transitioning countries. Table 2 (page 3) provides the estimated numbers of total new cancer cases and deaths in 2012 by United Nations (UN) area. In economically developed countries, the three most commonly diagnosed cancers were prostate, lung, and colorectal among males, and breast, colorectal, and lung among females (Figure 1, page 2). In economically developing countries, the three most

Tal	ole '	1. Leading	Causes of	of Death	Worldwide by	Income	Level, 2012	(Thousands)
-----	-------	------------	-----------	----------	--------------	--------	-------------	-------------

	Worldwide			Low-	and Middle-	income	High-income		
	Rank	Deaths	%	Rank	Deaths	%	Rank	Deaths	%
Cardiovascular diseases	1	17,513	31%	1	13,075	30%	1	4,438	38%
Malignant neoplasms	2	8,204	15%	3	5,310	12%	2	2,894	25%
Infectious and parasitic diseases	3	6,431	12%	2	6,128	14%	7	303	3%
Respiratory diseases	4	4,040	7%	4	3,395	8%	3	645	6%
Unintentional injuries	5	3,716	7%	5	3,212	7%	5	504	4%
Respiratory infections	6	3,060	5%	6	2,664	6%	6	396	3%
Digestive diseases	7	2,263	4%	7	1,748	4%	4	515	4%
Diabetes mellitus	8	1,497	3%	8	1,243	3%	9	254	2%
Intentional injuries	9	1,428	3%	9	1,185	3%	10	243	2%
Genitourinary diseases	10	1,195	2%	10	935	2%	8	260	2%
Nutritional deficiencies	11	559	1%	11	534	1%	14	25	0%
Congenital anomalies	12	556	1%	12	515	1%	13	42	0%
Maternal conditions	13	296	1%	13	293	1%	16	3	0%
Musculoskeletal diseases	14	216	0%	14	158	0%	12	58	1%
Other neoplasms	15	193	0%	15	116	0%	11	77	1%
All causes		55,843			44,172			11,671	

Source: World Health Organization Global Health Observatory Data Repository, Mortality and Global Health Estimates 2012. apps.who.int/gho/data/?theme=main. Accessed

American Cancer Society, Inc., Surveillance Research, 2015

Figure 1. Estimated New Cancer Cases and Deaths Worldwide for Leading Cancer Sites by Level of Economic Development, 2012

Estimated New Cases

Estimated Deaths

	zzamatea	Ten cases	Estimate	a Beating
	Male	Female	Male	Female
	Lung, bronchus, & trachea	Breast	Lung, bronchus, & trachea	Breast
	1,241,600	1,676,600	1,098,700	521,900
	Prostate	Colon & rectum	Liver	Lung, bronchus, & trachea
	1,111,700	614,300	521,000	491,200
	Colon & rectum 746,300	Lung, bronchus, & trachea 583,100	Stomach 469,000	Colon & rectum 320,300
	Stomach	Cervix uteri	Colon & rectum	Cervix uteri
	631,300	527,600	373,600	265,700
	Liver	Stomach	Prostate	Stomach
	554,400	320,300	307,500	254,100
Worldwide	Urinary bladder	Corpus uteri	Esophagus	Liver
vvoilavviae	330,400	319,600	281,200	224,500
	Esophagus 323,000	Ovary 238,700	Pancreas 173,800	Pancreas 156,600
	Non-Hodgkin lymphoma	Thyroid	Leukemia	Ovary
	217,600	229,900	151,300	151,900
	Kidney	Liver	Urinary bladder	Esophagus
	213,900	228,100	123,100	119,000
	Leukemia 200,700	Non-Hodgkin lymphoma 168,100	Non-Hodgkin lymphoma 115,400	Leukemia 114,200
	All sites*	All sites*	All sites*	All sites*
	7,427,100	6,663,000	4,653,400	3,548,200
	,,,,,,,	3,533,633	(13)	
	Male	Female	Male	Female
	Prostate	Breast	Lung, bronchus, & trachea	Lung, bronchus, & trachea
	758,700	793,700	416,700	209,900
	Lung, bronchus, & trachea	Colon & rectum	Colon & rectum	Breast
	490,300 Colon & rectum	338,000 Lung, bronchus, & trachea	175,400 Prostate	197,600 Colon & rectum
	398,900	267,900	142,000	157,800
	Urinary bladder	Corpus uteri	Stomach	Pancreas
	196,100	167,900	106,700	91,300
	Stomach	Ovary	Pancreas	Stomach
	175,100	99,800 Stampsh	93,100	68,000
Developed	Kidney 125,400	Stomach 99,400	Liver 80,400	Ovary 65,900
Countries	Non-Hodgkin lymphoma	Thyroid	Urinary bladder	Liver
	101,900	93,100	58,900	42,700
	Melanoma of skin	Pancreas	Esophagus	Leukemia
	99,400	92,800	56,100	40,300
	Pancreas 94,700	Melanoma of skin 91,700	Leukemia 51,300	Cervix uteri 35,500
	Liver	Non-Hodgkin lymphoma	Kidney	Corpus uteri
	92,000	88,500	47,900	34,700
	All sites*	All sites*	All sites*	All sites*
	3,243,500	2,832,400	1,591,500	1,287,000
	84-1-	Famala	86-1-	FI-
	Male	Female Proast	Male	Female
	Lung, bronchus, & trachea 751,300	Breast 882,900	Lung, bronchus, & trachea 682,000	Breast 324,300
	Liver	Cervix uteri	Liver	Lung, bronchus, & trachea
	462,400	444,500	440,600	281,400
	Stomach	Lung, bronchus, & trachea	Stomach	Cervix uteri
	456,200 Prostate	315,200 Colon & rectum	362,300 Esophagus	230,200 Stomach
	353,000	276,300	225,100	186,100
	Colon & rectum	Stomach	Colon & rectum	Liver
	347,400	220,900	198,200	181,800
Developing	Esophagus	Liver	Prostate	Colon & rectum
Countries	255,300	185,800	165,500	162,500
	Urinary bladder 134,300	Corpus uteri 151,700	Leukemia 100,000	Esophagus 103,700
	Lip, oral cavity	Ovary	Pancreas	Ovary
	130,900	139,000	80,700	86,000
	Leukemia	Thyroid	Non-Hodgkin lymphoma	Leukemia
	120,400	136,800	74,500	73,800
	Non-Hodgkin lymphoma 115,800	Esophagus 114,400	Lip, oral cavity 74,500	Pancreas 65,300
	All sites*	All sites*	All sites*	All sites*
	4,183,600	3,830,600	3,061,900	2,261,200

^{*}Excluding non-melanoma skin cancers. Estimates may not sum to worldwide total due to rounding.

Source: GLOBOCAN 2012.

Table 2. Estimated Number of New Cancer Cases and Deaths by World Area, 2012*

		Cases		Deaths					
	Male	Female	Overall	Male	Female	Overall			
Eastern Africa	116,800	170,500	287,300	92,400	116,100	208,500			
Middle Africa	30,300	43,800	74,100	25,600	31,200	56,900			
Northern Africa	105,800	114,800	220,600	77,000	66,500	143,400			
Southern Africa	39,900	43,000	82,900	25,100	25,900	51,000			
Western Africa	69,200	112,900	182,100	57,800	73,600	131,400			
Eastern Asia	2,431,500	1,713,500	4,145,000	1,756,100	1,002,200	2,758,200			
South-central Asia	711,800	802,300	1,514,000	533,000	490,400	1,023,400			
South-eastern Asia	382,900	403,500	786,400	290,200	238,300	528,500			
Western Asia	168,700	148,900	317,600	110,100	79,200	189,400			
Caribbean	48,300	42,500	90,800	29,500	23,700	53,200			
Central America	87,300	110,300	197,600	53,900	56,800	110,700			
Northern America	920,600	865,700	1,786,400	362,800	328,700	691,500			
South America	397,500	410,200	807,700	230,500	209,000	439,500			
Central and Eastern Europe	513,800	523,100	1,036,900	351,200	287,000	638,200			
Northern Europe	271,600	254,200	525,900	129,300	115,800	245,100			
Southern Europe	430,500	338,700	769,200	227,600	162,800	390,500			
Western Europe	614,700	495,700	1,110,300	268,700	213,900	482,600			
Australia/New Zealand	81,000	62,400	143,400	29,000	23,000	52,000			
Melanesia	4,000	6,100	10,000	2,900	3,700	6,600			
Micronesia	500	400	800	200	100	400			
Polynesia	700	600	1,200	400	300	700			

^{*}Excludes nonmelanoma skin cancer.

Source: GLOBOCAN 2012.

American Cancer Society, Inc., Surveillance Research, 2015

commonly diagnosed cancers were lung, liver, and stomach in males, and breast, cervix uteri, and lung in females. In both economically developed and developing countries, the three most common cancer sites were also the three leading causes of cancer death (Figure 1). Rates of cancers common in Western countries will continue to rise in developing countries if preventive measures are not widely applied.

The most common types of cancer also vary by geographic area (Table 3, page 4). For example, among women breast cancer was the most common cancer in 19 out of the 21 world areas, while cervical cancer was the most common in the remaining two areas (Table 3, page 4). Further variations are observed by examining individual countries (Figure 2, page 5). In 2012, the most common cancer site among males in most economically developed countries was prostate, with the exception of certain countries of Southern and Eastern Europe (lung cancer), Slovakia (colorectal cancer), and Japan (stomach cancer). Lung and stomach cancer were the top cancer sites in Asia. The greatest variation among males was in Africa, where the most common cancer was prostate, liver, Kaposi sarcoma, lung, non-Hodgkin lymphoma, colorectum, leukemia, esophagus, or stomach. Among females, the most common cancer sites were either breast or cervical cancer, with the exceptions of China and North Korea (lung), South Korea (thyroid), and Mongolia and Laos (liver) (Figure 2, page 5). Additional geographic variations are presented in the Selected Cancers section of this document beginning on page 12.

What Factors Contribute to Geographic Variation in Cancer Occurrence?

Factors that contribute to geographic differences in cancer occurrence include variations in the age structure of the population, the prevalence of risk factors, the availability and use of diagnostic tests (e.g., for cancer screening) and the availability and quality of treatment. For example, infections associated with cancer are more common in developing than developed countries. As a result, in 2012, two of the five leading cancers in men (liver and stomach) and women (cervix and stomach) in developing countries were related to infection. Stomach cancer continued to be the most common infection-related cancer worldwide, followed closely by liver and cervix (Figure 1). Approximately 16% of all incident cancers worldwide are attributable to infections.² This percentage is about three times higher in developing countries (23%) than in developed countries (7%) (Figure 3, page 6).

Table 3. The Two Most Common Types of New Cancer Cases and Deaths by World Area, 2012

Cancer Cases

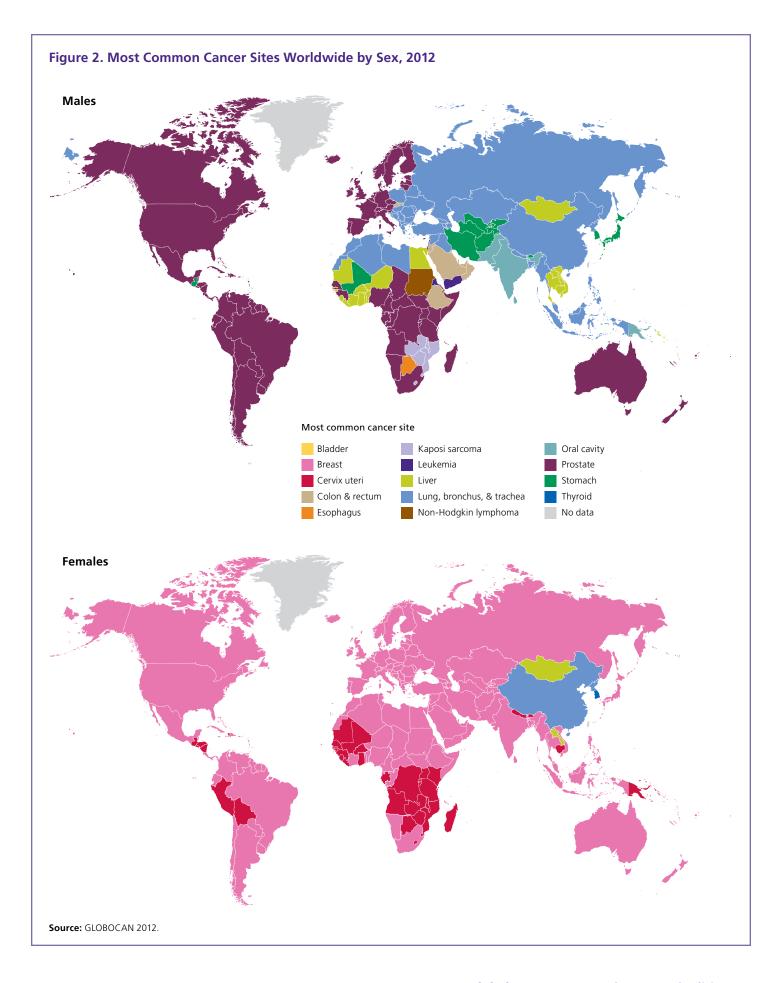
		Ma	ales		Females			
	First		Second	Second			Second	
Eastern Africa	Kaposi sarcoma	17%	Prostate	15%	Cervix uteri	27%	Breast	20%
Middle Africa	Prostate	23%	Liver	12%	Cervix uteri	26%	Breast	25%
Northern Africa	Liver	12%	Lung	11%	Breast	34%	Colorectum	5%
Southern Africa	Prostate	26%	Lung	12%	Breast	24%	Cervix uteri	20%
Western Africa	Prostate	25%	Liver	22%	Breast	35%	Cervix uteri	24%
Caribbean	Prostate	39%	Lung	12%	Breast	27%	Cervix uteri	12%
Central America	Prostate	22%	Stomach	8%	Breast	23%	Cervix uteri	17%
South America	Prostate	29%	Lung	10%	Breast	28%	Cervix uteri	11%
Northern America	Prostate	28%	Lung	14%	Breast	30%	Lung	13%
Eastern Asia	Lung	23%	Stomach	16%	Breast	16%	Lung	14%
South-eastern Asia	Lung	19%	Liver	15%	Breast	27%	Cervix uteri	13%
South-central Asia	Lung	11%	Lip, oral cavity	10%	Breast	28%	Cervix uteri	19%
Western Asia	Lung	19%	Prostate	13%	Breast	29%	Colorectum	8%
Central and Eastern Europe	Lung	21%	Colorectum	14%	Breast	24%	Colorectum	13%
Northern Europe	Prostate	30%	Colorectum	13%	Breast	31%	Colorectum	12%
Southern Europe	Prostate	21%	Lung	16%	Breast	30%	Colorectum	13%
Western Europe	Prostate	29%	Lung	13%	Breast	33%	Colorectum	12%
Australia/New Zealand	Prostate	31%	Colorectum	13%	Breast	28%	Colorectum	14%
Melanesia	Lip, oral cavity	15%	Prostate	12%	Breast	23%	Cervix uteri	20%
Micronesia	Prostate	27%	Lung	23%	Breast	34%	Lung	15%
Polynesia	Prostate	35%	Lung	17%	Breast	38%	Thyroid	8%

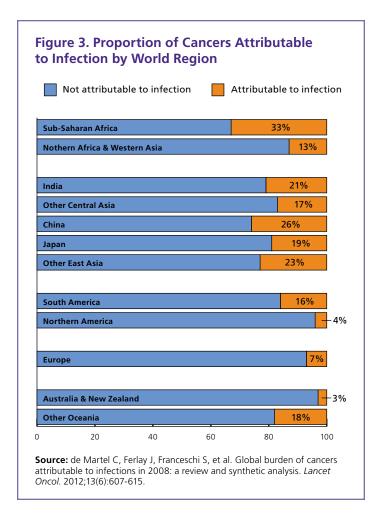
Cancer Deaths

		Ma	ales		Females			
	First		Second	1		Tem	Second	<u> </u>
Eastern Africa	Kaposi sarcoma	15%	Prostate	15%	Cervix uteri	24%	Breast	15%
Middle Africa	Prostate	23%	Liver	12%	Cervix uteri	25%	Breast	19%
Northern Africa	Liver	17%	Lung	14%	Breast	23%	Liver	8%
Southern Africa	Lung	17%	Prostate	15%	Cervix uteri	18%	Breast	16%
Western Africa	Liver	26%	Prostate	25%	Breast	28%	Cervix uteri	22%
Caribbean	Prostate	27%	Lung	19%	Breast	17%	Lung	14%
Central America	Prostate	17%	Lung	11%	Breast	13%	Cervix uteri	12%
South America	Lung	15%	Prostate	15%	Breast	15%	Lung	10%
Northern America	Lung	28%	Prostate	9%	Lung	26%	Breast	15%
Eastern Asia	Lung	29%	Liver	18%	Lung	21%	Stomach	13%
South-eastern Asia	Lung	23%	Liver	19%	Breast	18%	Lung	12%
South-central Asia	Lung	14%	Stomach	11%	Breast	21%	Cervix uteri	17%
Western Asia	Lung	26%	Prostate	9%	Breast	19%	Colorectum	9%
Central and Eastern Europe	Lung	27%	Colorectum	12%	Breast	17%	Colorectum	15%
Northern Europe	Lung	23%	Prostate	14%	Lung	20%	Breast	16%
Southern Europe	Lung	27%	Colorectum	12%	Breast	17%	Colorectum	13%
Western Europe	Lung	25%	Colorectum	11%	Breast	17%	Lung	15%
Australia/New Zealand	Lung	20%	Prostate	14%	Lung	18%	Breast	16%
Melanesia	Liver	15%	Lip, oral cavity	12%	Cervix uteri	19%	Breast	17%
Micronesia	Lung	39%	Liver	12%	Lung	37%	Breast	19%
Polynesia	Lung	28%	Prostate	12%	Breast	17%	Lung	16%

Source: GLOBOCAN 2012.

American Cancer Society, Inc., Surveillance Research, 2015





Can Cancer Be Prevented?

A substantial proportion of cancers could be prevented. All cancers caused by tobacco use and heavy alcohol consumption could be prevented completely. In 2010, almost 1.5 million of the estimated 8 million cancer deaths in the world were caused by tobacco smoking.^{3,4} In addition, the World Cancer Research Fund has estimated that between one-fifth and one-fourth of cancers worldwide are related to overweight or obesity, physical inactivity, and/or poor nutrition, and thus could also be prevented.⁵ Many of the cancers related to infectious agents, such as human papillomavirus (HPV), hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV), and Helicobacter pylori (H. pylori), could be prevented through behavioral changes, infection control procedures, vaccinations, or treatment of the infection. Many cases of skin cancer could be prevented by protecting skin from excessive sun exposure and avoiding indoor tanning.

Screening can prevent colorectal and cervical cancers by allowing for the detection and removal of precancerous lesions. Screening can also detect cancer early, before symptoms appear, which usually results in less extensive treatment and better outcomes. Screening is known to reduce mortality for cancers of the breast, colon, rectum, cervix, and lung (among long-term and/

or heavy smokers). A heightened awareness of changes in the breast, skin, testicles, or oral cavity may also result in the early detection of cancer.

Who Is at Risk of Developing Cancer?

Anyone can develop cancer. However, the risk of being diagnosed with cancer increases substantially with age. In economically developed countries, 58% of all newly diagnosed cancer cases occur at 65 years of age and older, compared with 40% in developing countries. The difference is largely due to variations in age structure of the populations. The populations of developing countries are younger and have a smaller proportion of older individuals in whom cancer most frequently occurs (Figure 4). Table 4 shows the estimated age-standardized incidence and mortality rates (per 100,000) in 2012 for various types of cancers by sex and level of economic development. The incidence rate for all cancers combined was higher in more developed countries compared with less developed countries in both males (308.7 vs. 163, respectively) and females (240.6 vs. 135.8). In contrast, the mortality rate for all cancers combined was generally similar between more developed and less developed countries, particularly among females (86.2 vs. 79.8, respectively). Larger differences in incidence than mortality relate to variations in both the types of major cancers and the availability of early detection and treatment services.

For most types of cancer, risk is higher with a family history of the disease. It is now thought that many familial cancers arise not exclusively from genetic makeup, but from the interplay between common gene variations and lifestyle and environmental risk factors. Only a small proportion of cancers are strongly hereditary, in that an inherited genetic alteration confers a very high risk.

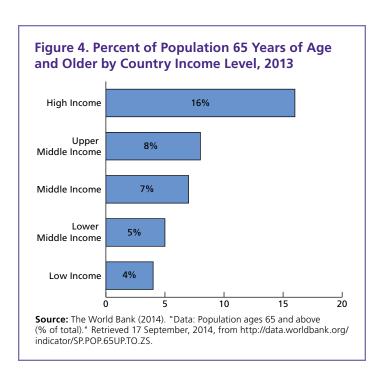


Table 4. Estimated Incidence and Mortality Rates* by Sex, Cancer Site, and Level of Economic Development, 2012

Malac

		Ma	ales		Females				
	Developed	d countries	Developin	g countries	Developed	d countries	Developin	g countries	
Site	Incidence	Mortality	Incidence	Mortality	Incidence	Mortality	Incidence	Mortality	
Bladder	16.9	4.5	5.3	2.6	3.7	1.1	1.5	0.7	
Brain, nervous system	5.9	4.0	3.3	2.6	4.4	2.7	2.7	1.9	
Breast	_	_	_	_	74.1	14.9	31.3	11.5	
Cervix uteri	_	_	_	_	9.9	3.3	15.7	8.3	
Colon and rectum	36.3	14.7	13.7	7.8	23.6	9.3	9.8	5.6	
Corpus uteri	_	_	_	_	14.7	2.3	5.5	1.5	
Esophagus	6.4	5.2	10.1	9.0	1.2	0.9	4.1	3.6	
Hodgkin lymphoma	2.3	0.4	0.8	0.4	1.9	0.3	0.5	0.3	
Kidney	12.6	4.2	3.4	1.7	6.2	1.7	1.8	0.9	
Larynx	5.1	2.2	3.5	2.0	0.6	0.2	0.4	0.3	
Leukemia	8.8	4.6	4.4	3.7	5.8	2.8	3.2	2.6	
Lip, oral cavity	7.0	2.3	5.0	2.8	2.6	0.6	2.5	1.4	
Liver	8.6	7.1	17.8	17.0	2.7	2.5	6.6	6.4	
Lung	44.7	36.8	30.0	27.2	19.6	14.3	11.1	9.8	
Melanoma of skin	10.2	2.0	0.8	0.4	9.3	1.2	0.7	0.3	
Multiple myeloma	3.3	1.8	1.0	0.8	2.2	1.2	0.7	0.6	
Nasopharynx	0.6	0.2	2.0	1.3	0.2	0.1	0.8	0.5	
Non-Hodgkin lymphoma	10.3	3.5	4.3	2.8	7.1	2.0	2.8	1.8	
Other pharynx	4.7	2.2	2.8	2.2	0.8	0.3	0.7	0.5	
Ovary	_	_	_	_	9.1	5.0	5.0	3.1	
Pancreas	8.6	8.3	3.3	3.2	5.9	5.5	2.4	2.3	
Prostate	69.5	10.0	14.5	6.6	_	_	_	-	
Stomach	15.6	9.2	18.1	14.4	6.7	4.2	7.8	6.5	
Testis	5.2	0.3	0.7	0.3	_	_	_	-	
Thyroid	3.6	0.3	1.4	0.4	11.1	0.4	4.7	0.7	
All sites [†]	308.7	138.0	163.0	120.1	240.6	86.2	135.8	79.8	

*Per 100,000, age standardized to the World Standard Population. †Excludes nonmelanoma skin cancer.

Source: GLOBOCAN 2012.

American Cancer Society, Inc., Surveillance Research, 2015

Famales

What Percentage of People Will **Survive Cancer?**

Survival statistics vary greatly by cancer type and stage at diagnosis. Survival is expressed as the percentage of people who are alive a certain period of time (usually 5 years) following a cancer diagnosis. It does not distinguish between patients who have no evidence of cancer and those who have relapsed or are still in treatment. While 5-year 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 because cancer death can occur beyond 5 years after diagnosis. In addition, although survival provides some indication about the average survival experience of cancer patients in a given population, it may not predict individual prognosis and should be interpreted with caution.

Cancer survival rates in a population are affected by a number of factors, most importantly, the types of cancer that occur, the stages at which cancers are diagnosed, and whether treatment is available (Table 5, page 9). For cancers that are affected by screening and/or treatment, such as female breast, colorectal, and certain childhood cancers, there are large survival differences between economically developed and developing countries. For example, the five-year survival rate for breast cancer in the United States in 2005-2009 is 89%, compared with 53% in South Africa and 60% in Algeria (Table 5, page 9). In contrast, for cancer sites without early detection or effective treatment, such as esophagus, liver, lung, or pancreatic cancer, survival rates vary little between developing and developed countries. In addition to differences in screening and treatment, international differences in cancer survival rates are also affected by differences in detection practice, awareness, and data quality.

There are different methods for calculating cancer survival. For most sites, we present net survival, which is useful for international comparisons because it is not influenced by mortality from other diseases, which may vary between countries.⁶ However, for some cancers (childhood, esophagus, non-Hodgkin lymphoma, and urinary bladder), net survival estimates were not available so relative survival rates are presented. Relative and net survival estimates are calculated differently and should not be directly compared.

Cancer survival is difficult to calculate because it requires an established cancer registration system with good case ascertainment, as well as follow-up of patients for several years following diagnosis. For this reason, cancer survival statistics are generally more available for developed countries. However, efforts are underway to establish and strengthen cancer registries in developing countries through the International Agency for Research on Cancer's Global Initiative for Cancer Registry Development.⁷

How Is Cancer Staged?

Staging describes the extent or spread of cancer at the time of diagnosis. Proper staging is essential in determining the choice of therapy and in assessing prognosis. A cancer's stage is based on the size or extent of the primary tumor and whether it has spread to nearby lymph nodes or other areas of the body. A number of different staging systems are used to classify cancer. A system of summary staging is used for descriptive and statistical analysis of tumor registry data and is particularly useful for looking at trends over time. According to this system, 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 beyond the original layer of tissue, the cancer has become invasive and is categorized as local, regional, or distant based on the extent of spread.

Clinicians use a different staging system, called TNM, for most cancers. The TNM system assesses cancer growth and spread in three ways: size 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 categories are determined, a stage of 0, I, II, III, or IV is assigned, with stage 0 being in situ, stage I being early, and so on, with stage IV being the most advanced disease. Some cancers (e.g., leukemia and lymphoma) have different staging systems. As the biology of cancer has become better understood, genetic features of tumors have been incorporated into treatment plans and/or stage for some cancer sites.

Comprehensive and complete information on stage at diagnosis is not available for most parts of the world. Table 6 (page 10) illustrates the wide geographic variation in stage at diagnosis for breast cancer. Only about 5% of women diagnosed with this cancer in Malaysia, Iraq, and and Nigeria had early stage disease (stage I), compared with about 40% in Canada and the United Kingdom and 48% in the US.

What Are the Costs of Cancer?

In addition to the human toll of cancer, the financial cost is substantial. Direct costs include expenditures for treatment, as well as the cost of care and rehabilitation related to the illness. Indirect costs include the loss of economic output due to missed work (morbidity costs) and premature death (mortality costs). There are also hidden costs of cancer, such as health insurance premiums and nonmedical expenses (transportation, child or elder care, housekeeping assistance, wigs, etc.).8 The exact global cost of cancer is unknown, but it is thought to be in the hundreds of billions of dollars per year. In the United States alone, the estimated direct medical cost for cancer in 2011 was \$88.7 billion.9 The estimated cost of lost productivity due to premature cancer mortality in Europe in 2008 was €75 billion.¹0 The global cost of cancer is expected to increase due to increases in the number of new cancer cases, as well as the increasing cost of cancer therapies.11

Interventions for Cancer Prevention and Control

In response to the urgency of the rising incidence of cancer, global public health organizations are taking action. Each year on February 4, the American Cancer Society works with its strategic partner, the Union for International Cancer Control (UICC), to raise awareness of cancer prevention through World Cancer Day. At the World Cancer Congress in 2006 in Washington DC, the global cancer community united behind a call for urgent action to deal with the growing worldwide cancer burden by launching the first World Cancer Declaration, which outlined the steps to reverse the global cancer crisis by 2020.12 The declaration was updated in 2011 to reflect the conclusions of a landmark high-level meeting of the UN General Assembly to address chronic noncommunicable diseases (NCDs), including cancer, as a major development challenge. Leaders from more than 120 nations committed to work to prevent, treat, and manage these diseases, and in 2013 the World Health Assembly adopted the World Health Organization (WHO) Global Action Plan on NCDs, emphasizing whole-of-society approaches to reduce the major drivers of preventable cancer. The plan also endorsed a global monitoring framework including nine voluntary global targets, such as decreasing premature mortality from NCDs by 25% by 2025. Following this advance, the World Cancer Declaration was refreshed in 2013 to align with the global NCD framework and the evolving discourse on NCDs. The updated declaration targets resonate more widely with the cancer community, as well as partners in other development sectors aside from health, to support more innovative partnerships and collaborations.

A balanced approach to cancer control includes prevention, early detection, and effective treatment, including palliative care.¹³ Successful national cancer control policies and programs raise awareness of cancer, reduce exposure to cancer risk factors,

Table 5. Five-year Net Survival Rates* (%) for Selected Cancers among Adults 15 Years of Age and Older in Select Countries, 2005-2009

	Stomach	Colon	Rectum	Liver	Lung	Female Breast	Cervix	Ovary	Prostate	Leukemia
Africa										
Algerian registries	10 [†]	57 [†]	46^{\dagger}	18†	15 [†]	60 [†]	55 [†]	42 [†]	59†	14 [†]
South Africa (Eastern Cape)	_	_	_	10 [†]	19†	53	55	91 [†]	100 [†]	_
Asia										
Chinese registries	31	55	53	13	18	81	60	39	64	21
Indian registries	19	37	29	4	10	60	46	14†	58	6^{\dagger}
Indonesia (Jakarta)	18	28	58	20	12 [†]	78	65	40 [†]	44	40
Israel	29	69	67	14^{\dagger}	24	87	66	42	94	50
South Korea	58	66	66	20	19	83	77	44	82	23
Mongolia	15	31	16	9	7	57	60	52	40	36
Thai registries	12	50	40	8	8	71	56	41	58	14
Turkey (Izmir)	17	53	45	14	10	79	61	39	81	33
Northern America										
Canada	25	63	63	18	17	86	67	38	92	55
US registries	29	65	64	15	19	89	63	41	97	52
Central and South America										
Brazilian registries	25	58	56	12 [†]	18	87	61	32	96	20 [†]
Chilean registries	18	43	38	8 [†]	6	77	51	32	89	16
Colombian registries	17	43	_	5	9	76	59	31	79	20
Ecuadorian registries	32 [†]	68	53	18†	29 [†]	83	62	47	92	34
Europe										
Austria	33	63	62	13	18	83	66	42	91	46
Belgium	33	65	65	20	17	85	65	43	93	59
Czech Republic	23	55	50	7 [†]	12	80	65	37	83	46
Denmark	18	56	58	6	11	82	65	37	77	57
Finland	25	63	63	8	12	87	65	45	93	51
German registries	32	65	62	14	16	85	65	40	91	54
Italian registries	32	63	60	18	15	86	68	39	90	47
Poland	19	50	47	10 [†]	13	74	53	34	74	49
Slovenia	27	56	55	5	11	80	69	38	78	38
Spanish registries	27	59	58	16	13	84	65	38	87	52
United Kingdom	19	54	57	9	10	81	60	36	83	47
Oceania										
Australian registries	28	64	64	15	15	86	67	38	89	51
New Zealand	27	62	61	17	12	84	64	34	89	58

^{*}Survival rates are age-standardized. †Data are subject to limitations. Please see source.

Source: Allemani C, Weir HK, Carreira H, et al. Global surveillance of cancer survival 1995-2009: analysis of individual data for 25,676,887 patients from 279 populationbased registries in 67 countries (CONCORD-2). Lancet. 2014. doi:10.1016/S0140-6736(14)62038-9

American Cancer Society, Inc., Surveillance Research, 2015

provide information and support for the adoption of healthy lifestyles, and increase the proportion of cancers detected early. The WHO emphasizes that countries should consider the following four broad approaches based on their economic development when creating national strategies for controlling cancer.14

Prevention: The goal of prevention is to reduce or eliminate exposure to cancer-causing agents, which include modifiable factors related to tobacco use, nutrition, physical inactivity, occupational exposures, and infections. Primary prevention

offers the greatest public health potential and the most costeffective, long-term cancer control. Approaches to primary prevention include immunization against, or treatment of, infectious agents that cause cancer; application of effective tobacco control measures; reduction of excessive alcohol consumption; maintenance of healthy body weight and physically active lifestyles; promotion of a healthy diet; avoidance of excess sun exposure and indoor tanning; and reduction in occupational exposure to carcinogens. The WHO has assessed public health interventions and declared the hepatitis B vaccination

Table 6. Stage Distribution (%) for Breast Cancer in Selected Countries

Country	Stage I	Stage II	Stage III	Stage IV
Brazil (2008-2009)†	20	47	28	5
Canada (2000-2007)*	41	38	13	8
China (1999-2008)†	19	55	23	3
Denmark (2000-2007)*	29	47	16	8
Egypt (South Cancer Inst., 2001-2008) [†]	11	39	25	25
Iraq (Kurdistan, 2006-2008)†	5	53	32	10
Libya (2008-2009)†	9	26	54	12
Malaysia (E. coast and Kuala Lumpur, 2005-2007)†	5	39	45	11
Nigeria (Lagos, 2009-2010)†	6	15	63	16
Thailand (2009)†	12	38	41	9
United Kingdom (2000-2007)*	40	45	9	5
United States (2004-2010)*	48	34	13	5

Percentages corrected to exclude stage 0 and unknown stage. Percentages may not sum to 100 due to rounding. *Population-based data. †Hospital-based data. Sources: China: Wang, Q., et al. (2012). "Breast cancer stage at diagnosis and area-based socioeconomic status: a multicenter 10-year retrospective clinical epidemiological study in China." BMC Cancer 12: 122. Brazil: Liedke, P. E., et al. (2014). "Outcomes of breast cancer in Brazil related to health care coverage: a retrospective cohort study." Cancer Epidemiol Biomarkers Prev 23(1): 126-133. Canada, Nigeria, Thailand, Denmark, United Kingdom, Egypt, Iraq, Libya, Malaysia: Unger-Saldana, K. (2014). "Challenges to the early diagnosis and treatment of breast cancer in developing countries." World J Clin Oncol 5(3): 465-477. **United States:** Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence - SEER 18 Regs Research Data + Hurricane Katrina Impacted Louisiana Cases, Nov 2013 Sub (1973-2011 varying) - Linked To County Attributes - Total U.S., 1969-2012 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, Surveillance Systems Branch, released April 2014 (updated 5/7/2014), based on the November 2013 submission.

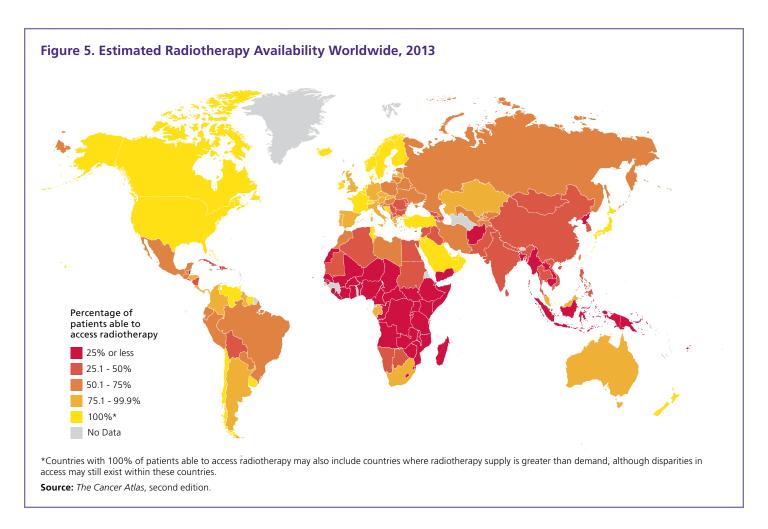
American Cancer Society, Inc., Surveillance Research, 2015

and cervical cancer screening to be "best buys" because they have a potentially large public health impact while being costeffective, inexpensive, and feasible to implement.¹⁵

The Framework Convention on Tobacco Control (FCTC), the first health treaty negotiated under the auspices of the WHO, was promulgated in May 2003 in response to the global tobacco pandemic with the objective of substantially reducing the worldwide prevalence of tobacco use and exposure to tobacco smoke. The FCTC provides a framework for national legislation and enforcement of tobacco control measures. As of October 2014, 179 out of 196 eligible countries had ratified the treaty, representing approximately 89% of the world population. A number of major tobacco-producing nations, including Argentina, Indonesia, Zimbabwe, and the United States, have not ratified the treaty. FCTC provisions establish international standards for tobacco taxation; tobacco advertising and sponsorship; regulation of tobacco products; tobacco product disclosure; packaging and labeling; education, communication, training, and public awareness; cessation measures; measures to eliminate illicit trade; sales to minors; support for economically viable alternatives; liability issues; and scientific and technical cooperation and exchange of information.16

The WHO also adopted the Global Strategy on Diet and Physical Activity in 2004. The four main objectives of the strategy are to: 1) Reduce risk factors for chronic diseases that stem from unhealthy diet and physical inactivity through public health actions. 2) Increase awareness and understanding of the influences of diet and physical activity on health. 3) Develop, strengthen, and implement global, regional, and national policies, as well as action plans, to improve diets and increase physical activity that are sustainable, comprehensive, and actively engage all sectors. 4) Monitor science and promote research on diet and physical activity.17

Early detection: The main objective of early detection is to diagnose precancerous changes or early stage cancers when they can be treated most effectively. Early detection is only valuable if it leads to timely diagnostic follow-up and effective treatment. Strategies for early detection through screening include: 1) opportunistic screening requested by a physician or an individual or 2) organized screening in which a defined population is contacted and invited to be screened at regular intervals. In practice, many cancer screening programs have elements of each of these approaches.¹⁸ Cancers that have proven early detection tests include cervix, colon and rectum, breast, and lung (among long-term and/or heavy smokers). However, wide implementation of screening for these cancers has not been fully achieved even in economically developed countries. Lung cancer screening in particular, due to the technical expertise and infrastructure required, is unlikely to be feasible in developing countries in the near future. The Institute of Medicine of the National Academies recommends that low-resource countries that cannot afford the infrastructure required for organized screening programs should focus on increasing awareness of signs and symptoms of cancer in the general population to promote earlier diagnosis and treatment. 19 In developing countries, cervical cancer is one of the most important health problems for women. The WHO provides a variety of resources to assist countries with comprehensive cervical cancer control program implementation. If Pap test screening for cervical cancer is considered in developing countries, it should focus primarily on women 30 years of age or older since these women are generally at highest risk of developing the disease or precancerous lesions.²⁰ Methods of screening for cervical cancer using visual inspection with acetic acid and HPV testing may be effective and affordable in developing countries;²¹ work is ongoing to make HPV testing in particular available at a low price.²² One study found that once-in-a-lifetime screening with these methods at age 35 reduces lifetime cervical cancer risk by 25% to 36%.²³



Diagnosis and treatment: Cancer diagnosis, including careful clinical and pathological assessments, is the first step to cancer management. Once a diagnosis is confirmed, the cancer must be staged to determine treatment options and prognosis, and to apply the appropriate research treatment protocols. The primary modalities of cancer treatment are surgery, chemotherapy, radiotherapy, hormone therapy, immune therapy, and targeted therapy; these may be used alone or in combination.

There is increasing emphasis worldwide on the development of specialized cancer centers that apply evidence-based multimodal therapies and provide rehabilitation and palliative care. The International Atomic Energy Agency has created a Programme of Action for Cancer Therapy that advises developing countries in the fight against cancer by integrating radiotherapy into sustainable comprehensive cancer control programs. Many countries, especially low- and middle-income countries, do not have sufficient radiotherapy centers to provide treatment for all of the cancer patients in need (Figure 5).

Palliative care: In low-resource countries, the majority of cancer patients are diagnosed with advanced-stage disease. For these patients, the only effective treatment options are pain relief and palliative care. The most basic approach to palliative care for terminally ill cancer patients, especially in low-resource settings, involves using inexpensive oral pain medications ranging from aspirin to opiates, depending on individual patient needs.

Unfortunately, sufficient access to opioid drugs for use in palliative care is often not available in resource-limited countries because of regulatory or pricing obstacles, lack of training and knowledge among health workers, and weak health care systems. The WHO has developed guidelines for cancer pain management based on the three-step analgesic ladder. These steps comprise a sequential approach according to the individual pain intensity, which begins with non-opioid analgesics and progresses to increasing-strength opioids for moderate and severe pain. When pain treatment is administered according to the ladder, it is effective in 80-90% of patients.²⁴ The WHO also elaborated on guidelines for assessing national drug policies to ensure the availability of opioids for medical and scientific use, while at the same time safeguarding against abuse and diversion.²⁵ The WHO has played an important role in encouraging effective pain management and monitoring the availability of opioids internationally.26 Surgery, chemotherapy, and radiotherapy are also important components of palliative care. Radiotherapy in particular is often used for pain relief without curative intent.27,28

Selected Cancers

Breast (see Special Section on page 37)

Childhood Cancer

Although childhood cancers are rare, they are one of the leading causes of childhood death in developed countries such as the United States. Childhood cancer is generally not a public health priority in most developing countries. With the burden of HIV/ AIDS, malaria, and other infectious diseases - even the lack of clean drinking water - treatment for cancer is often regarded as unaffordable. In developing countries, many children who have cancer are never diagnosed, are diagnosed too late for treatment to be effective, or go without treatment because it is limited or unavailable. The Union for International Cancer Control (UICC) My Child Matters initiative aims to improve the early diagnosis, treatment, care, and support of children with cancer in the developing word. Projects focus on disseminating information about cancer in children to health professionals, children's organizations, and the general public; improving early diagnosis and access to health care; and strengthening support for children with cancer and their families.²⁹ In addition, the International Network for Cancer Treatment and Research (INCTR) has established networks for acute lymphocytic leukemia, retinoblastoma, and Burkitt lymphoma. Partnerships between institutions in high- and lower-income countries, such as the Asociación de Hemato-Oncología Pediátrica de Centro América, have also been successful in improving outcomes for children with cancer.30

New cases: An estimated 163,300 new cancer cases occurred among children 0-14 years of age in 2012. Childhood cancer incidence rates are generally higher in developed than in developing countries. 1 It is more difficult to measure the incidence of childhood cancer accurately in developing countries, where cases are often unreported due to the greater frequency of death from infectious diseases and malnutrition.31 However, the great majority of children, and 84% of children with cancer, live in developing countries.1 Leukemia is the most common form of cancer among children in most parts of the world, except in Africa, where non-Hodgkin lymphomas (including Burkitt lymphoma) predominate (Figure 6).

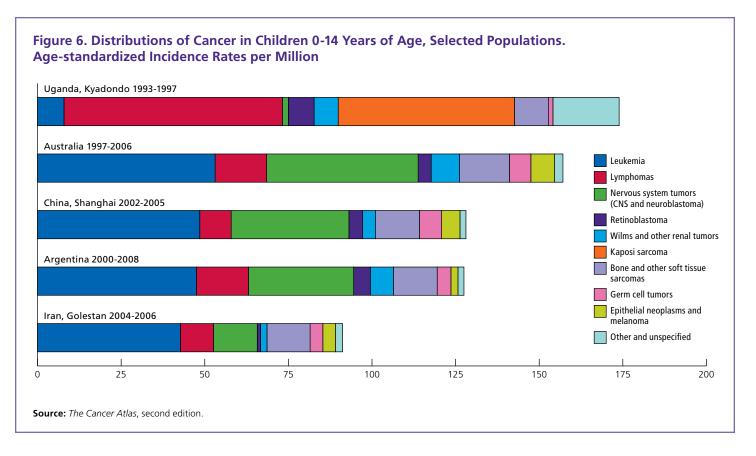
Deaths: Worldwide, about 80.000 children died from cancer in 2012. Mortality rates are lowest in developed countries, despite higher incidence rates, because of the availability of high-quality diagnosis and treatment.^{1,31} Cancer is emerging as a major cause of childhood death in Asia, Central and South America, North Africa, and the Middle East, where fewer children are dying from preventable infectious diseases.

Global trends: Mortality rates for childhood cancer in general, and childhood leukemia in particular, have sharply declined in Northern America, Europe, Oceania, and Japan over the past 40 years because of improvements in disease management, including diagnosis and treatment.32 Concern has been raised in the United States and Europe that overall incidence rates of childhood cancer have been increasing since 1970. In the United States, the incidence rate increased about 35% between 1975 and 2011.33 The reasons for these trends are largely unknown, although they may be in part the result of improved diagnosis and reporting methods. In developing countries, incidence and mortality trends for childhood cancers are much more difficult to analyze due to inadequate reporting and competing causes of death.32,34

Risk factors: The causes of most childhood cancers are unknown. Some relatively rare cancers are known to be attributable to inherited genetic conditions. Exposure to ionizing radiation is a risk factor for several types of leukemia. In recent years, a number of studies have demonstrated associations between fetal growth and/or high birth weight and childhood and adolescent cancers, while low birth weight has been associated with acute myeloid leukemia and some CNS tumor subtypes.³⁵ Worldwide, the most common examples of infection-related childhood cancers are Burkitt lymphoma, Hodgkin lymphoma and nasopharyngeal carcinoma (all associated with Epstein-Barr virus), liver carcinoma (HBV), and Kaposi sarcoma (human herpes virus 8). Some of these cancers, such as Burkitt lymphoma and Kaposi sarcoma, are the most common childhood cancers in some parts of developing countries, but account for a very small proportion of childhood cancer in Western countries.

Early detection: The early diagnosis of childhood cancer is often hampered by nonspecific symptoms that are similar to those of more common childhood diseases. Parents should ensure that children have regular medical checkups and be alert to any unusual, persistent symptoms. Signs and symptoms of childhood cancer include an unusual mass or swelling; unexplained paleness or loss of energy; a sudden increase in the tendency to bruise or bleed; a persistent, localized pain or limping; a prolonged, unexplained fever or illness; frequent headaches, often with vomiting; sudden eye or vision changes; and excessive, rapid weight loss. Major categories of pediatric cancer (including benign brain tumors) and more specific symptoms include:

- · Leukemia, which may manifest as bone or joint pain, weakness, pale skin, bleeding or bruising, and fever or infection
- · Brain and other central nervous system tumors, which may cause headaches, nausea, vomiting, blurred or double vision, seizures, dizziness, and difficulty walking or handling objects



- Non-Hodgkin lymphoma and Hodgkin lymphoma, which are most common in children during adolescence, affect lymph nodes but may involve the bone marrow and other organs; may cause swelling of lymph nodes in the neck, armpit, or groin, as well as general weakness and fever
- Neuroblastoma, a cancer of the nervous system that is most common in children younger than 5 years of age and usually appears as a swelling in the abdomen
- Wilms tumor, a kidney cancer (also called nephroblastoma) that may be recognized by a swelling or lump in the abdomen
- Rhabdomyosarcoma, 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
- Osteosarcoma, a bone cancer that most often occurs in adolescents and commonly appears as sporadic pain in the affected bone that may worsen at night or with activity, with eventual progression to local swelling
- Retinoblastoma, an eve cancer that usually occurs in children younger than 5 years of age and is typically recognized because the pupil appears white or pink instead of the normal red color in flash photographs or during examination with an ophthalmoscope
- Ewing sarcoma, another type of cancer that usually arises in bone, is most common in adolescents, and typically appears as pain at the tumor site.

- Kaposi sarcoma, a cancer that develops from the cells that line lymph or blood vessels, is characterized by purple, red, or brown lesions on the skin and in some cases causes painful swelling, especially in the legs, groin area, or skin around the eyes.
- · Burkitt lymphoma, which is endemic in many countries of sub-Saharan Africa and occurs with a considerable frequency (although it is rare in developed countries), usually first recognized by swelling of the lymph nodes in the neck, groin, or under the arm

Treatment: Childhood cancers can be treated by one or more therapies (surgery, radiation, and chemotherapy/targeted therapy) based on the type and stage of cancer. In countries with highly developed medical systems, treatment is coordinated by a team of experts, including pediatric oncologists and nurses, social workers, psychologists, and others trained to assist children and their families. Because these cancers are uncommon, outcomes are most successful when treatment is managed by specialists at a children's cancer center.

Treatment for childhood cancer can be expensive, although evidence shows that in low- and middle-income countries, it can be achieved at a fraction of the cost of that in developed countries.³¹ For example, Burkitt lymphoma can be treated in children in sub-Saharan Africa for as little as \$50 US dollars per patient.³⁶ Governments should be encouraged to make the necessary investments to address the limited access to cancer therapy for many children in developing countries.31

Table 7. Five-year Observed Survival Rates (%) for Select Childhood Cancers (0-14 years) in European Regions and the United States

	Northern Europe (2005-2007)	UK and Ireland (2005-2007)	Central Europe (2005-2007)	Southern Europe (2005-2007)	Eastern Europe (2005-2007)	US (2005-2007)
Lymphoid leukemia	87	89	90	87	80	89
Acute myeloid leukemia	67	67	67	67	49	64
Hodgkin lymphoma	95	97	97	96	91	97
Non-Hodgkin lymphoma	87	89	87	84	78	88
Burkitt lymphoma	95	93	94	96	85	92
All CNS tumors	65	54	57	65	55	72
Neuroblastoma	80	65	70	72	62	79
Retinoblastoma	95*	99*	99*	100*	81*	97
Wilms tumor	86	91	94	86	84	-
Osteosarcoma	62 [†]	67 [†]	71 ⁺	57 [†]	56 [†]	71
Ewing sarcoma	71	68	70	74	46	75
Rhabdomyosarcoma	69	64	76	78	39	68

CNS = central nervous system. *Children aged 0-4 years only. †Children aged 10-14 years only.

Sources: Europe: Gatta, G., et al. (2014). "Childhood cancer survival in Europe 1999-2007: results of EUROCARE-5 – a population-based study." Lancet Oncol 15(1): 35-47. US: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence - SEER 18 Regs Research Data + Hurricane Katrina Impacted Louisiana Cases, Nov 2013 Sub (1973-2011 varying) - Linked To County Attributes - Total U.S., 1969-2012 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, Surveillance Systems Branch, released April 2014 (updated 5/7/2014), based on the November 2013 submission.

American Cancer Society, Inc., Surveillance Research, 2015

Survival: Survival from childhood cancer largely depends on timely diagnosis and the availability of effective treatment,³⁷ although rates also vary considerably depending on cancer type, patient age, and other characteristics. Significant advances have been made in diagnosis and therapy during the past four decades. Relative survival rates for most of Europe are similar to those in the United States, although they are lower in Eastern Europe (Table 7). In general, overall survival rates are much lower in the developing world. The estimated overall five-year relative survival rates for childhood cancer were 40% in Chennai, India (1990-2001); 55% in Thailand (2003-2005); and 56% in Shanghai, China (2002-2005).³⁸⁻⁴⁰ Among those who survive childhood cancers, side effects of treatment and quality of life are important issues, as childhood cancer treatments can have significant lifelong neurologic, developmental, and reproductive effects.35

Colon and Rectum

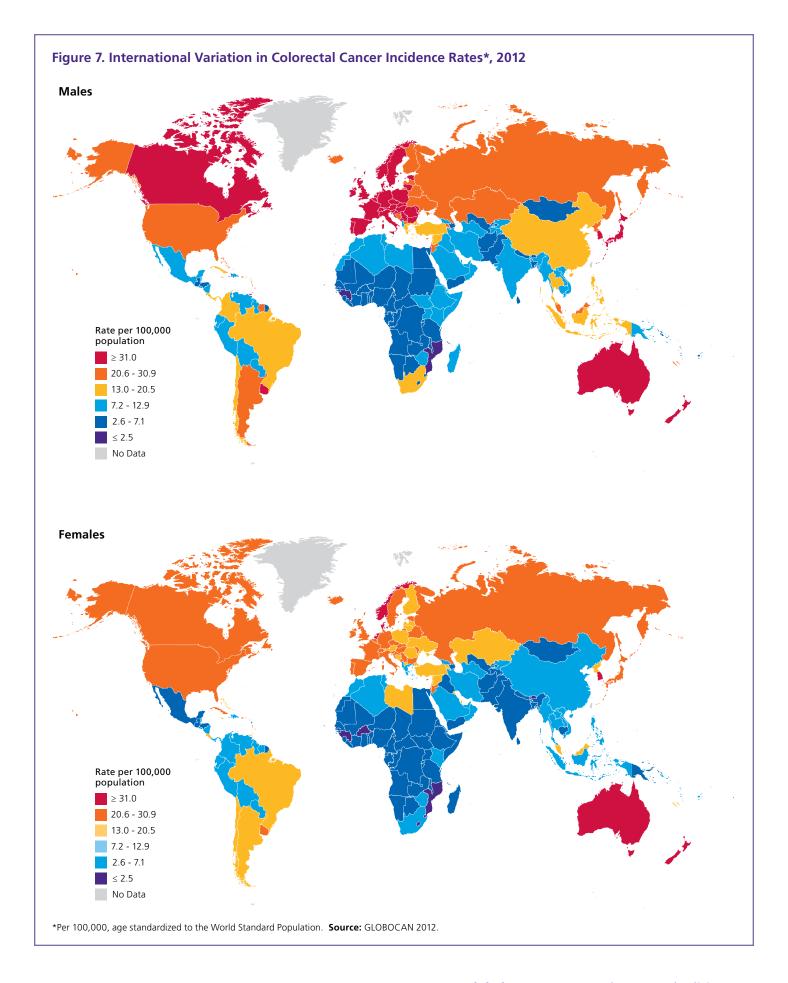
New cases: Colorectal cancer is the third most common cancer in men and the second in women. Worldwide, an estimated 1.4 million cases of colorectal cancer occurred in 2012. The highest incidence rates were in Northern America, Australia, New Zealand, Europe, and South Korea (Figure 7). Rates were low in Africa and South Central Asia.

Deaths: About 693,900 deaths from colorectal cancer occurred in 2012 worldwide, accounting for 8% of all cancer deaths.

Global trends: The incidence of colorectal cancer is increasing in certain countries where risk was historically low (e.g., Japan).41 The greatest increases are in Asia (Japan, Kuwait, and Israel) and Eastern Europe (Czech Republic, Slovakia, and Slovenia). In fact, incidence rates among males in the Czech Republic, Slovakia, and Japan have exceeded the peak rates observed in longstanding developed countries, such as the United States, Canada, and Australia, and continue to increase. 41 In high-risk/high-income countries, trends over the past 20 years have either gradually increased (Finland and Norway), stabilized (France and Australia), or declined (United States) with time. The decrease in colorectal cancer incidence in the United States among those 50 years of age and older partially reflects the increase in detection and removal of precancerous lesions through screening.⁴² In contrast to the stabilizing rates observed in most Western and Northern European countries, relatively large increases have been observed in Spain, which may be related to the increasing prevalence of obesity in recent years in that country.^{43,44} The increase in several Asian and Eastern European countries may also reflect increased prevalence of risk factors for colorectal cancer associated with westernization such as unhealthy diet, obesity, and smoking.45

In contrast to incidence trends, decreasing colorectal cancer mortality rates have been observed in a large number of countries worldwide and are most likely due to colorectal cancer screening and/or improved treatments. However, increases in mortality rates are still occurring in countries that have more limited resources, including Brazil and Chile in South America and Romania and Russia in Eastern Europe. 45

Signs and symptoms: Early stage colorectal cancer typically does not have symptoms, which is why screening is usually nec-



essary to detect this cancer early. Symptoms may include rectal bleeding, blood in the stool, a change in bowel habits or stool shape (e.g., narrower than usual), the feeling that the bowel is not completely empty, cramping pain in the lower abdomen, decreased appetite, or weight loss. In some cases, blood loss from the cancer leads to anemia (low red blood cells), causing symptoms such as weakness and excessive fatigue. Timely evaluation of symptoms consistent with colorectal cancer is essential.

Risk factors: The risk of colorectal cancer increases with age. Modifiable factors associated with increased risk include obesity, physical inactivity, moderate to heavy alcohol consumption, long-term smoking, high consumption of red or processed meat, low calcium intake, and very low intake of whole-grain fiber, fruit, and vegetables. Hereditary and medical factors that increase risk include a personal or family history of colorectal cancer and/or polyps, a personal history of chronic inflammatory bowel disease (e.g., ulcerative colitis or Crohn disease), certain inherited genetic conditions (e.g., Lynch syndrome [also known as hereditary nonpolyposis colorectal cancer or HNPCC] and familial adenomatous polyposis [FAP]), and type 2 diabetes.

Regular use of nonsteroidal anti-inflammatory drugs, such as aspirin, reduces risk. However, these drugs are not recommended for the prevention of colorectal cancer among individuals at average risk because they can have serious adverse health effects, such as stomach bleeding. Accumulating evidence suggests that use of menopausal hormone therapy (particularly combined estrogen and progesterone) also lowers risk. However, hormone therapy is not recommended for the prevention of colorectal cancer because it increases risk of breast cancer, stroke, heart attack, and blood clots.

Prevention and early detection: Screening can detect colorectal polyps that can be removed before becoming cancerous, as well as detect cancer at an early stage, when treatment is usually less extensive and more successful. The current recommendation for colorectal cancer screening in most countries is to begin screening at age 50 for men and women who are at average risk for developing colorectal cancer. People at higher risk should begin screening at a younger age and may need to be tested more frequently.

There are several accepted screening options, which include fecal occult blood test (FOBT), flexible sigmoidoscopy, doublecontrast barium enema, stool DNA test, and colonoscopy. These tests differ with respect to the need for bowel preparation, test performance and limitations, frequency of administration, and cost. While colonoscopy is a highly sensitive test, it requires a skilled examiner, involves greater cost, is less convenient, and has more risk for the patient compared with other tests.⁴⁶ Therefore, FOBT, which is inexpensive and easy to perform, is a more practical screening option in many areas of the world.⁴⁵ Country-specific colorectal cancer screening programs, recommendations, and guidelines vary greatly worldwide. While some countries have implemented national screening programs (Australia, Czech Republic, Germany, Israel, Japan, Poland, South Korea, and the United Kingdom), the majority of initiatives consist of recommendations and/or guidelines with opportunistic screening. 45,47 However, ongoing regional research studies and/or pilot studies are in place in many countries (United States, Canada, Belgium, Finland, France, Italy, Norway, Spain, Switzerland, Thailand, and Taiwan) with the intent to evaluate the potential for implementing colorectal cancer screening programs. Additionally, studies are underway to evaluate alternatives to FOBT. For instance, a randomized trial in the United Kingdom reported one-time flexible sigmoidoscopy screening between 55 and 64 years of age reduced colorectal cancer incidence by 33% and mortality by 43%.⁴⁸ Colorectal cancer screening initiatives are scarce in Africa, Asia, and South America.

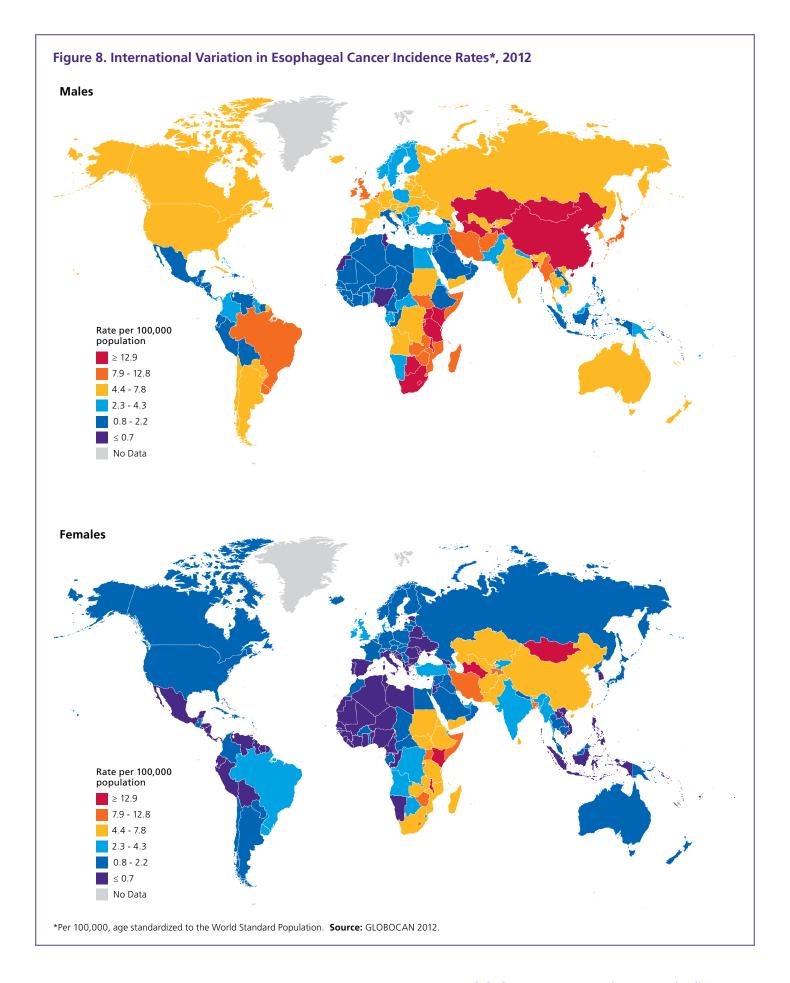
Other preventive measures for colorectal cancer include maintaining a healthy body weight, being physically active, minimizing consumption of red and processed meat and alcohol, and not smoking.

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 waste) is rarely needed for colon cancer and is infrequently required for rectal cancer. Chemotherapy alone, or in combination with radiation, is given before (neoadjuvant) or after (adjuvant) surgery to most patients whose cancer has penetrated the bowel wall deeply or spread to lymph nodes.

Survival: Survival rates for colorectal cancer vary worldwide. In Northern America, Australia/New Zealand, and many countries of Europe, colon and rectum five-year net survival is about 60% to 65% (Table 5, page 9). In Asia, five-year colon and rectal cancer survival rates of more than 65% have been reported in Israel and South Korea, while they range from about 20% to 55% in remaining countries (Table 5, page 9). Survival is much higher when colorectal cancer is detected at an early stage; however, fewer than half are diagnosed early, even in developed countries, mainly due to suboptimal screening rates. For example, about 40% of colorectal cancers are diagnosed at an early stage in Canada, Denmark, and the United Kingdom.49

Esophagus

New cases: An estimated 455,800 new cases occurred in 2012 worldwide. Esophageal cancer incidence rates vary internationally by more than 50-fold. The highest rates are found in Asia, including China and Central Asia, and in East and South Africa. The lowest rates are found in Western Africa in both men and women and in parts of Europe and South America in women (Figure 8). Esophageal cancer is usually three to four times more common among men than women. The two main types of esophageal cancer are squamous cell carcinoma and ade-



nocarcinoma. In the highest-risk area, often referred to as the "esophageal cancer belt," which stretches from Northern Iran through the Central Asian republics to North-Central China, 90% of cases are squamous cell carcinomas, compared with about 26% in the United States. $^{\rm 33,50-52}$

Deaths: About 400,200 people died from esophageal cancer in 2012, with more than 80% of those deaths occurring in developing countries.

Global trends: Geographic variations in the incidence rates of esophageal cancer are larger than for any other cancer. Temporal trends also vary greatly. For example, while the incidence of esophageal squamous cell carcinoma has been increasing in some Asian countries, such as Taiwan,53 it has been steadily declining in Northern America and Europe due to reductions in alcohol and tobacco use.54-56 In contrast, the incidence of adenocarcinoma of the esophagus has been increasing rapidly in Western countries, such as the United States, Australia, France, and England, in recent decades, most likely as a result of increases in overweight/obesity, chronic gastric reflux, and the premalignant condition Barrett's esophagus.⁵⁷ These increases may also be related to the declining prevalence of *H. pylori* infection, as *H. pylori* appears to be associated with a reduced risk of esophageal adenocarcinoma.58-60

Signs and symptoms: Esophageal cancer usually has no signs or symptoms in the early stages of the disease. When cancer is more advanced, the most common signs are painful or difficult swallowing and weight loss.

Risk factors: The primary risk factors for squamous cell esophageal cancer in Western countries are heavy drinking and smoking, which account for almost 90% of total cases. In high-risk areas, such as Golestan (Iran) and Linxan (China), contributing risk factors are not well understood, but are thought to include poor nutritional status, low intake of fruits and vegetables, and drinking beverages at high temperatures.⁶¹⁻⁶⁴ HPV infection has been detected in squamous cell carcinomas, particularly in high-risk areas in Asia. However, more research is needed to determine whether HPV or other infectious agents increase risk.65-68

The main known risk factors for esophageal adenocarcinoma are overweight and obesity and chronic gastroesophageal reflux disease (GERD). GERD (when stomach contents enter the lower section of the esophagus) irritates the esophagus and, over time, can lead to Barrett's esophagus, a condition in which the cells lining the lower part of the esophagus have changed or been replaced with abnormal cells that could lead to adenocarcinoma of the esophagus. Nevertheless, only a small proportion of those with Barrett's esophagus go on to develop esophageal cancer. 69 GERD is more common in overweight men and women. Smoking and low fruit and vegetable consumption are also risk factors for adenocarcinoma of the esophagus.

Prevention and early detection: Eliminating the use of tobacco and reducing alcohol consumption, maintaining a healthy body weight, and being physically active are the best ways to reduce the incidence of esophageal cancer. In addition, a healthy diet rich in fruits and vegetables may lower a person's risk. Research is ongoing to determine whether surveillance of those with Barrett's esophagus is a feasible method to reduce esophageal cancer mortality.70,71 Treating gastric reflux with proton pump inhibitor drugs or surgery may prevent Barrett's esophagus, although preventive measures once Barrett's esophagus has developed have not been shown to prevent esophageal cancer.⁵⁷ Further risk factor studies are necessary to elucidate primary prevention measures in high-risk areas (Northern Iran and Central Asia) because the prevalence of established major risk factors for esophageal cancer (smoking and alcohol intake) is low in those regions.

Treatment: Options for treatment include surgery, radiation therapy, chemotherapy, targeted therapy, and endoscopic treatments. Palliative treatment may also be used to relieve symptoms, such as pain and trouble swallowing.

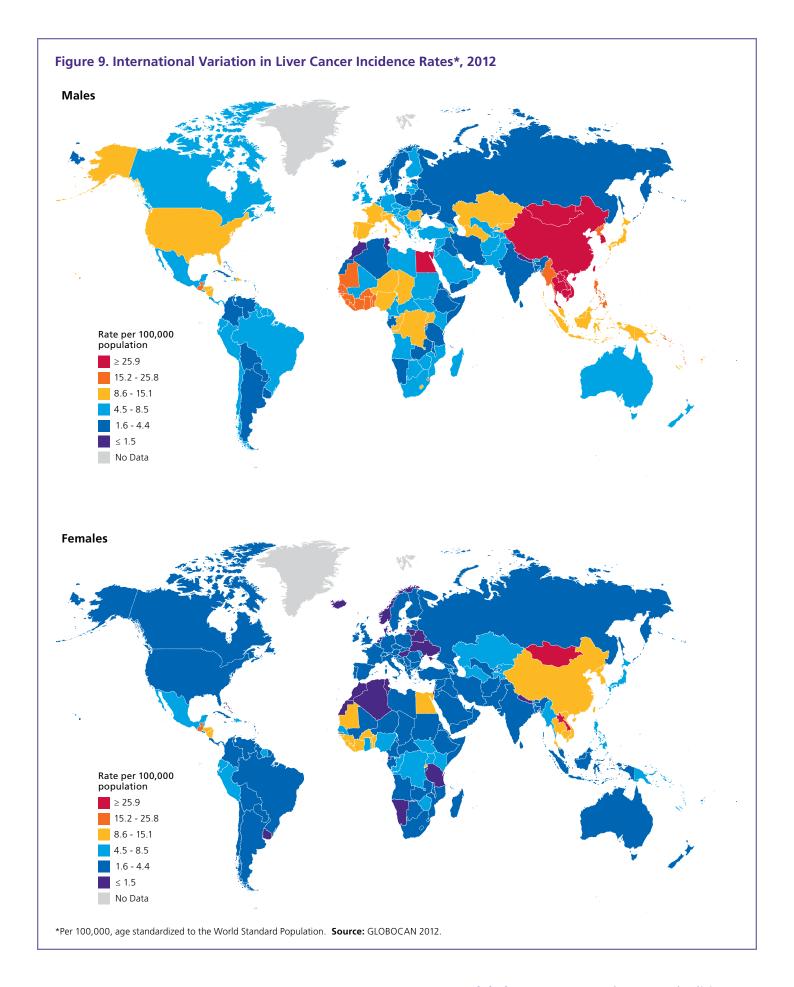
Survival: Most people with esophageal cancer eventually die of the disease because it is usually diagnosed at a late stage. In the United States, 18% of white patients and 12% of black patients survive (relative survival) at least five years after diagnosis.³³ In Europe, the average five-year relative survival rate is 12%.⁷²

Liver

New cases: Liver cancer is the fifth most common cancer in men and the ninth in women. An estimated 782,500 new liver cancer cases occurred in the world during 2012, with China alone accounting for about 50% of the total. Rates are more than twice as high in men as in women. Liver cancer rates are the highest in Central America, West and Central Africa, and East and Southeast Asia (Figure 9). Most primary liver cancers occurring worldwide are hepatocellular carcinoma (HCC), which likely accounts for 70% to 90% of cases. 73 One type of liver cancer (cholangiocarcinoma) that is rare in most parts of the world has high incidence rates in Thailand and other parts of Asia due to the high prevalence of liver fluke infection.

Deaths: Worldwide, liver cancer is the second leading cause of cancer death in men and the sixth leading cause among women, with about 745,500 deaths in 2012.

Global trends: Liver cancer incidence is increasing in areas with historically low rates, including parts of Oceania, Western Europe, and Northern America. In the United States, age-adjusted incidence rates of liver cancer more than tripled between 1975 and 2011.33 This increase is thought to be attributable to increases in chronic hepatitis C virus (HCV) infection due to injection drug abuse, which was common in the 1960s and 1970s, or possibly increases in the prevalence of obesity and



diabetes mellitus.74,75 In contrast, liver cancer rates are decreasing in some historically high-risk areas, including China and Japan, most likely due to reductions in hepatitis C virus (HCV) infection in Japan and hepatitis B virus (HBV) infection in China through improved hygiene and sanitation conditions.⁷⁶ A more than 80% decline in liver cancer incidence rates among youth and young adults in Taiwan has been reported as a result of a universal HBV childhood vaccination program begun in 1984.77 However, HBV vaccination programs cannot be responsible for the decreasing liver cancer rates among adults in most parts of Asia because of their relatively recent implementation.

Signs and symptoms: Common symptoms, which do not usually appear until the cancer is advanced, include abdominal pain and/or swelling, weight loss, weakness, loss of appetite, jaundice (a yellowish discoloration of the skin and eyes), and fever. Enlargement of the liver is the most common physical sign.

Risk factors: Liver cancer is strongly associated with chronic infection of HBV or HCV. Both HBV and HCV are transmitted by intimate person-to-person contact or direct contact with infectious blood or blood-derived body fluids. This can occur through contaminated injections or blood transfusions, sexual intercourse with an infected partner, birth to an infected mother, or contact with contaminated surfaces. Other risk factors for liver cancer include smoking, type 2 diabetes, and cirrhosis related to heavy alcohol consumption or non-alcoholic fatty liver disease (associated with obesity).75,78 A study in Europe estimated that almost half of HCC cases were attributable to smoking and about 20% were due to HCV infection.79

Additional risk factors for liver cancer, which are more prevalent in economically developing countries, include consumption of food contaminated with aflatoxin (a toxin produced by a fungus that infests grains, peanuts, soybeans, and corn that have been stored in warm, moist conditions) and infection with parasitic liver flukes. In 2008, an estimated 77% of about 750,000 liver cancers worldwide were attributable to HBV, HCV, and liver fluke infection, with about 68% of those cases occurring in less developed regions.2

Prevention and early detection: The primary causes of liver cancer can be prevented through public health measures, including vaccination, sanitary medical practices, healthy lifestyle choices, and environmental management strategies.

A vaccine that protects against HBV has been available since 1982. The WHO recommends that all countries include hepatitis B vaccine in routine infant immunization programs. By the end of 2012, 181 countries (93%) had introduced the hepatitis B vaccine into their national infant immunization schedules, with many countries achieving more than 80% coverage for the full recommended dose (Figure 10). While there is no vaccine available to protect against HCV, new antiviral therapies may prevent chronic infection among those with acute (new) infection. Hepatitis C prevention strategies include screening of blood, organ, and tissue donors for antibodies to HCV; adherence to infection control practices during all medical, surgical, and dental procedures; and needle-exchange programs for injection drug users. However, these preventive measures have not been implemented in many developing countries due to resource constraints. Among individuals who are already infected with HBV or HCV, a reduction in the risk of liver cancer has been shown with the use of antiviral treatments.^{75,80} However, these treatments may be costly and unfeasible in many low-resource countries.⁷⁵ The United States Centers for Disease Control and Prevention recommends a one-time test for HCV infection for all adults born between 1945 and 1965 because people in this birth cohort account for three-quarters of both HCV-infected individuals and HCV-related deaths in the United States.81

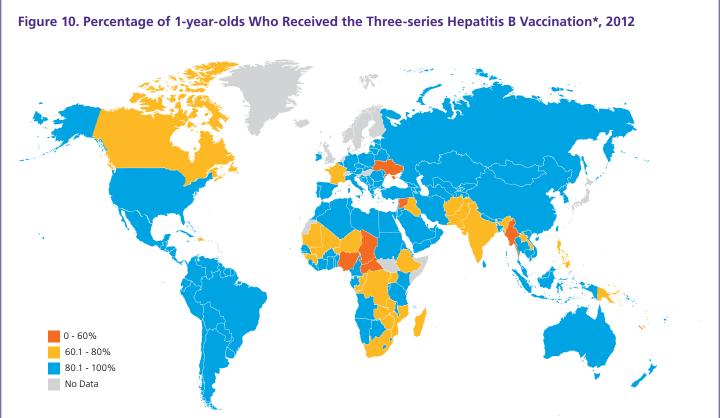
Additional preventive strategies also include avoiding smoking and limiting alcohol consumption. In economically developing countries, liver cancer can be prevented by reducing aflatoxin contamination of foods and preventing and treating parasitic infections with liver flukes. Crop substitution and improved grain storage practices have been used to reduce contamination with aflatoxin in areas such as sub-Saharan Africa. Mass drug administration and public health campaigns may contribute to prevention of cholangiocarcinoma, a highly fatal form of liver cancer caused by chronic infection by the liver fluke. 82,83

Screening for liver cancer has not been shown to reduce mortality. Nonetheless, many doctors in the United States screen individuals at high risk for the disease (e.g., those with cirrhosis) with ultrasound or blood tests.

Treatment: In countries with developed health care systems, early stage liver cancer can sometimes be treated successfully with surgery to remove part of the liver (partial hepatectomy); however, only a limited number of patients have sufficient healthy liver tissue for this option. Liver transplantation may be an option for individuals with small tumors who are not candidates for partial hepatectomy. Other treatments include ablation (tumor destruction) or embolization (blocking blood flow to the tumor).

Fewer treatment options exist for patients diagnosed at an advanced stage. Sorafenib (Nexavar) is a targeted drug approved for the treatment of HCC in patients who are not candidates for surgery and do not have severe cirrhosis.

Survival: Liver cancer is one of the most fatal cancers, with five-year survival rates less than 20% even in developed countries. Net survival ranges from less than 10% (India, Mongolia, Thailand, Chile, Colombia, Czech Republic, Denmark, Finland, Slovenia, United Kingdom) to about 20% (Jakarta, Indonesia; South Korea; Belgium) (Table 5, page 9).



*Countries with no data may represent countries where hepatitis B is not endemic (e.g. Scandinavian countries) and national hepatitis B vaccination programs have not been introduced.

Source: World Health Organization. Global Health Observatory Data Repository, Hepatitis B (HepB3) Immunization Coverage of 1-year-olds, Data by Country, 1985-2013 [online database]. Available from: http://apps.who.int/ghodata/, accessed November 14, 2014.

Lung and Bronchus

New cases: An estimated 1.8 million new cases occurred in 2012, accounting for about 13% of total cancer diagnoses. In males, the highest lung cancer incidence rates were in Northern America, Europe, Eastern Asia, and Uruguay, and the lowest rates were in sub-Saharan Africa (Figure 11, page 22). Among females, the highest lung cancer rates were in Northern America, Europe, Australia, New Zealand, North Korea, and China (Figure 11, page 22). Lung cancer rates in Chinese females (20.4 cases per 100,000 females) were higher than rates among females in some European countries despite a lower prevalence of smoking. This is thought to reflect indoor air pollution from unventilated coalfueled stoves and cooking fumes.84

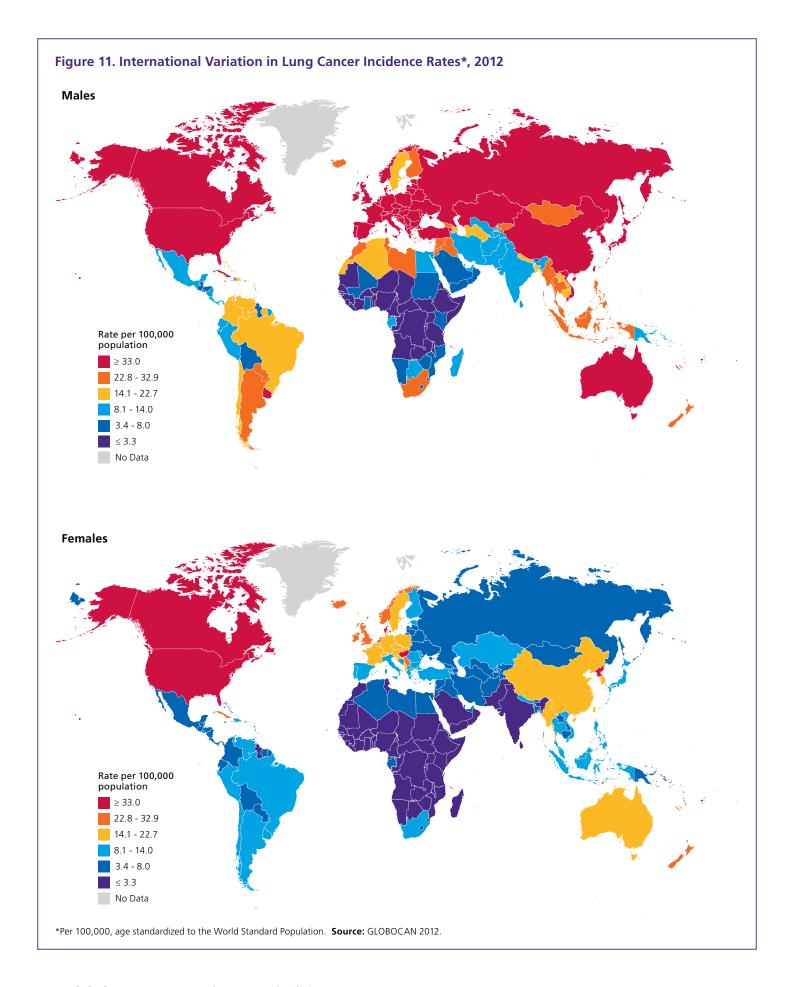
Deaths: Worldwide, lung cancer is the leading cause of cancer death in men and the second leading cause in women, with an estimated 1.6 million deaths in 2012 (1.1 million in men and 491,200 deaths in women). However, in developed countries, it is now the leading cause of cancer death in females, surpassing breast cancer.

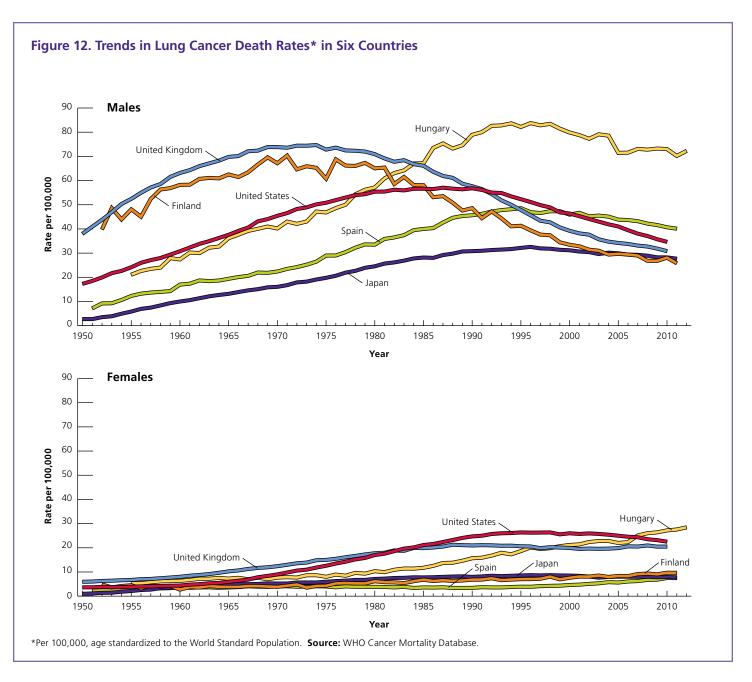
Global trends: International variations in lung cancer rates and trends largely reflect differences in the stage and degree of the tobacco epidemic.85-87 In several Western countries, where

the tobacco epidemic began earliest and peaked by the middle of the past century, such as the United States, the United Kingdom, and Denmark, lung cancer rates have been decreasing in men and plateauing in women.88-91 Lung cancer rates are also decreasing in men, but continuing to increase in women, in countries where the tobacco epidemic peaked later, such as Spain and Hungary (Figure 12, page 23).91 Sex differences in lung cancer trends reflect historic differences in patterns of smoking uptake and cessation. In contrast, in countries where the epidemic has been established more recently and smoking has just peaked or continues to increase, such as China, Indonesia, and several countries in Africa, lung cancer rates are likely to continue to increase for at least the next few decades without large-scale interventions to accelerate smoking cessation and reduce initiation.87,92,93

Signs and symptoms: Symptoms do not usually occur until the cancer is advanced, and may include persistent cough, sputum streaked with blood, chest pain, voice change, worsening shortness of breath, and recurrent pneumonia or bronchitis.

Risk factors: Cigarette smoking is by far the most important risk factor for lung cancer, accounting for about 80% of lung cancer deaths in men and 50% in women worldwide.94 Risk increases





with both quantity and duration of smoking. Cigar and pipe smoking also increase risk. Exposure to radon gas released from soil and building materials is the leading cause of lung cancer after smoking in Europe and Northern America (8%-15% of cases).95 Air pollution, both outdoor and indoor, is also a risk factor for lung cancer. Indoor air pollution due to the burning of solid fuels such as coal for heating and cooking, which occurs mostly in low- and middle-income countries, is estimated to account for 2% of lung cancer deaths in these countries.96 Other risk factors include occupational or environmental exposure to secondhand smoke, asbestos (particularly among smokers), certain metals (chromium, cadmium, and arsenic), some organic chemicals, radiation, air pollution, and diesel exhaust. Additional occupational exposures that increase risk include rubber manufacturing, paving, roofing, painting, and chimney sweeping. Risk is also probably increased among people with a medical history of tuberculosis. Genetic susceptibility plays a contributing role in the development of lung cancer, especially in those who develop the disease at a young age.

Prevention and early detection: Lung cancer is one of the most preventable cancers. Most lung cancers could be averted by preventing smoking initiation among adolescents and increasing smoking cessation among adults. This requires a comprehensive tobacco control program that includes raising the price of tobacco products through excise taxes, banning smoking in public places and tobacco sales to minors, restricting tobacco advertising and promotion, counter-advertising, and providing treatment and counseling for tobacco dependence. In the

United States, state comprehensive tobacco control programs have markedly decreased smoking rates and accelerated the reduction in lung cancer occurrence, particularly in California. 97,98 In the developing world, many of the most populous countries, such as China and India, are in the earlier stages of the tobacco epidemic. 99 If these and other developing countries take swift action to promote smoking cessation and prevent initiation, they can attenuate future lung cancer rates and avoid the extraordinary burden of smoking-related diseases experienced in developed countries.

Results from the National Lung Screening Trial, a clinical trial in the United States designed to determine the effectiveness of lung cancer screening in high-risk individuals, showed 20% fewer lung cancer deaths among current or former heavy or long-term smokers (30 pack-years) who were screened with spiral CT compared with standard chest x-ray. 100 However, it is unknown whether these results are relevant for individuals who have smoked less. In addition, the potential risks associated with screening, including the high rate of false positive results, cumulative radiation exposure from multiple CT scans, and unnecessary lung biopsy and surgery, are important considerations. These potential harms may be substantially greater in settings that lack access to high-quality screening. 101 The World Health Organization also recommends that effective treatment capable of reducing morbidity and mortality should be available.102 Thus, residents of low-resource countries with limited health care resources will not likely benefit from lung cancer screening in the near future.

Treatment: Lung cancer is classified as small cell or non-small cell for the purposes of treatment. Based on type and stage of cancer, treatments include surgery, radiation therapy, chemotherapy, and/or targeted therapies. For early stage non-small cell lung cancers, surgery is usually the treatment of choice; chemotherapy (sometimes in combination with radiation therapy) may be given as well. Advanced-stage non-small cell lung cancer patients are usually treated with chemotherapy, targeted drugs, or some combination of the two. Chemotherapy alone or combined with radiation is the usual treatment for small cell lung cancer; on this regimen, a large percentage of patients experience remission, though the cancer often returns.

Survival: Despite some improvements in surgical techniques and combined therapies over the past several decades, lung cancer is one of the most lethal cancers. Five-year net survival is generally similar worldwide, ranging from about 10% to 20% (Table 5, page 9). Survival is somewhat higher for the small fraction of cases detected when the disease is still localized.

Non-Hodgkin Lymphoma

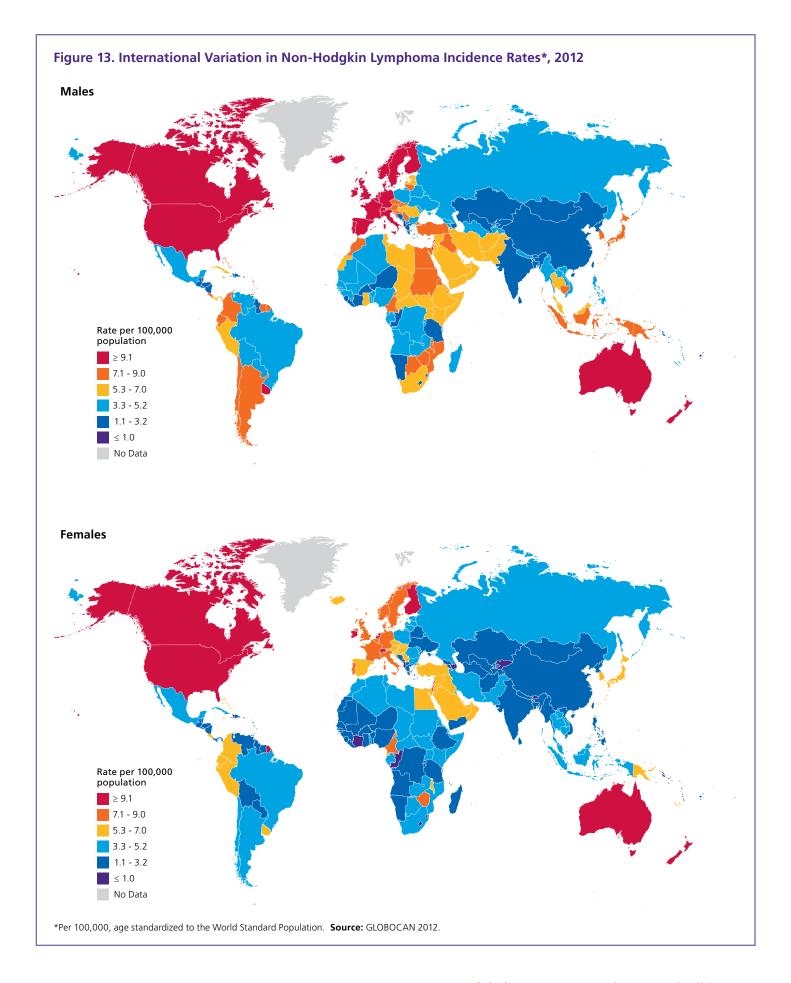
New cases: An estimated 385,700 new cases of non-Hodgkin lymphoma (NHL) occurred in 2012. NHL encompasses a wide variety of disease subtypes for which incidence patterns vary. NHL is more common in developed regions, with the highest incidence rates found in Australia, Western and Northern Europe, and Northern America. The lowest rates are found in Asia and Eastern Europe (Figure 13). In general, the incidence of NHL is low in Africa with the exception of some sub-Saharan areas (particularly in East Africa) because of high incidence among children of a subtype of NHL called Burkitt lymphoma.

Deaths: An estimated 199,700 deaths from NHL occurred in 2012.

Global trends: The incidence of NHL increased in most developed countries through 1990 and leveled off thereafter. 103, 104 While the increase may be due in part to improvements in diagnostic procedures and changes in classification, much of this trend reflects a true increase in disease occurrence. 105 In the United States, some of the increase throughout the 1980s, particularly among white males, has been attributed to the onset of the AIDS epidemic, while the decline after 1990 likely reflects the declining incidence of HIV infection and the success of antiretroviral therapies. Non-AIDS-associated NHL subtypes continued to increase or stabilized during this time period. 106 In developing countries, the incidence of NHL is increasing in some populations, also likely due in part to the AIDS epidemic. In Kampala, Uganda, and among the black population of Harare, Zimbabwe, NHL incidence rates increased 5-7% annually between 1991 and 2010; however, among young adults in these same populations, rates peaked in the early 2000s and decreased slightly through 2010, again perhaps reflecting the use of antiretroviral therapies. 107, 108

Signs and symptoms: Symptoms may include swollen lymph nodes or abdomen, feeling full after only a small amount of food, night sweats, fatigue, chest pain or pressure, unexplained weight loss, and fever.

Risk factors: Like most cancers, the risk of developing NHL increases with age. Most of the few known risk factors for lymphoma are associated with altered immune function. NHL risk is elevated in people who receive immune suppressants to prevent organ transplant rejection, people with severe autoimmune conditions, and people infected with HIV, human T-cell leukemia virus type I (HTLV-I), and probably HCV. NHL is classified as an AIDS-defining illness among HIV-positive people, and the risk is 60 times greater among AIDS patients compared with the general population. Epstein-Barr virus causes Burkitt lymphoma and a number of autoimmune-related NHLs. In addition, chronic infection with some other viruses and types of bacteria (e.g., H. pylori) that cause the immune system to be continuously active are associated with certain NHL subtypes. A family history of lymphoma confers increased risk of NHL uniformly across subtypes, and a growing number of confirmed common genetic variations are associated with modestly increased risk, including variations in the human leukocyte antigen (HLA) system. Studies indicate that excess body weight may increase the risk of some



NHL subtypes. Working in the rubber manufacturing industry and occupational and environmental exposure to certain chemicals (e.g., solvents such as dichloromethane) may also increase risk for some NHL subtypes.

Treatment: NHL patients are usually treated with chemotherapy; radiation, alone or in combination with chemotherapy, is used less often. Targeted drugs directed at lymphoma cells, such as rituximab (Rituxan®) and alemtuzumab (Campath®), are used for some types of NHL, as are antibodies linked to a radioactive atom, such as ibritumomab tiuxetan (Zevalin[®]). If NHL persists or recurs after standard treatment, stem cell transplantation (with high-dose or nonmyeloablative chemotherapy) may be an option.

Survival: Survival varies widely by cell type and stage of the disease. In the United States, the five-year relative survival for all ages is 69%.33 In Europe, the average is 59%, ranging from 44% in Poland to 74% in Iceland.⁷²

Prostate

New cases: Prostate cancer is the second most frequently diagnosed cancer in men, with 1.1 million new cases estimated to have occurred in 2012. About two-thirds of these cases were diagnosed in economically developed countries, where only 17% of the world's male population resides. Incidence rates vary by more than 100-fold worldwide, and are highest in Northern and Western Europe, Northern America, Oceania, and some Caribbean island nations, and lowest in Asia (Figure 14). Much of the variation reflects differences in the use of prostate specific antigen (PSA) testing.109

Deaths: With an estimated 307,500 deaths in 2012, prostate cancer was the fifth leading cause of cancer death in men worldwide. Men in the Caribbean region have the highest prostate cancer mortality rates in the world.1

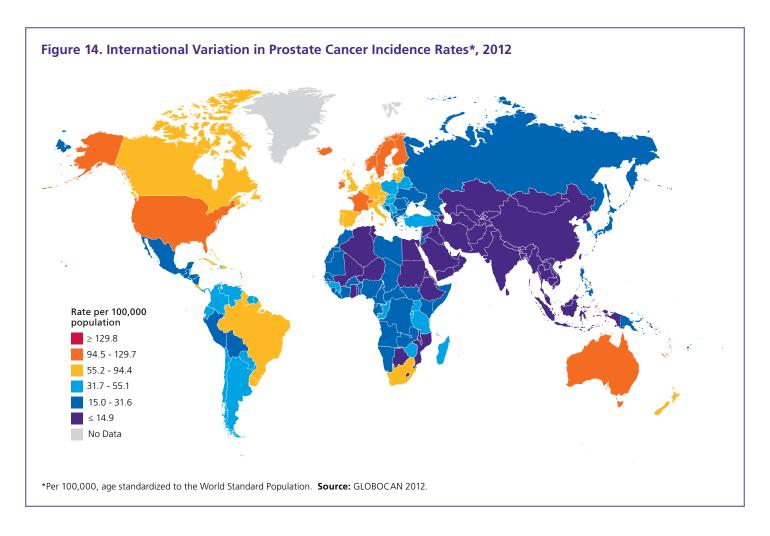
Global trends: Incidence trends in countries with rapid uptake of PSA screening, such as Australia, Canada, and the United States, follow a consistent pattern with a rapid rise in incidence in prostate cancer in the early 1990s soon after the introduction of PSA testing, followed by a sharp decline. 109, 110 In other highincome countries with more gradual adoption of PSA testing, such as many countries in Western Europe, the dramatic peak in incidence is not observed, though rates continue to increase.¹⁰⁹ Rates are also increasing in some countries where PSA testing began later or remains uncommon, such as the United Kingdom, Japan, and Thailand.109

Death rates for prostate cancer have been decreasing in most developed countries, including those in Northern America, Oceania, and Northern and Western Europe. 109 This decrease has been attributed mainly to improved treatment and/or early detection, although the specific contribution of PSA testing is debated.¹⁰⁹ In contrast, mortality rates are rising in some Asian and Central and Eastern European countries, such as Korea, China (Hong Kong), and Russia. 109 The increase is thought to reflect trends in risk factors associated with economic development, including increased consumption of animal fat, obesity, and physical inactivity. 109

Signs and symptoms: Early prostate cancer usually has no symptoms. With more advanced disease, men may experience weak or interrupted urine flow; the 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.

Risk factors: The only well-established risk factors for prostate cancer are increasing age, African ancestry, a family history of the disease, and certain inherited genetic conditions. About 56% of all prostate cancer cases in the United States are diagnosed in men 65 years of age and older, and 97% occur in men 50 and older.33 Men of African descent in Northern America and the Caribbean have the highest documented prostate cancer incidence rates in the world. The reason for the high prostate cancer risk among some populations of African descent is still poorly understood, though it may in part reflect differences in genetic susceptibility.109, 111 Genetic studies suggest that strong familial predisposition may be responsible for 5%-10% of all prostate cancers. Inherited conditions associated with increased risk include Lynch syndrome (hereditary nonpolyposis colorectal cancer) and BRCA1 and BRCA2 mutation phenotypes. Studies suggest that a diet high in processed meat or dairy foods may increase risk, that obesity increases the risk of aggressive prostate cancer, and that smoking is associated with prostate cancer death, but not incidence. 112 There is some evidence that occupational exposures of firefighters (e.g., toxic combustion products) increase risk.

Prevention and early detection: There are few known modifiable risk factors for prostate cancer. Risk may be reduced by not smoking, maintaining a healthy body weight, getting regular physical activity, and consuming a diet low in animal fat and high in fruits and vegetables. The chemoprevention of prostate cancer is an active area of research. Two drugs of interest, finasteride and dutasteride, reduce the amount of certain male hormones in the body and are used to treat the symptoms of benign prostate enlargement. Both drugs have been found to lower the risk of prostate cancer by 25% in large clinical trials and have similar potential side effects, including reduced libido and risk of erectile dysfunction. However, a study of long-term survival among participants in the finasteride trial reported that the drug had no effect on overall survival or survival after the diagnosis of prostate cancer. Neither finasteride nor dutasteride is approved for the prevention of prostate cancer at this time.



Whether PSA screening reduces deaths from prostate cancer remains controversial; studies are ongoing to clarify its impact.113 Routine PSA screening is no longer recommended for men at average risk given the large potential for serious side effects associated with prostate cancer treatment and concerns about frequent overdiagnosis, estimated at 23% to 42% for screen-detected cancers.114 However, PSA is widely used in Northern America, Australia, and parts of Europe. 110 The American Cancer Society recommends that beginning at age 50, men who are at average risk of prostate cancer and have a life expectancy of at least 10 years have a conversation with their health care provider about the benefits and limitations of PSA testing. Risks of PSA testing include the early detection and treatment of indolent (low-risk) cancers. Men should have an opportunity to make an informed decision about whether to be tested based on their personal values and preferences. Men at high risk of developing prostate cancer (African Americans or men with a close relative diagnosed with prostate cancer before the age of 65) should have this discussion with their health care provider 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. Studies

are underway to evaluate new tests for prostate cancer that could distinguish more aggressive cancers from those less likely to be lethal, and to identify men at higher risk of developing prostate cancer.113

Treatment: Treatment options vary depending on age, stage, and grade of cancer, as well as other medical conditions. The grade assigned to the tumor, typically called the Gleason score, indicates the aggressiveness of the cancer. In practice, most cancers are assigned scores ranging from 6 (low grade, less aggressive) to 10 (high grade, very aggressive). Careful observation (called active surveillance) instead of immediate treatment is appropriate for many patients, particularly men with less aggressive tumors and for older men.

There is no current evidence supporting a "best" treatment for prostate cancer. Treatment options for early stage disease that is not a candidate for active surveillance include surgery (open, laparoscopic, or robotic-assisted), external beam radiation, or radioactive seed implants (brachytherapy). Data show similar survival rates for patients treated with any of these methods. Hormonal therapy may be used along with surgery or radiation therapy for advanced early stage disease. Treatment often

impacts a man's quality of life due to side effects or complications, such as urinary and erectile difficulties, that may be short or long term. Current research is exploring new biologic markers for prostate cancer in order to improve the distinction between indolent and aggressive disease diagnoses to minimize unnecessary treatment.

More advanced disease is treated with hormonal therapy, chemotherapy, radiation therapy, and/or other treatments. 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. An option for some men with advanced prostate cancer that is no longer responding to hormones is a cancer vaccine known as sipuleucel-T (Provenge®). This treatment is designed to stimulate the patient's immune system to specifically attack prostate cancer cells.

Survival: Over the past 25 years, the dramatic improvement in survival in high-income countries largely reflects lead time bias attributable to the early diagnosis of asymptomatic cancers (some of which would never have become clinically evident) through PSA testing. The five-year net survival rate for patients diagnosed with prostate cancer is more than 90% in some countries (Eastern Cape, South Africa; Israel; Canada; United States; Brazil; Ecuador; Austria; Belgium; Finland; Germany) (Table 5, page 9). Survival rates are lower in Mongolia (40%); Jakarta, Indonesia (44%); Thailand (58%); India (58%); and Algeria (59%) (Table 5, page 9).

Stomach

New cases: Stomach cancer was the fourth most common malignancy in the world in 2012, with an estimated 951,600 new cases, approximately 71% of which occurred in developing countries. Generally, stomach cancer rates are about twice as high in men as in women. Stomach cancer incidence rates vary widely across countries, ranging from about 1 case (per 100,000) in countries such as Mozambique and Botswana to about 62 in South Korea for men and from less than 1 in Guam to about 25 in South Korea for women (Figure 15). In general, the highest incidence rates are in Asia (particularly in Korea, Mongolia, Japan, and China) and many parts of South America, and the lowest rates are in Northern America and most parts of Africa.

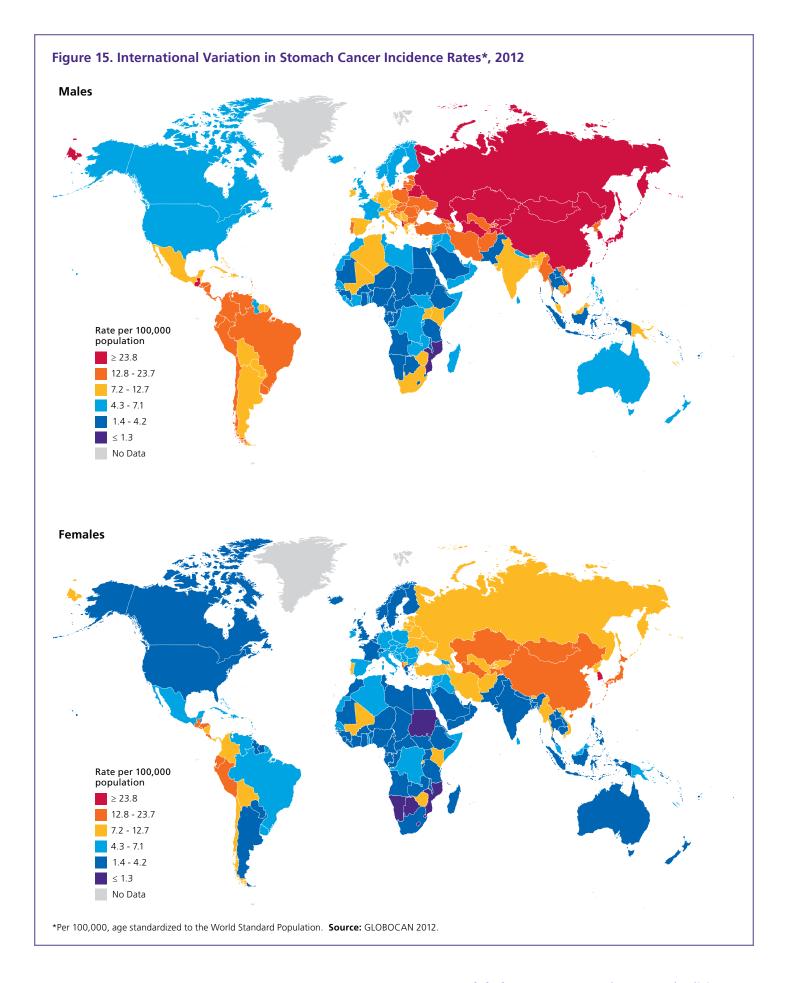
Deaths: Stomach cancer is the third and fifth leading cause of cancer death in men and women, respectively. About 723,100 people worldwide died from stomach cancer in 2012.

Global trends: A steady decline in stomach cancer incidence and mortality rates has been observed in most developed countries of Northern America and Europe since the mid-20th century. 115,116 Similar decreasing trends have been noted in more recent years in areas with historically high rates, including several countries in Asia (Japan, China, and Korea), Latin America (Colombia and Ecuador) and Europe (Ukraine).117 Factors thought to have contributed to these declines include increased availability of fresh fruits and vegetables, decreased reliance on salted and preserved foods, and reduction in chronic H. pylori infection due to sanitation and antibiotics. 118 In developed countries, decreases in smoking prevalence may also account for some of the decline. 117,119 Although stomach cancer is declining overall, adenocarcinoma of the gastric cardia (the part of the stomach attached to the esophagus) is increasing in Northern America and Europe and is thought to be related to increased obesity and perhaps improvements in diagnosis. 119

Signs and symptoms: Stomach cancer has very few symptoms in the early stages, but may include indigestion, a bloated sensation after eating, and heartburn. As it progresses, symptoms may include nausea, abdominal pain or discomfort in the upper abdomen, diarrhea or constipation, bloody stools, vomiting blood, loss of appetite, weight loss, anemia, and feelings of fullness or pressure in the stomach.

Risk factors: Chronic infection with *H. pylori* is the strongest identified risk factor for stomach cancer, with more than 60% of new stomach cancer cases worldwide attributed to this bacteria. 118 It is not known with certainty how *H. pylori* is spread, but the most likely route of transmission is from person to person through fecal-oral or oral-oral routes. Possible environmental sources include water contaminated with human waste. Prevalence of *H. pylori* infection is higher in developing countries (74%) than in developed countries (58%).¹¹⁸ Notably, less than 5% of chronically infected individuals will develop stomach cancer. 120 Dietary risk factors for stomach cancer include a diet rich in smoked foods, salted meat or fish, and pickled vegetables; fresh fruits and vegetables appear to lower risk. Smoking also increases risk of stomach cancer.84 Smokers have a 50% to 60% increased risk for stomach cancer compared with nonsmokers.84 Obesity is associated with increased risk of adenocarcinoma of the gastric cardia, possibly due to gastroesophageal reflux disease or chronic inflammation.¹²¹

Prevention and early detection: The primary prevention strategies for stomach cancer include reducing intake of foods preserved by salting, pickling, or smoking; increasing consumption of fresh fruits and vegetables; not smoking; and reducing H. pylori infection prevalence through improvement of hygienic conditions. Screening for and eradication of H. pylori using antibiotics has been shown to reduce the risk of stomach cancer in recent randomized trials.122 While this approach requires further study in additional settings and populations, it represents a promising intervention for stomach cancer prevention in the future. However, there are also concerns about whether widespread H. pylori eradication using antibiotics would result in antibiotic resistance or have other unknown harms. 122 Stomach cancers are believed to develop slowly over many years, usually beginning with asymptomatic precancerous changes in the lining of the stomach. National stomach cancer screening programs



Global Refe



rence Map



are available in some countries in Asia where the disease burden is the highest, such as Japan and Korea. 123 This intervention has resulted in detection of many cancers at an earlier, more treatable stage, although its contribution to decreasing mortality rates is unclear. 117,123,124 General population screening is not recommended in low-incidence countries such as the United States, where the disease is less common.

Treatment: The main treatments for stomach cancer are surgery, chemotherapy, targeted therapy, and radiation therapy. Often the best approach uses two or more of these treatment methods. Treatment for advanced stage cancer is often aimed at relieving symptoms.

Survival: In Japan, about half of stomach cancers are diagnosed at an early stage due to early detection services; as a result, the five-year net survival rate for all stages combined is 54%. 125,126 In contrast, in the United States, where only about 26% of cases are diagnosed at an early stage, the overall five-year survival rate is 29% (Table 5, page 9).33 In Europe, five-year survival ranges from about 18% in Poland, the United Kingdom, and Denmark to more than 30% in Austria, Belgium, Germany, and Italy (Table 5, page 9). In developing countries, survival rates are generally below 20% (Table 5, page 9).

Urinary Bladder

New cases: An estimated 429,800 new cases of bladder cancer occurred in 2012, making it the ninth most common cancer worldwide. The majority of bladder cancer occurs in men, and there is about a 15-fold variation in incidence rates internationally. The highest incidence rates are found in Europe, Northern Africa, the Middle East, and Northern America, and the lowest rates are in Southeast Asia and Middle Africa (Figure 16). Some of this variation reflects differences in the reporting of low-grade urinary bladder tumors (malignant but noninvasive tumors detected with endoscopy).127

Deaths: Bladder cancer is the 13th leading cause of cancer death among men and women worldwide. An estimated 165,100 deaths from bladder cancer occurred in 2012. The highest mortality among men was in Turkey, where the estimated death rate (12.8 per 100,000) in 2012 was 50% higher than the highest rates in Europe (8.3 in Latvia, 8.0 in Poland) and three times higher than that in the United States (4.0).

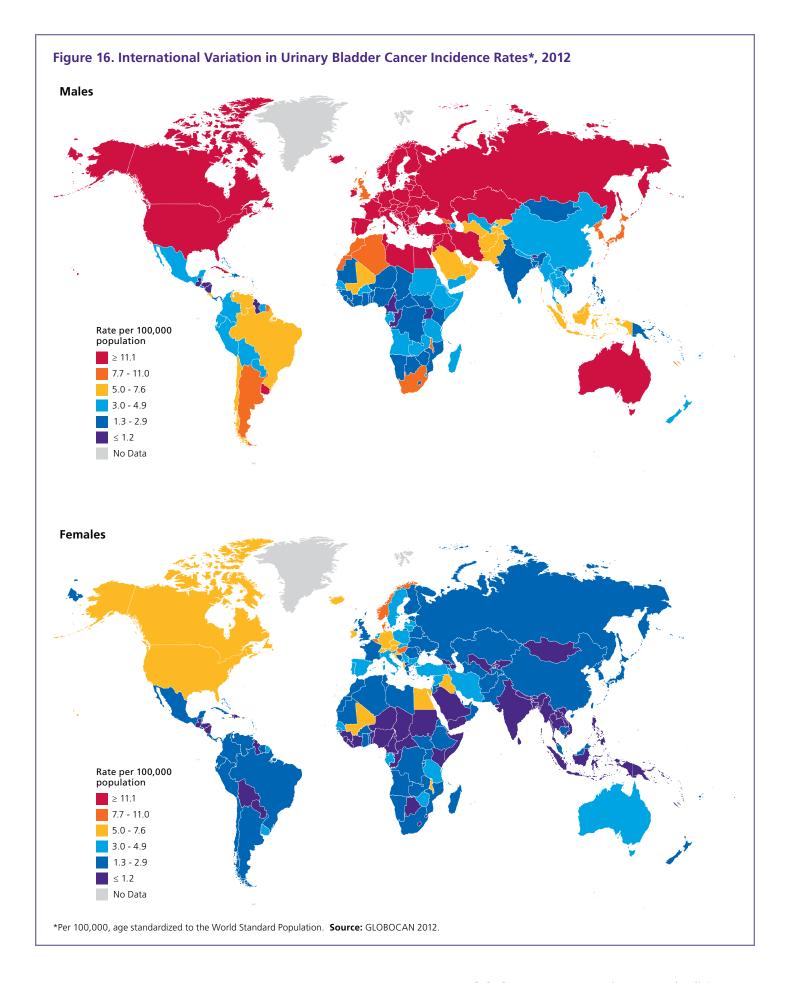
Global trends: Bladder cancer incidence rates were declining or stable in most Western countries in recent decades following a prior period of increase. Incidence trends across countries are difficult to interpret due to differences in reporting of low-grade tumors. In the United States, mortality rates in males decreased from 1975 through 1987 and have subsequently stabilized, while in females rates have been decreasing since 1975. 103 In most countries of Europe and in urban China, declines have been observed since the 1990s. 128,129 In Latin America and the Caribbean, mortality has been largely stable. 127 Decreasing mortality trends among males reflect reductions in smoking prevalence in Western countries along with reductions in occupational exposures known to cause bladder cancer, such as toxic compounds used to make dyes.

Signs and symptoms: Bladder cancer is usually detected early because of blood in the urine or other symptoms, including increased frequency or urgency of urination or pain or irritation during urination.

Risk factors: Smoking is the most well-established risk factor for bladder cancer. The risk of bladder cancer among smokers is approximately two- to six-fold that among nonsmokers.¹³⁰ Smoking is estimated to cause about 31% of bladder cancer deaths among men and 14% among women worldwide.³ Workers in the dye, rubber, leather, and aluminum industries, painters, people who live in communities with high levels of arsenic in the drinking water, and people with certain bladder birth defects also have an increased risk. Eating more fruits and vegetables and possibly drinking more fluids may lower the risk of bladder cancer.¹³¹ In the developing world, particularly Africa and the Middle East, chronic infection with Schistosoma haematobium (a parasitic worm causing urinary schistosomiasis) is associated with an increased risk of bladder cancer. This parasite, which is transmitted through contaminated water, is responsible for an estimated 50% of bladder cancer cases in some parts of Africa and about 3% of cases worldwide. 118 Bladder cancers caused by schistosomiasis have a different histology (squamous cell carcinoma) compared with those associated with other risk factors (transitional cell carcinoma).

Prevention and early detection: Not smoking, increasing the intake of fruits and vegetables, and schistosomiasis control and treatment are the best measures for bladder cancer prevention. In Egypt, schistosomiasis control has substantially reduced the burden of bladder cancer, once the most common cancer in Egyptian men.¹²⁷ There is currently no screening method recommended for people at average risk. Bladder cancer is diagnosed by microscopic examination of cells from urine or bladder tissue and examination of the bladder wall with a cystoscope, a slender tube fitted with a lens and light that is inserted through the urethra. These and other tests may be used to screen people at increased risk, as well as during 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 in the United States. Early stage cancers may be treated by removing the tumor and then administering immunotherapy or chemotherapy drugs directly into the bladder after surgery. More advanced cancers may require removal of the entire bladder (cystectomy). Patient outcomes are improved with the use of chemotherapy, alone



or with radiation, before cystectomy. Timely follow-up care is extremely important because of the high rate of bladder cancer recurrence.

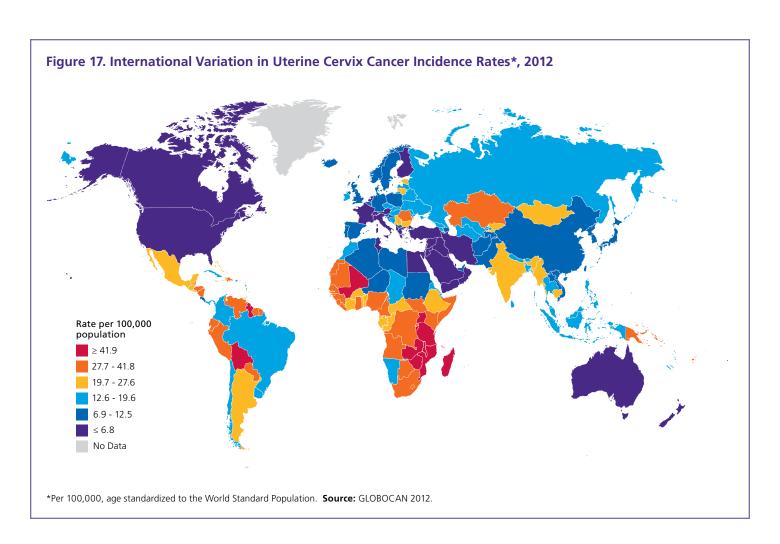
Survival: For all stages combined, the five-year relative survival rate in the United States is 77%. 33 Half of all bladder cancer patients in the United States are diagnosed while the tumor is in situ (noninvasive, present only in the layer of cells in which the cancer developed), for which cases the five-year survival rate is 96%.³³ In Europe, the overall five-year relative survival rates average 72% and range from 57% in Slovenia to 78% in Germany.¹³² Relative survival rates are low in the developing countries of Asia, such as Thailand (48%) and India (39%). 133

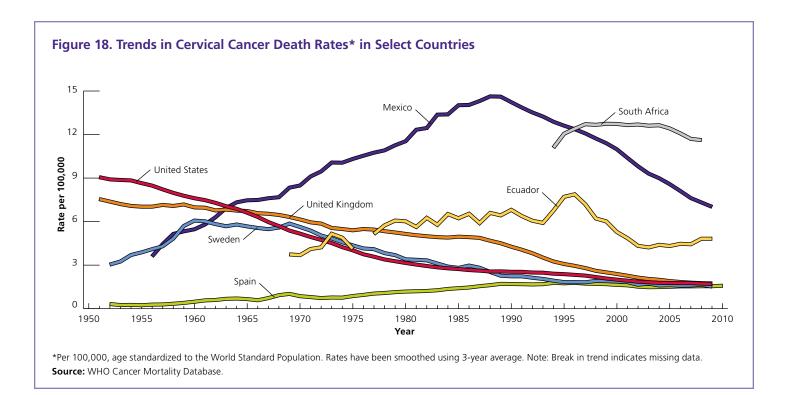
Uterine Cervix

New cases: Cervical cancer was the fourth most commonly diagnosed cancer in women in 2012, with an estimated 527,600 new cases worldwide. The highest incidence rates were in Central and South America and sub-Saharan Africa. Rates were lowest in the Middle East, Northern America, Australia and New Zealand, China, and parts of Western Europe (Figure 17). The disproportionately high burden of cervical cancer in subSaharan Africa, parts of Latin America and the Caribbean, and elsewhere in medically underserved populations is mainly due to lack of screening.

Deaths: Cervical cancer was the fourth leading cause of cancer death in women worldwide in 2012, with an estimated 265,700 deaths. Nearly 90% of cervical cancer deaths occurred in developing parts of the world: 60,100 deaths in Africa, 28,600 in Latin America and the Caribbean, and 144,400 in Asia. India, the second most populous country in the world, accounted for 25% (67,500) of cervical cancer deaths. In Eastern, Middle, and Southern Africa, as well as Melanesia, cervical cancer is the leading cause of cancer death in females.

Global trends: The large geographic variation in cervical cancer rates reflects differences in both the availability of screening, which can detect and allow for the removal of precancerous lesions, and HPV infection prevalence. 134-136 In several Western countries, where screening programs have long been established, cervical cancer rates have decreased by as much as 65% over the past four decades (Figure 18). For example, in Norway, cervical cancer mortality rates decreased from 6.3 per 100,000 in 1970 to 1.5 per 100,000 in 2011. 137 Rates have also decreased in





some high-incidence areas, including Colombia, the Philippines, and India, likely due to improved screening activities and socioeconomic conditions.136

In contrast to favorable overall trends, cervical cancer rates have been reported to be rising in Uganda and in some countries of Eastern Europe (Estonia, Lithuania, Bulgaria). 136 Most affected are younger women in several countries, including many in Europe, Central Asia, Japan, and China;134,138 this cohort-driven trend is thought to reflect increases in high-risk HPV prevalence from changing sexual behaviors.^{134,138} The exceptionally low overall cervical cancer rates in the Middle East and parts of Asia are thought to reflect low prevalence of HPV infections due to societal disapproval of extramarital sexual activity. 139

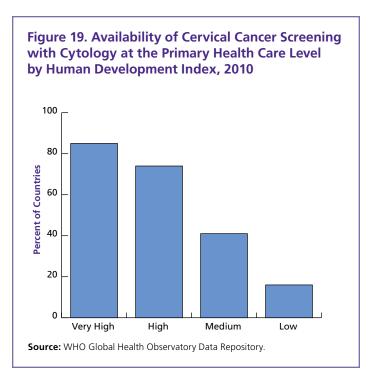
Signs and symptoms: Preinvasive cervical lesions often have no symptoms. Once abnormal cervical cells become cancerous and invade nearby tissue, the most common symptom is abnormal vaginal bleeding. Bleeding may start and stop between regular menstrual periods, or it may occur after sexual intercourse, douching, or a pelvic exam. Menstrual bleeding may be longer and/or heavier than usual. Bleeding after menopause or increased vaginal discharge may also be symptoms.

Risk factors: Most cervical cancers are caused by persistent infection with certain types of human papillomavirus (HPV). While women who begin having sex at an early age or who have had numerous sexual partners are at increased risk for HPV infection and cervical cancer, a woman may be infected with HPV even if she has had only one sexual partner. In fact, HPV infections are common in healthy women and are usually cleared successfully by the immune system. Only rarely does the infection become chronic, increasing the risk of cervical cancer. HPV infection prevalence varies widely, from 21% in Africa to 16% in Latin America and the Caribbean, 14% in Europe, 9% in Asia, and 5% in Northern America.¹³⁵ Both the persistence of HPV infection and the progression to cancer may be influenced by many factors, including a suppressed immune system, a high number of childbirths, and cigarette smoking. Long-term use of oral contraceptives (birth control pills) is also associated with increased risk of cervical cancer.

Prevention and early detection: There are two vaccines (Gardasil® and Cervarix®) available for protection against the two types of HPV that cause most (70%) cervical cancers. In economically developing countries, the major barrier to widespread use is the high cost of the vaccine. However, Gavi, the Vaccine Alliance has negotiated lower prices for these countries and began rolling out HPV vaccination demonstration projects in supported countries in 2013.140 It is extremely important that all women, even those who have been vaccinated, continue to be screened, as HPV vaccines cannot protect against established infections, nor do they protect against all of the types of HPV that cause cervical cancer.

Screening can prevent cervical cancer by detecting precancerous lesions that can be treated so they do not progress to cancer. The Papanicolaou (Pap) test is a simple procedure in which a small sample of cells is collected from the cervix and examined under a microscope. The HPV test detects HPV infections associated with cervical cancer and can forecast cervical cancer risk many years in the future. In the United States, the HPV test is currently recommended to be used in conjunction with the Pap test, either as an additional screening test or when Pap test results are uncertain. Many low-resource countries do not have the technical and public health infrastructure to support Pap testing for cervical cancer (Figure 19). Therefore, increasing access to and improving quality of screening programs in the high-risk age group of women 30 years of age or older has been identified as a key component of effective programs for the early detection of cervical cancer in these settings. 20, 21 The most efficient and cost-effective screening techniques in lowresource countries include visual inspection using acetic acid and HPV tests.²¹ A clinical trial in rural India found that a single round of HPV testing reduced the number of cervical cancer deaths by about 50%.141 In 2015, the American Cancer Society will release the Cost of Action Report, an economic analysis of comprehensive global cervical cancer control, including vaccination, screening, and all associated costs, in collaboration with researchers at Harvard University.

Treatment: Precancerous cervical lesions may be treated with a loop electrosurgical excision procedure (LEEP), which removes abnormal tissue with a wire loop heated by electric current; cryotherapy (the destruction of cells by extreme cold); cold-coagulation (the destruction of cells by extreme heat); laser ablation (removal of tissue); or conization (the removal of a cone-shaped piece of tissue containing the abnormal tissue). Invasive cervical cancers are generally treated with surgery or radiation (both external and internal) combined with chemotherapy. Chemotherapy alone is often used to treat advanced disease. However, for women with metastatic, recurrent, or persistent cervical cancer, the addition of the targeted drug bevacizumab (Avastin*) to standard chemotherapy has been shown to improve overall survival, and has recently been approved in the United States for this use. Cervical cancer survivors may suffer from side effects including sexual dysfunction and impaired fertility; those who are treated with a total hysterectomy will be infertile.¹⁴²



Survival: When detected at an early stage, invasive cervical cancer is one of the most successfully treated cancers. The five-year net survival rate ranges from 46% in India to 77% in South Korea, although it is between 60% and 70% in most countries (Table 5, page 9).

Special Section: Female Breast Cancer

Introduction

Breast cancer is the most commonly diagnosed cancer among women in the vast majority (140 of 184) of countries worldwide, making it the only cancer that is common among women in all regions of the world. Although once primarily considered a disease of Western women, more than half of new breast cancer cases and deaths occur in economically developing countries. In developed countries, many breast cancers are caught early and prognosis is often very good. By contrast, in economically developing countries, breast cancers are often diagnosed after the disease has progressed and survival is poorer.

Although we generally refer to breast cancer as a single disease throughout this section, it is important to note that it is biologically variable in presentation and outcomes, distinguished by different molecular subtypes, risk factors, clinical behaviors, and responses to treatment.2-5 This diversity depends to a significant degree on the genetic variability among tumors, which today is better understood through gene expression profiling techniques. These profiles allow tumors to be classified based on gene expression patterns that better explain variation in behavior and response to treatment.3

How Many Breast Cancer Cases and Deaths Occurred in 2012?

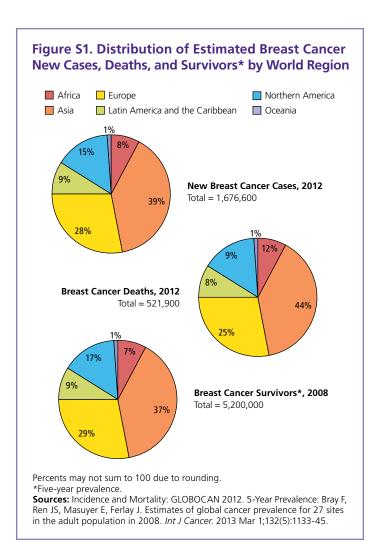
Breast cancer is the most frequently diagnosed cancer in women worldwide with nearly 1.7 million new cases diagnosed in 2012, accounting for 25% of all new cancer cases in women. A little more than half (53%) of these cases occurred in economically developing countries, which represents about 82% of the world population. An estimated 521,900 breast cancer deaths occurred in women in 2012. Breast cancer is the leading cause of cancer death among women in developing countries and the second leading cause of cancer death (following lung cancer) among women in developed countries.

The distribution of breast cancer cases, deaths, and 5-year survivors by world region is shown in Figure S1. Asian countries, which represent 59% of the global population, have the largest burden of breast cancer, with 39% of new cases, 44% of deaths, and 37% of the world's five-year survivors. Although Northern America (US and Canada) represents only 5% of the world population, it accounts for 15% of new cases, 9% of deaths, and 17% of survivors, reflecting the high incidence and survival rates in the region. In contrast, African countries (15% of world population) represent 8% of the total new cases, but 12% of breast cancer deaths because of poor survival due to late stage at diagnosis and limited treatment.

What Are the Symptoms of Breast Cancer?

The most common symptom of breast cancer is a lump or mass in the breast, which is usually painless. Although some breast cancers can cause pain, in general the presence of pain is not an indication of breast cancer. When the discomfort is diffuse in the breast, migrates to different areas, or comes and goes over time, it is more likely caused by benign conditions or hormonal cycling. In many developed countries, breast cancer is often identified by a screening mammogram before symptoms have developed.

Other symptoms of early breast cancer can be subtle and develop gradually. Early cancer may create a sense of "tugging" or "pulling" within the breast. Sometimes breast cancer can spread to lymph nodes under the arm, or, less often, above the collarbone, even before the original tumor can be felt in the breast. Enlarged lymph nodes may feel like a separate mass in the armpit or over the collarbone.



As cancers progress and evolve, they may cause breast swelling, fullness, or visible deformity. Sometimes cancers located centrally in the breast cause nipple retraction or thickening and swelling of the surrounding skin. Very advanced cancers can ulcerate through the skin and create sores that may bleed or become infected. These late cancers are more likely to be associated with cancer spreading to lymph nodes and/or distant organs.

There are a few exceptions to the typical presentations of breast cancer. For example, inflammatory breast cancer, which is an aggressive subtype of breast cancer, presents with rapidly worsening diffuse redness and swelling of the breast, often without a palpable mass. This condition is often painful and can be confused with mastitis. In women with Paget disease of the breast, a rare cancer involving the nipple and areola, the nipple can be crusted, scaly, and red, with areas of bleeding or oozing that may cause itching and/or burning. Most people with this cancer also have invasive or in situ tumors inside the same breast.

Factors Associated with Breast Cancer Risk

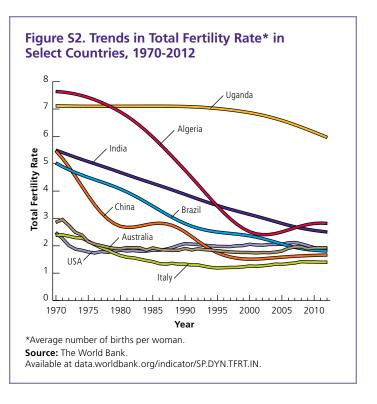
Much of the worldwide increase in breast cancer has been linked to the increasing prevalence of a number of breast cancer risk factors. These include changes in reproductive patterns as women increasingly enter the work force and have access to contraception, as well as increases in obesity and physical inactivity reflecting changes in diet and lifestyle. 6 These and other risk factors for breast cancer are discussed below:

Reproductive factors

Younger age at first full-term pregnancy (<30 years) and a greater number of childbirths are independently associated with an overall lower risk of breast cancer; however, there is a transient increase in breast cancer risk in the 5 to 10 years following a fullterm pregnancy, particularly among women who have a first birth after age 30.7-9 Over the past several decades, fertility rates have declined in many low- and middle-income countries such as Algeria, Brazil, and India (Figure S2).

Most studies suggest that breastfeeding for a year or more slightly reduces a woman's overall risk of breast cancer. 10 Longer duration is associated with greater risk reduction. In a review of 47 studies in 30 countries, the risk of breast cancer was reduced by 4% for every 12 months of breastfeeding.¹¹

Women who have had more menstrual cycles because they started menstruating early (before age 12) and/or went through menopause later (after age 55) have a slightly higher risk of breast cancer.¹² Numerous studies have reported that age at menarche has decreased worldwide, which probably reflects increased caloric intake and decreased levels of physical activity. 13-16

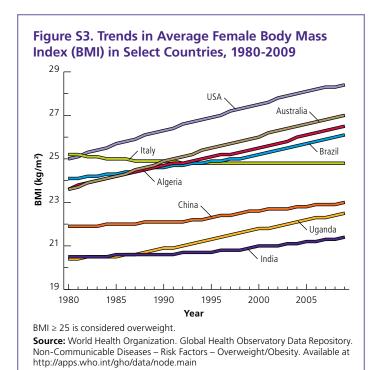


Obesity, diet, and physical activity

Obesity increases the risk of postmenopausal breast cancer.¹⁷ The risk is about 1.5 times higher in overweight women and about 2 times higher in obese women than in lean women.¹⁸ The average body mass index (BMI) has increased over the past several decades among women around the world (Figure S3). For example, from 1980 to 2010, the average BMI in Australia increased from about 23.6 kg/m 2 to 26.8 kg/m 2 .

In contrast, obesity appears to protect against breast cancer before menopause. A recent study based on women from 15 different countries found that an increase of 5 kg/m² in BMI was associated with a 7% reduction in risk of premenopausal breast cancer for Caucasian women and a 5% reduction in risk for women of African ancestry, but an increase in risk (5%) for Asian women.19

For decades there has been interest in whether dietary patterns contribute to global variation in breast cancer incidence. Research has produced inconsistent results, with some suggesting that a healthy diet (e.g., high intake of fruits and vegetables, poultry, fish, low-fat dairy, whole grains) is associated with lower breast cancer risk than a Western diet (e.g. red and/or processed meat, refined grains/sweets, high-fat dairy), while others have found no association. 20, 21 Nor has a clear association been found for specific dietary components. For example, it has been suggested that soy consumption may reduce breast cancer risk in part because of historically low breast cancer rates among Asian women who have a diet high in soy; however, a recent metaanalysis showed that soy intake was inversely associated with



breast cancer risk in Asian but not Western women.²² Animal fat intake was not linked to breast cancer risk in a large study that included more than 20,000 breast cancer patients.²³

Physical activity has been shown to reduce breast cancer risk. Women who engage in regular physical activity have about a 12% lower risk of breast cancer.24,25

Menopausal hormone therapy and oral contraceptives

Recent use of menopausal hormone therapy (MHT) with combined estrogen and progestin increases the risk of developing and dying from breast cancer, with higher risk associated with longer use.²⁶ Risk is also greater for women who start MHT soon after the onset of menopause compared to those who begin use later.^{27, 28} The increased risk appears to diminish within 5 years of discontinuation of hormone use.^{26, 27} Estrogen alone can be prescribed for women without a uterus (usually due to hysterectomy), and it is less clear if this therapy increases risk of breast cancer. 27, 29, 30

Recent use of oral contraceptives may increase the risk of breast cancer by about 10% to 30%; however, since most studies have looked at older, high-dose estrogen forms of oral contraceptives, the risk with current, low-dose formulations is not clear.³¹ Women who have stopped using oral contraceptives for 10 years or more have the same risk as women who never used them.³¹

Tobacco and alcohol

Accumulating research indicates that smoking increases breast cancer risk, particularly long-term, heavy smoking and among women who start smoking before their first pregnancy.³²⁻³⁸ A recent review by American Cancer Society researchers found that women who initiated smoking before the birth of their first child had a 21% higher risk of breast cancer than women who never smoked.³⁴ There is also increasing evidence linking secondhand smoke and breast cancer, particularly premenopausal breast cancer.32,36,39-42

Numerous studies have confirmed that alcohol consumption increases the relative risk of breast cancer in women by about 7% to 10% for each 10g (roughly one drink) of alcohol consumed per day.43-45

Environmental risk factors

The link between radiation exposure and breast cancer has been demonstrated in studies of atomic bomb survivors and women who have received high-dose radiation therapy to the chest, particularly for those who were first exposed at younger ages. 46, 47 Breast cancer is one of the most common types of second cancers among childhood cancer survivors, particularly in those women treated with high-dose radiation therapy to the chest between 10 and 30 years of age, such as for Hodgkin lymphoma.⁴⁸

Although animal studies have demonstrated that prolonged, high-dose exposure to many industrial chemicals can increase mammary tumor development, it is difficult to determine whether exposure to lower concentrations of these chemicals in the general environment increases the risk of human breast cancer.49 In general, epidemiological studies have not found clear relationships between environmental pollutants and breast cancer, though researchers have had limited capability to study effects on population subgroups or to quantify exposures at potentially critical periods of life, such as adolescence. An association between environmental exposures and breast cancer is difficult to quantify, partly because it may reflect an indirect pathway (e.g., an effect of these exposures on early onset puberty); however, it continues to be an active area of research.

A few occupations have been linked to breast cancer risk. For example, ethylene oxide, a fumigant used to sterilize surgical instruments, has been shown to cause breast cancer in experimental animals. One study found an increased risk of breast cancer among women employed in commercial sterilization facilities who were exposed to high levels of ethylene oxide.⁵⁰

According to the International Agency for Research on Cancer, shift work, particularly at night, is probably carcinogenic to humans.51 It is thought that the increased risk is a result of exposure to light at night. In an ecologic study of 164 countries, higher levels of light at night were associated with higher breast cancer rates.⁵² Additional studies are needed to confirm this relationship because shift work at night is a common exposure, involving about 15% to 20% of workers in the US and Europe, and because much of the population in industrialized countries is exposed to artificial light at night.

Chemoprevention and prophylactic surgery

Clinical trials have shown that the drugs tamoxifen and raloxifene reduce the risk of estrogen receptor-positive (ER+) breast cancer in women shown to be at high risk.^{53,54} Clinical trials also suggest that aromatase inhibitors reduce the risk of breast cancer in postmenopausal women; currently, these drugs are only FDA-approved to prevent breast cancer recurrence. 55,56

Some women at very high risk of breast cancer, such as those with a mutation in the genes BRCA1 or BRCA2 (lifetime risk of breast cancer is 45%-65%), may elect prophylactic (preventive) mastectomy. Removing both breasts reduces the risk of breast cancer in these women by 90% or more.^{57, 58} Women with these mutations are also at high risk of ovarian cancer, and many choose to have their ovaries removed as well. This surgery can also lower the risk of breast cancer by up to 50%.59

How Can Breast Cancer Be Detected Early?

Methods for the early detection of breast cancer are screening by mammography and physical examinations. Mammography screening aims to detect breast cancer before symptoms develop, whereas physical examinations, either through selfexamination or clinical breast examination by a health care worker, detect symptomatic breast cancer. When breast cancer is detected at an early stage, treatment is more effective and a cure is more likely. Pooled estimates of the results of older data from randomized trials of mammography screening suggest that mammography reduces the risk of dying from breast cancer by 15% to 20%, whereas pooled estimates from studies of modern mammography screening programs in Europe and Canada have found that women who have been screened have 30% to 40% lower risk of dying from breast cancer compared to women who have not.60-65 Early detection of breast cancer by mammography also leads to a greater range of treatment options, including less-extensive surgery (e.g., breast-conserving surgery versus mastectomy) and the use of chemotherapy with fewer serious side effects, or even, in some cases, the option to forgo chemotherapy.

While mammographic screening has considerable advantages over physical exams, it is not perfect. Not all breast cancers will be detected by a mammogram, and some breast cancers that are screen-detected still have poor prognosis. In addition, most women who are recalled for further evaluation, perhaps including biopsy, after a suspicious mammogram, do not have cancer. These are referred to as false-positive test results. Mammography also results in overdiagnosis and overtreatment of some breast cancers, that is, the diagnosis and treatment of cancers that would not have progressed or otherwise been detected without screening.

A number of countries, primarily in Europe, have implemented organized, population-based mammography screening programs.66 Organized screening programs consist of a system for proactively offering all eligible people screening at appropriate intervals, rather than offering screening only when people are seeking care. A recent analysis of mammography screening programs from 18 countries in Europe reported that 48% (ranging from 28% in Italy to 92% in Navarra, Spain) of eligible women received a recent screening mammogram.⁶⁷ Unlike Europe, the US does not have an organized screening program; according to the 2010 National Health Interview Survey, 72% of US women ages 50-74 years received a recent mammogram.⁶⁸ In many developing countries, mammography screening is neither cost-effective nor feasible; therefore, recommendations for mammography screening are limited to countries with high incidence rates and good health care infrastructure that can afford long-term screening programs and access to diagnostic and treatment services.⁶⁹ Countries with limited resources should prioritize increasing public awareness and access to prompt and effective diagnosis for women with symptomatic breast cancer. Although it has not been demonstrated by a randomized clinical trial, clinical breast examination may be an effective and low-cost screening method for these settings. A simulation study using data from India predicted that annual clinical breast exams from ages 40 to 60 years could lower the breast cancer death rate by 23%.70

Programs to raise public awareness and promote clinical breast examination have been successfully implemented in some lowincome countries. For example, a program in Sudan increased early stage breast cancer detection by training female volunteers to go door to door in their villages conducting physical breast exams.⁷¹ In Sarawak, Malaysia, the proportion of late-stage breast cancers declined from 77% in 1993 to 37% in 1998, following the introduction of a program to increase public awareness and train health staff in breast examination.⁷²

Misconceptions about the nature or curability of breast cancer are still prevalent in many communities. Thus, in order to successfully implement any early detection program, it is necessary to increase awareness about breast cancer and the benefits of early detection.73

How Is Breast Cancer Diagnosed?

When cancer is suspected based on clinical exam or breast imaging, microscopic analysis of breast tissue is necessary for a definitive diagnosis. The tissue for microscopic analysis can be obtained via a needle or surgical biopsy. Selection of the type of biopsy is based on individual patient clinical factors, availability of specific biopsy devices, and resources. In particular, needle biopsy requires adequate pathology services that may not be available in many low- and middle-income countries.

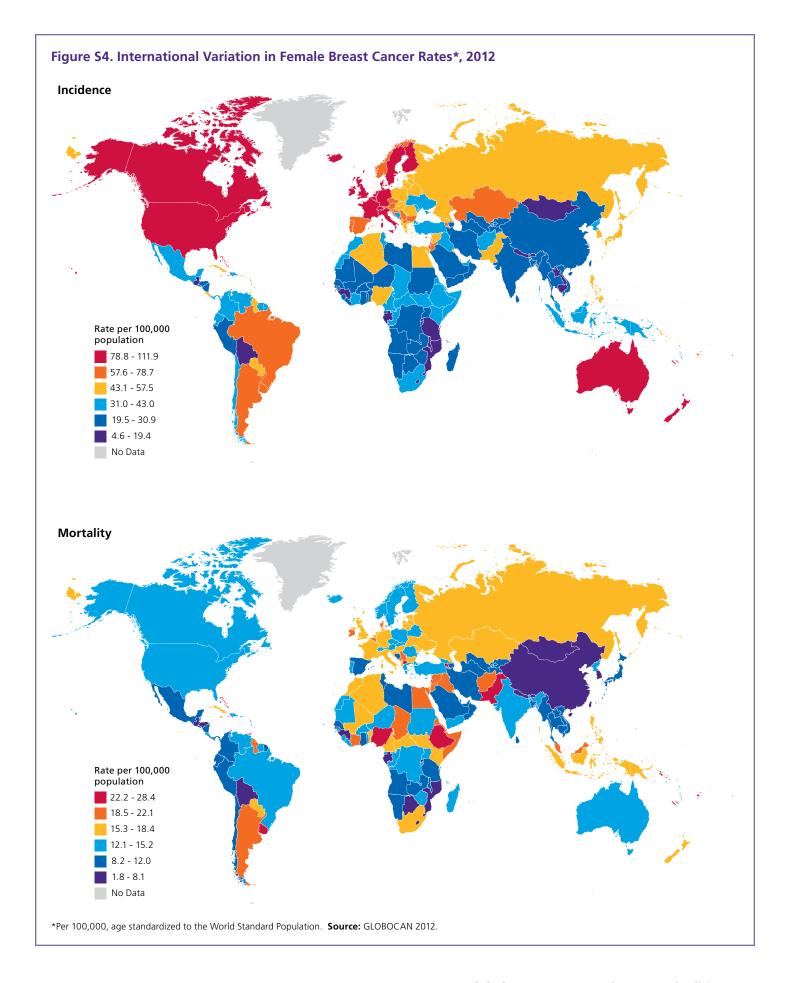
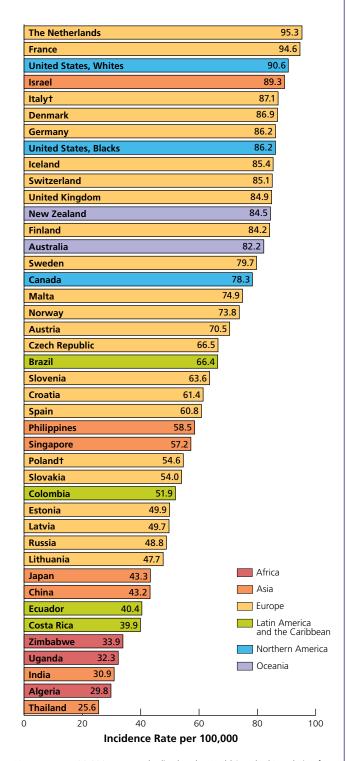


Figure S5. Breast Cancer Incidence Rates* in Select Countries, 2006-2007



^{*}Rates are per 100,000, age standardized to the World Standard Population for countries with high-quality cancer registry data. Rates for some countries are not based on complete national data. For more information on contributing registries, see Sources of Statistics on page 53. †Data for Italy are from 2004-2005 and data for Poland are from 2005-2006.

Source: Ferlay J, Bray F, Steliarova-Foucher E and Forman D. Cancer Incidence in Five Continents, CI5plus: IARC CancerBase No. 9. Lyon, France: International Agency for Research on Cancer; 2014.

Are There Geographic Differences in Breast **Cancer Rates?**

There are large variations in breast cancer incidence rates around the world (Figure S4, page 41). Higher incidence rates are observed in Northern America, Australia, and Northern and Western Europe, while incidence rates are lower in parts of Africa and Asia. Results from migrant studies suggest that international variations in breast cancer incidence largely reflect differences in lifestyle or environmental factors rather than genetic differences.74,75 Lower incidence rates in developing countries also reflect low screening rates and incomplete data. Countries with high mammographic screening rates have higher breast cancer incidence overall in part due to the detection of asymptomatic tumors.

Age-standardized incidence rates in 2006-2007 for countries with high-quality cancer registries according to the International Agency for Research on Cancer are presented in Figure S5. Incidence rates vary nearly four-fold, ranging from 25.6 cases per 100,000 females in Thailand to 95.3 per 100,000 in The Netherlands. Wide variation is also seen within regions. For example, incidence rates in Israel are at least 1.5 times higher than other Asian countries, which may be in part due to the high prevalence of BRCA1 and BRCA2 mutations in the Ashkenazi Jewish population. ⁷⁶ Incidence rates also tend to be higher in Northern and Western European countries than in Eastern Europe. These variations are likely due to differences in population makeup, health resources, detection practices, and/or lifestyle factors.

Breast cancer incidence rates increase with advancing age; however, the age-specific patterns differ across countries.⁷⁷ Rates increase rapidly until approximately age 50 in most countries, which likely reflects the influence of reproductive hormones on breast cancer occurrence. After age 50, the pattern differs with a slowed increase in more developed countries and a leveling off in less economically developed countries. This pattern is likely due to increasing risk of breast cancer in younger generations of women.⁷⁸ The distribution of ER+ and estrogen receptor negative (ER-) breast cancers, which have distinct age-specific patterns, also varies worldwide.⁷⁷ However, this may partly reflect differences in testing since many regions do not have or consistently employ ER testing. In addition, the quality of tissue preservation and adherence to testing protocols affect the accuracy of the test results.79,80

Figure S4, page 41 also shows geographic variation in breast cancer death rates. Age-standardized female breast cancer death rates for select countries in 2008-2009 are shown in Figure S6. Breast cancer death rates were highest in Denmark (19.4 per 100,000), Israel, and Argentina (both 17.9 per 100,000), and lowest in the Republic of Korea (5.2 per 100,000), Egypt (5.7), and Ecuador (6.4). The smaller geographic variation in mortality than in incidence is in part due to more favorable survival of breast cancer in countries with higher incidence rates (more

Figure S6. Breast Cancer Death Rates* in Select Countries, 2008-2009



*Per 100,000, age standardized to the World Standard Population. †Data are for 2008.

Source: WHO Cancer Mortality Database.

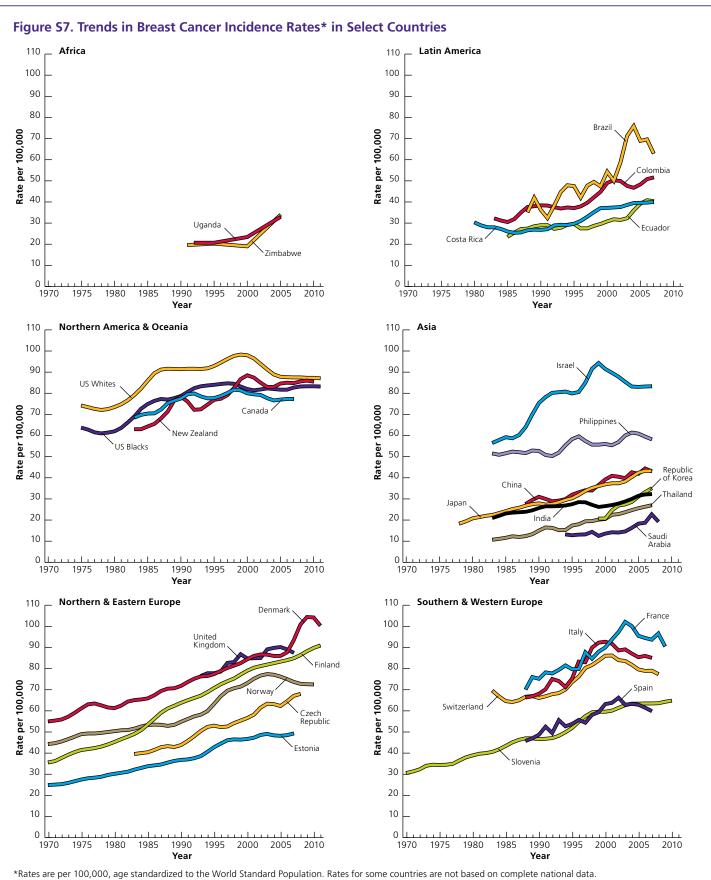
developed countries), where cancers are detected earlier and effective cancer treatment is more available.

How Has the Occurrence of Breast Cancer Changed over Time?

Trends in breast cancer incidence rates for select countries are shown in Figure S7, page 44. Between 1980 and the late 1990s, breast cancer incidence rates rose approximately 30% in westernized countries because of changes in reproductive patterns, increased screening, and increased use of MHT.6 However, these increases halted around the early 2000s, and a decline in incidence was seen in many countries including the US, Canada, United Kingdom, France, and Australia, which coincided with the publication of a major study on the adverse health effects of MHT use in postmenopausal women.⁸¹⁻⁸⁵ The continued decline or stabilization of rates in Western countries may also be due to plateaus in participation in mammographic screening.66

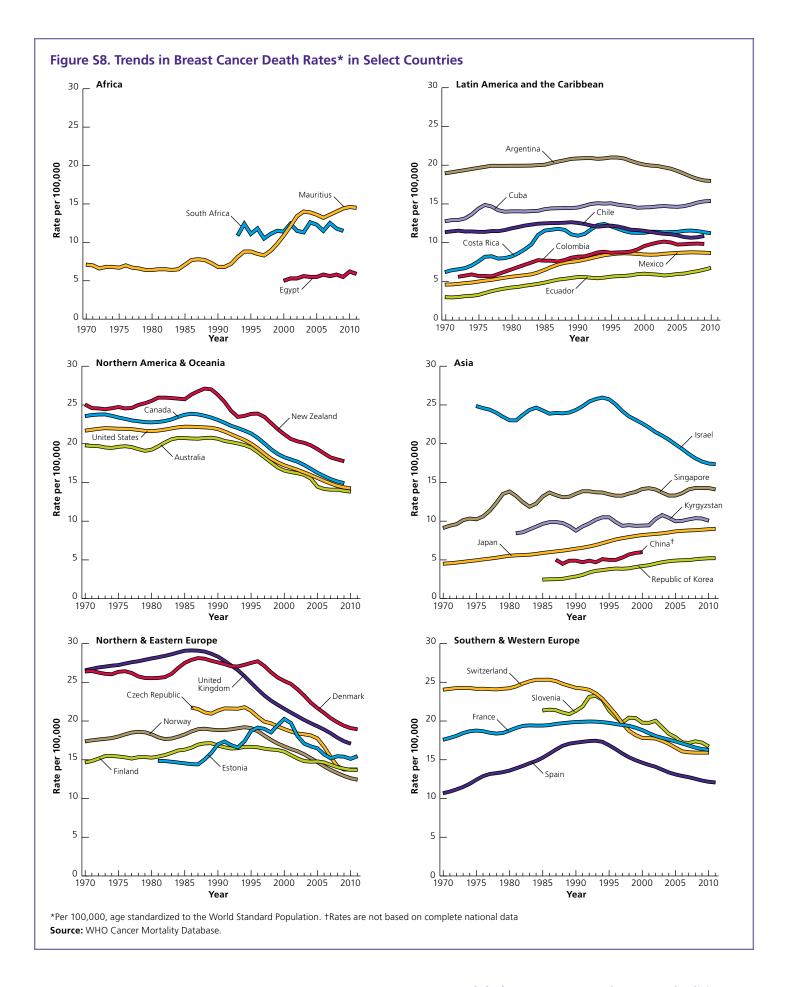
In contrast, breast cancer incidence rates have been rising more rapidly in historically lower-risk areas, such as in many countries of Latin America, Africa, and Asia. These rising trends likely reflect changes in risk factors associated with economic development and urbanization, including obesity, physical inactivity, delayed childbearing and/or having fewer children, earlier age at menarche, and shorter duration of breastfeeding, as well as increases in breast cancer screening and awareness.86 For example, in Brazil, incidence rates nearly doubled from the late 1980s to the late 2000s. Over this same period, the fertility rate declined from more than 5 children per family in 1970 to less than 2 in 2010 (Figure S2, page 38) and the average BMI increased by 2 kg/m² (Figure S3, page 39). In Japan, breast cancer incidence rates increased rapidly from 1999 to 2008 by an average of 6% per year.87

Although breast cancer incidence rates increased through the late 1990s in westernized countries, breast cancer mortality has been stable or decreasing since around 1990 in the US, Canada, and many European countries (Figure S8, page 45). These reductions have been attributed to early detection through mammography and improved treatment, although the respective contributions of each are unclear and likely vary depending on the level of participation in regular screening and availability of state-of-the-art treatment.^{6, 88-90} In contrast, mortality rates continue to increase in many countries of Asia, Africa, and Latin America reflecting increasing incidence trends and in some cases, limited access to treatment (Figure S8, page 45).91,92 For example, death rates have increased continuously in Japan (1.1% per year from 1997 to 2011) and in Korea (2.1% per year from 1994 to 2011).87 Notably, these are both high-income countries where cancer treatment is available, but mammography screening has not been widely embraced at the population level.



*Rates are per 100,000, age standardized to the World Standard Population. Rates for some countries are not based on complete national data For more information on contributing registries, see Sources of Statistics on page 53.

Source: Cancer Incidence in Five Continents, CI5plus: IARC CancerBase No. 9. Lyon, France: International Agency for Research on Cancer; 2014.



Breast Cancer Survival and Stage at Diagnosis

Five-year net survival rates for breast cancer among women in select countries are presented in Table 5 (page 9).93 Survival rates for breast cancer are 85% or higher in the US, Canada, Australia, Israel, Brazil, and many Northern and Western European countries but are 60% or lower in many developing countries, such as South Africa, Mongolia, Algeria, and India. Differences in survival reflect variations in stage at diagnosis and access to appropriate treatment.

There is wide international variation in the stage distribution for breast cancer (Table 6, page 10). In the United Kingdom, the US, Canada and Denmark, more than three-quarters (76%-85%) of breast cancers are diagnosed at an early stage (I or II). Notably, the vast majority of breast cancers in China (74%) are also diagnosed at an early stage, which is reflected in the high five-year overall survival rate (81%). In contrast, in several developing countries, the majority of women are diagnosed with late-stage disease. For example, 77% of breast cancer cases in Nigeria, 66% in Libya, and 56% in Malaysia are diagnosed at late stage (III or IV).

Reasons for late-stage diagnoses include lack of awareness as well as limited access to adequate detection and diagnostic services.⁹⁴ In some countries there are also social barriers such as reluctance or refusal to have one's breasts examined by a male doctor and stigma associated with breast cancer and its treatment.⁷¹ Cancer fatalism – the cultural belief that cancer is invariably fatal and cannot be changed through individual action - has been documented in Latin American, Arabic, and Ethiopian populations. 95-97 Fatalistic belief systems can adversely affect participation in early detection programs and may delay or prevent the receipt of comprehensive curative cancer treatment. In some societies, a woman may avoid revealing that she has breast cancer out of fear that she will be rejected by her family and community or that her daughter's potential for future marriage may be adversely affected. For these reasons, cancer education about the value and efficacy of early detection is fundamental to any successful early detection program.

How Is Breast Cancer Treated?

Taking into account tumor size, extent of spread, and other characteristics, as well as patient preference, treatment usually involves breast-conserving surgery (surgical removal of the tumor and surrounding tissue) or mastectomy (surgical removal of the breast) with removal of some of the axillary (underarm) lymph nodes to obtain accurate information on stage of disease. In addition, radiation therapy; chemotherapy (before or after surgery); hormone therapy; and/or targeted biologic therapy may be used depending on the stage of the cancer, its biologic characteristics, and the type of surgery used.

In low-income countries, women are more likely to be diagnosed with advanced-stage disease and optimal breast cancer treatment is often not available. Effective breast cancer treatment may be limited by small numbers of trained medical personnel; insufficient modern equipment, including pathology services and radiotherapy machines; and the high cost of cancer drugs.98 Even in middle- and high-resource countries, which are more likely to have adequate breast cancer treatments, many individuals cannot afford or otherwise access necessary treatments.

Surgery

Most women with breast cancer have surgery to remove the tumor. Surgical treatment for breast cancer has evolved over the past several decades as understanding of the molecular biology and natural history of breast cancer has improved. Historically, surgical treatment was aggressive with the goal to remove as much of the breast and surrounding area as feasible. For patients with early stage disease, modern treatment often consists of more limited, breast-conserving surgery. In low-resource settings, however, mastectomy remains the most common surgical treatment due to more advanced disease presentation and limited availability of radiotherapy (Figure 5, page 11).

Radiation therapy

Radiation therapy is required following breast-conserving surgery to avoid an excessive number of local cancer recurrences in the breast. Numerous studies have shown that for early breast cancer, long-term survival for women treated with breast-conserving surgery plus radiation therapy is similar to that for those treated with mastectomy. 99-101 Radiation is also recommended after mastectomy for patients with tumors larger than 5 cm or when cancer is found in the lymph nodes. In low-resource countries, radiation therapy is more often used for symptom control rather than as a component of treatment with curative intent due to the large proportion of patients presenting at advanced stages with metastatic disease. Radiation is particularly effective for controlling painful symptoms associated with bone metastases.

The International Atomic Energy Agency (IAEA) has estimated that there is a shortage of at least 5,000 radiotherapy machines in developing countries. As a result, up to 70% of cancer patients who may benefit from radiation do not receive it.¹⁰² The IAEA has established the Programme of Action for Cancer Therapy (PACT) to build global partnerships to support cancer control programs in its low- and middle-income member states through the development and implementation of radiotherapy capacities. The IAEA and its partners have: provided radiotherapy equipment, trained more than 115 professionals, and provided expertise for cancer control capacity in 8 countries since 2006 (Albania, Ghana, Mongolia, Nicaragua, Sri Lanka, Tanzania, Vietnam, and Yemen). For countries that have radiotherapy

equipment, routine maintenance and calibration is essential. The IAEA developed the Quality Assurance Team for Radiation Oncology (QUATRO) to facilitate quality improvement in radiation therapy through expert assessment of radiotherapy centers.103

Systemic therapy

Systemic therapy for breast cancer includes chemotherapy, hormone therapy, and targeted biological therapies. The benefit of chemotherapy is dependent on multiple factors, including the size of the cancer, the number of lymph nodes involved, the presence of hormone receptors, and the amount of human epidermal growth receptor 2 (HER2) protein made by the cancer cells. Recommended therapeutic agents vary based on available resources.¹⁰⁴ The availability of medical oncologists is limited in some areas; therefore, chemotherapy may be administered by other medical providers. Women with ER+ breast cancer can be given hormone therapy such as tamoxifen or aromatase inhibitors. Although tamoxifen is a relatively affordable treatment, adequate pathology services to measure hormone receptor status are often not available in lower-resource settings. Further, proper tissue handling and processing is essential for valid hormone test results. The use of the HER2-targeted monoclonal antibody-based treatment trastuzumab together with chemotherapy has been shown to be highly effective in treating HER2-positive cancer, but is cost-prohibitive in most of the world. Trastuzumab has been considered for inclusion in the World Health Organization (WHO) Essential Medicine list, sparking a debate about how health care systems can and should balance high cost against proven curative benefit.

Supportive care

There are wide variations in the availability of supportive and palliative care around the world. Breast cancer patients may suffer immediate or delayed effects of treatment, which can include swelling, nausea, fatigue, pain, sexual dysfunction, and infertility. For women with metastatic breast cancer, pain management should be a priority. Common sites for breast cancer metastases are bone, brain, liver, and lung. Pain management often requires multimodal approaches and can include the use of pain medications and radiotherapy. Access to pain control is limited in some countries where pain control medications such as opioids (e.g., morphine) are restricted or prohibited.

What Is the American Cancer Society Doing about Breast Cancer around the World?

The American Cancer Society Global Health, Cancer Control, and Intramural Research departments are promoting evidencebased cancer control programs and participating in breast cancer research around the world. This section provides highlights and information on some of these efforts.

The Breast Health Global Initiative

Established in 2002, the Breast Health Global Initiative (BHGI) created an international health alliance to develop evidencebased guidelines for countries with limited resources to improve breast health outcomes. The following cancer control strategies for low- and middle-income countries are a result of the 2010 consensus summit.98

Visit the BHGI website at portal.bhgi.org for more information.

Breast Health Global Initiative recommendations for low- and middle-resource countries

- Cancer registries are needed so that disease prevalence, stage, and treatment outcome can be measured.
- National cancer plans should define health care networks in which centers of excellence become connected through outreach to rural and surrounding areas for consultation and patient triage.
- Resource-adapted multidisciplinary cancer care models should be used to avoid system fragmentation and to facilitate consistent health-policy reform.
- Training for physician and non-physician staff should be linked to equipment acquisition and quality care initiatives that measure utilization and clinical outcomes.
- Public awareness that breast cancer outcomes are improved through early detection should be promoted in conjunction with the development of resource-appropriate early detection programs.
- Clinical breast examination should be promoted as a necessary method for clinical diagnosis of breast abnormalities.
- Diagnostic services, surgical treatment, radiotherapy, systemic therapy, and palliative care should become integrated within coordinated multidisciplinary environments.
- Systems for coordinated tissue sampling and pathology services should be developed to optimize pathology practices for accurate diagnosis and effective treatment planning.
- Barriers to accessing cancer drugs need to be addressed in conjunction with the deployment of properly trained physicians and staff.
- Workforce issues should be addressed through resourcesensitive strategies that provide quality care but without limiting access.

Adapted with permission from Anderson BO, Cazap E, El Saghir NS, et al. Optimisation of breast cancer management in low-resource and middleresourcecountries: executive summary of the Breast Health Global Initiative consensus, 2010. Lancet Oncol. 2011;12: 387-398.

The Global Health department of the American Cancer Society supports partnerships and advocacy coalitions that increase breast cancer awareness and early detection in low- and middleincome countries. To this end, the Society provides guidance, training, and tools across the cancer continuum and leverages the expertise and resources of established global health institutions. The Society is a founding partner of the newly established Global Breast Cancer Alliance, which calls for reducing the burden of breast cancer, as measured by improved health, enhanced well-being, and increased survival, for at least 2.5 million women in low- and middle-income countries by the year 2025. Other key founding partners include the Breast Health Global Initiative, the Harvard Global Equity Initiative, the National Cancer Institute's Center for Global Health, the Pan American Health Organization, Susan G. Komen for the Cure, and the Union for International Cancer Control.

The Society's Cancer Control department is collaborating with researchers from Europe and Asia to continue the evaluation of data from randomized controlled trials and large national databases of breast cancer screening in order to further quantify the effectiveness of early detection, and in particular to estimate prognosis based on tumor size, mammographic appearance, and molecular subtypes. In a separate study organized through the International Cancer Screening Network, a collaboration of US and European investigators is evaluating the relative contribution of system influences and individual expertise on the accuracy of mammography in different countries. The goal of this investigation is to better understand the differences in the sensitivity, specificity, and cancer detection rate between radiologists within and between countries, and to attempt to identify factors that can improve the accuracy and effectiveness of mammography screening.

The Society's Surveillance & Health Services Research program is collaborating with researchers at Martin Luther University (Germany) and Addis Ababa University (Ethiopia) to create an electronic database for breast cancer patients seen at the Addis Ababa University's teaching hospital in order to examine demographic and tumor characteristics, treatment, and survival and to enhance research capacity of residents and staff of the hospital's Oncology Department. Notably, this teaching hospital houses the only radiation treatment facility in Ethiopia and offers a unique opportunity to study breast cancer care and outcomes in a country with one of the fastest-growing economies in the world.

References

- 1. Bray F, Jemal A, Grey N, Ferlay J, Forman D. Global cancer transitions according to the Human Development Index (2008-2030): a populationbased study. Lancet Oncol. 2012;13: 790-801.
- 2. Cancer Genome Atlas Network. Comprehensive molecular portraits of human breast tumours. Nature. 2012;490: 61-70.

- 3. Perou CM, Sorlie T, Eisen MB, et al. Molecular portraits of human breast tumours. Nature. 2000;406: 747-752.
- 4. Tamimi RM, Colditz GA, Hazra A, et al. Traditional breast cancer risk factors in relation to molecular subtypes of breast cancer. Breast Cancer Res Treat. 2012;131: 159-167.
- 5. Yang XR, Chang-Claude J, Goode EL, et al. Associations of breast cancer risk factors with tumor subtypes: a pooled analysis from the Breast Cancer Association Consortium studies. J Natl Cancer Inst. 2011;103: 250-263.
- 6. Althuis MD, Dozier JM, Anderson WF, Devesa SS, Brinton LA. Global trends in breast cancer incidence and mortality 1973-1997. Int J Epidemiol. 2005;34: 405-412.
- 7. Kelsey JL, Gammon MD, John EM. Reproductive factors and breast cancer. Epidemiol Rev. 1993;15: 36-47.
- 8. Lambe M, Hsieh C, Trichopoulos D, Ekbom A, Pavia M, Adami HO. Transient increase in the risk of breast cancer after giving birth. N Engl IMed. 1994;331: 5-9.
- 9. Bruzzi P, Negri E, La Vecchia C, et al. Short term increase in risk of breast cancer after full term pregnancy. BMJ. 1988;297: 1096-1098.
- 10. Faupel-Badger JM, Arcaro KF, Balkam JJ, et al. Postpartum remodeling, lactation, and breast cancer risk: summary of a National Cancer Institute-sponsored workshop. J Natl Cancer Inst. 2013;105: 166-174.
- 11. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50,302 women with breast cancer and 96,973 women without the disease. Lancet. 2002;360: 187-195.
- 12. Collaborative Group on Hormonal Factors in Breast Cancer. Menarche, menopause, and breast cancer risk: individual participant metaanalysis, including 118,964 women with breast cancer from 117 epidemiological studies. Lancet Oncol. 2012;13: 1141-1151.
- 13. Ahn JH, Lim SW, Song BS, et al. Age at menarche in the Korean female: secular trends and relationship to adulthood body mass index. Ann Pediatr Endocrinol Metab. 2013;18: 60-64.
- 14. Krieger N, Kiang MV, Kosheleva A, Waterman PD, Chen JT, Beckfield J. Age at menarche: 50-year socioeconomic trends among US-born black and white women. Amer J Public Health. 2014: e1-e10.
- 15. Lewington S, Li L, Murugasen S, et al. Temporal trends of main reproductive characteristics in ten urban and rural regions of China: the China Kadoorie Biobank study of 300,000 women. Int J Epidemiol. 2014;43: 1252-1262.
- 16. Talma H, Schonbeck Y, van Dommelen P, Bakker B, van Buuren S, Hirasing RA. Trends in menarcheal age between 1955 and 2009 in the Netherlands. PLoS One. 2013;8: e60056.
- 17. World Cancer Research Fund/American Institute for Cancer Research. Food, nutrition, physical activity, and the prevention of cancer: a global perspective. Washington, DC: American Institute for Cancer Research, 2007.
- 18. La Vecchia C, Giordano SH, Hortobagyi GN, Chabner B. Overweight, obesity, diabetes, and risk of breast cancer: interlocking pieces of the puzzle. Oncologist. 2011;16: 726-729.
- 19. Amadou A, Ferrari P, Muwonge R, et al. Overweight, obesity and risk of premenopausal breast cancer according to ethnicity: a systematic review and dose-response meta-analysis. Obesity Reviews. 2013;14: 665-
- 20. Teegarden D, Romieu I, Lelievre SA. Redefining the impact of nutrition on breast cancer incidence: is epigenetics involved? Nutr Res Rev. 2012;25: 68-95.

- 21. Chlebowski RT. Nutrition and physical activity influence on breast cancer incidence and outcome. Breast. 2013;22S2: S30-S37.
- 22. Chen M, Rao Y, Zheng Y, et al. Association between soy isoflavone intake and breast cancer risk for pre- and post-menopausal women: a meta-analysis of epidemiological studies. PLoS One. 2014;9: e89288.
- 23. Alexander DD, Morimoto LM, Mink PJ, Lowe KA. Summary and meta-analysis of prospective studies of animal fat intake and breast cancer. Nutr Res Rev. 2010;23: 169-179.
- 24. Wu Y, Zhang D, Kang S. Physical activity and risk of breast cancer: a meta-analysis of prospective studies. Breast Cancer Res Treat. 2013;137: 869-882.
- 25. Lee IM, Shiroma EJ, Lobelo F, et al. Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy. Lancet. 2012;380: 219-229.
- 26. Chlebowski RT, Anderson GL, Gass M, et al. Estrogen plus progestin and breast cancer incidence and mortality in postmenopausal women. JAMA. 2010;304: 1684-1692.
- 27. Beral V, Reeves G, Bull D, Green J. Breast cancer risk in relation to the interval between menopause and starting hormone therapy. J Natl Cancer Inst. 2011;103: 296-305.
- 28. Chlebowski RT, Anderson GL. The influence of time from menopause and mammography on hormone therapy-related breast cancer risk assessment. J Natl Cancer Inst. 2011;103: 284-285.
- 29. Anderson GL, Chlebowski RT, Aragaki AK, et al. Conjugated equine oestrogen and breast cancer incidence and mortality in postmenopausal women with hysterectomy: extended follow-up of the Women's Health Initiative randomised placebo-controlled trial. Lancet Oncol. 2012:13:476-486.
- 30. Bakken K, Fournier A, Lund E, et al. Menopausal hormone therapy and breast cancer risk: impact of different treatments. The European Prospective Investigation into Cancer and Nutrition. Int J Cancer. 2011;128: 144-156.
- 31. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormonal contraceptives: collaborative reanalysis of individual data on 53,297 women with breast cancer and 100,239 women without breast cancer from 54 epidemiological studies. Lancet. 1996;347: 1713-1727.
- 32. Dossus L, Boutron-Ruault MC, Kaaks R, et al. Active and passive cigarette smoking and breast cancer risk: results from the EPIC cohort. Int J Cancer. 2014;134: 1871-1888.
- 33. Catsburg C, Miller AB, Rohan TE. Active cigarette smoking and risk of breast cancer. Int J Cancer. 2014: doi 10.
- 34. Gaudet MM, Gapstur SM, Sun J, Diver WR, Hannan LM, Thun MJ. Active smoking and breast cancer risk: original cohort data and metaanalysis. J Natl Cancer Inst. 2013;105: 515-525.
- 35. Bjerkaas E, Parajuli R, Weiderpass E, et al. Smoking duration before first childbirth: an emerging risk factor for breast cancer? Results from 302,865 Norwegian women. Cancer Causes Control. 2013;24: 1347-1356.
- 36. US Department of Health and Human Services. The Health Consequences of Smoking - 50 Years of progress. A Report of the Surgeon General. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2014. Printed with corrections, January 2014.
- 37. International Agency for Research on Cancer. IARC Monographs on the Evaluation of: Volume 100E-Tobacco Smoking. Carcinogenic Risks to Humans. Lyon, France: IARC Press, 2012.

- 38. Secretan B, Straif K, Baan R, et al. A review of human carcinogens-Part E: tobacco, areca nut, alcohol, coal smoke, and salted fish. Lancet Oncol. 2009;10: 1033-1034.
- 39. Pirie K, Beral V, Peto R, Roddam A, Reeves G, Green J. Passive smoking and breast cancer in never smokers: prospective study and metaanalysis. Int J Epidemiol. 2008;37: 1069-1079.
- 40. Luo J, Margolis KL, Wactawski-Wende J, et al. Association of active and passive smoking with risk of breast cancer among postmenopausal women: a prospective cohort study. BMJ. 2011;342: d1016.
- 41. Xue F, Willett WC, Rosner BA, Hankinson SE, Michels KB. Cigarette smoking and the incidence of breast cancer. Arch Intern Med. 2011;171: 125-133.
- 42. Anderson LN, Cotterchio M, Mirea L, Ozcelik H, Kreiger N. Passive cigarette smoke exposure during various periods of life, genetic variants, and breast cancer risk among never smokers. Am J Epidemiol. 2012;175: 289-301.
- 43. Hamajima N, Hirose K, Tajima K, et al. Alcohol, tobacco and breast cancer--collaborative reanalysis of individual data from 53 epidemiological studies, including 58,515 women with breast cancer and 95,067 women without the disease. Br J Cancer. 2002;87: 1234-1245.
- 44. Chen WY, Rosner B, Hankinson SE, Colditz GA, Willett WC. Moderate alcohol consumption during adult life, drinking patterns, and breast cancer risk. JAMA. 2011;306: 1884-1890.
- 45. Allen NE, Beral V, Casabonne D, et al. Moderate alcohol intake and cancer incidence in women. J Natl Cancer Inst. 2009;101: 296-305.
- 46. Preston DL, Mattsson A, Holmberg E, Shore R, Hildreth NG, Boice JD, Jr. Radiation effects on breast cancer risk: a pooled analysis of eight cohorts. Radiat Res. 2002;158: 220-235.
- 47. Travis LB, Hill DA, Dores GM, et al. Breast cancer following radiotherapy and chemotherapy among young women with Hodgkin disease. JAMA. 2003;290: 465-475.
- 48. Clemons M, Loijens L, Goss P. Breast cancer risk following irradiation for Hodgkin's disease. Cancer Treat Rev. 2000;26: 291-302.
- 49. Brody JG, Moysich KB, Humblet O, Attfield KR, Beehler GP, Rudel RA. Environmental pollutants and breast cancer. Cancer. 2007;109: 2667-
- 50. Steenland K, Whelan E, Deddens J, Stayner L, Ward E. Ethylene oxide and breast cancer incidence in a cohort study of 7576 women (United States). Cancer Causes Control. 2003;14: 531-539.
- 51. International Agency for Research on Cancer. IARC monographs on the evaluation of carcinogenic risks to humans. Volume 98. Shiftwork, painting and fire-fighting. Lyon, France: International Agency for Research on Cancer, 2007.
- 52. Kloog I, Stevens RG, Haim A, Portnov BA. Nighttime light level codistributes with breast cancer incidence worldwide. Cancer Causes Control. 2010:21: 2059-2068.
- 53. Nelson HD, Smith ME, Griffin JC, Fu R. Use of medications to reduce risk for primary breast cancer: a systematic review for the U.S. Preventive Services Task Force. Ann Intern Med. 2013;158: 604-614.
- 54. Vogel VG, Costantino JP, Wickerham DL, et al. Update of the National Surgical Adjuvant Breast and Bowel Project Study of Tamoxifen and Raloxifene (STAR) P-2 Trial: Preventing breast cancer. Cancer Prev Res. 2010:3: 696-706.
- 55. Goss PE, Ingle JN, Ales-Martinez JE, et al. Exemestane for breastcancer prevention in postmenopausal women. N Engl J Med. 2011;364: 2381-2391.

- 56. Cuzick J, Sestak I, Forbes JF, et al. Anastrozole for prevention of breast cancer in high-risk postmenopausal women(IBIS-II): an international, double-blind, randomised placebo-controlled trial. Lancet. 2014:383: 1041-1048.
- 57. Lostumbo L, Carbine NE, Wallace J. Prophylactic mastectomy for the prevention of breast cancer. Cochrane Database Syst Rev. 2010: CD002748.
- 58. Domchek SM, Friebel TM, Singer CF, et al. Association of risk-reducing surgery in BRCA1 or BRCA2 mutation carriers with cancer risk and mortality. JAMA. 2010;304: 967-975.
- 59. Rebbeck TR, Lynch HT, Neuhausen SL, et al. Prophylactic oophorectomy in carriers of BRCA1 or BRCA2 mutations. N Engl J Med. 2002;346: 1616-1622.
- 60. Independent U. K. Panel on Breast Cancer Screening. The benefits and harms of breast cancer screening: an independent review. Lancet. 2012;380: 1778-1786.
- 61. Gotzsche PC, Jorgensen KJ. Screening for breast cancer with mammography. Cochrane Database Syst Rev. 2013;6: CD001877.
- 62. Nelson HD, Tyne K, Naik A, et al. Screening for Breast Cancer: Systematic Evidence Review Update for the US Preventive Services Task Force. Rockville MD, 2009.
- 63. Paci E, Broeders M, Hofvind S, Puliti D, Duffy SW. European breast cancer service screening outcomes: a first balance sheet of the benefits and harms. Cancer Epid Biomarkers Prev. 2014;23: 1159-1163.
- 64. Weedon-Fekjaer H, Romundstad PR, Vatten LJ. Modern mammography screening and breast cancer mortality: population study. BMJ. 2014;348: g3701.
- 65. Coldman A, Phillips N, Wilson C, et al. Pan-Canadian study of mammography screening and mortality from breast cancer. J Natl Cancer Inst. 2014;106.
- 66. Youlden DR, Cramb SM, Dunn NA, Muller JM, Pyke CM, Baade PD. The descriptive epidemiology of female breast cancer: an international comparison of screening, incidence, survival and mortality. Cancer Epidemiol. 2012;36: 237-248.
- 67. Giordano L, von Karsa L, Tomatis M, et al. Mammographic screening programmes in Europe: organization, coverage and participation. J Med Screen. 2012;19 Suppl 1: 72-82.
- 68. Centers for Disease Control and Prevention. Cancer Screening -United States, 2010. Morb Mortal Wkly Rep. 2012;61:3.
- 69. World Health Organization. WHO position paper on mammogrpahy screening. Switzerland: World Health Organization, 2014.
- 70. Okonkwo QL, Draisma G, der Kinderen A, Brown ML, de Koning H. Breast cancer screening policies in developing countries: a cost-effectiveness analysis for India. J Natl Cancer Inst. 2008;100: 1290-1300.
- 71. Abuidris DO, Elsheikh A, Ali M, et al. Breast-cancer screening with trained volunteers in a rural area of Sudan: a pilot study. Lancet Oncol.
- 72. Devi BC, Tang TS, Corbex M. Reducing by half the percentage of late-stage presentation for breast and cervix cancer over 4 years: a pilot study of clinical downstaging in Sarawak, Malaysia. Ann Oncol. 2007;18: 1172-1176.
- 73. Yip CH, Smith RA, Anderson BO, et al. Guideline implementation for breast healthcare in low- and middle-incomecountries: early detection resource allocation. Cancer. 2008;113: 2244-2256.
- 74. Ziegler RG, Hoover RN, Pike MC, et al. Migration patterns and breast cancer risk in Asian-American women. J Natl Cancer Inst. 1993;85: 1819-1827.

- 75. Tominaga S. Cancer incidence in Japanese in Japan, Hawaii, and western United States. Natl Cancer Inst Monogr. 1985;69: 83-92.
- 76. Roa BB, Boyd AA, Volcik K, Richards CS. Ashkenazi Jewish population frequencies for common mutations in BRCA1 and BRCA2. Nat Genet. 1996:14: 185-187.
- 77. Kamangar F, Dores GM, Anderson WF. Patterns of cancer incidence, mortality, and prevalence across five continents: defining priorities to reduce cancer disparities in different geographic regions of the world. J Clin Oncol. 2006;24: 2137-2150.
- 78. Bray F, McCarron P, Parkin DM. The changing global patterns of female breast cancer incidence and mortality. Breast Cancer Res. 2004;6:
- 79. Anderson BO. Breast cancer hormone receptor status in Egypt: are we asking the questions that matter most? Breast Cancer Res Treat.
- 80. Hammond ME, Hayes DF, Dowsett M, et al. American Society of Clinical Oncology/College of American Pathologists guideline recommendations for immunohistochemical testing of estrogen and progesterone receptors in breast cancer. *Arch Pathol Lab Med*. 2010;134: e48-72.
- 81. Ravdin PM, Cronin KA, Howlader N, et al. The decrease in breastcancer incidence in 2003 in the United States. N Engl J Med. 2007;356:
- 82. Canfell K, Banks E, Moa AM, Beral V. Decrease in breast cancer incidence following a rapid fall in use of hormone replacement therapy in Australia. Med J Aust. 2008;188: 641-644.
- 83. Parkin DM. Is the recent fall in incidence of post-menopausal breast cancer in UK related to changes in use of hormone replacement therapy? Eur J Cancer. 2009;45: 1649-1653.
- 84. Seradour B, Allemand H, Weill A, Ricordeau P. Changes by age in breast cancer incidence, mammography screening and hormone therapy use in France from 2000 to 2006. Bull Cancer. 2009;96: E1-6.
- 85. De P, Neutel CI, Olivotto I, Morrison H. Breast cancer incidence and hormone replacement therapy in Canada. J Natl Cancer Inst. 2010;102: 1489-1495.
- 86. Colditz GA, Sellers TA, Trapido E. Epidemiology identifying the causes and preventability of cancer? Nature Rev Cancer. 2006;6: 75-83.
- 87. Youlden DR, Cramb SM, Yip CH, Baade PD. Incidence and mortality of female breast cancer in the Asia-Pacific region. Cancer Biol Med. 2014;11: 101-115.
- 88. Bosetti C, Bertuccio P, Levi F, Chatenoud L, Negri E, La Vecchia C. The decline in breast cancer mortality in Europe: an update (to 2009).
- 89. Autier P, Boniol M, Middleton R, et al. Advanced breast cancer incidence following population-based mammographic screening. Ann Oncol. 2011;22: 1726-1735.
- 90. Berry DA, Cronin KA, Plevritis SK, et al. Effect of screening and adjuvant therapy on mortality from breast cancer. N Engl J Med. 2005;353: 1784-1792.
- 91. Jemal A, Center MM, DeSantis C, Ward EM. Global patterns of cancer incidence and mortality rates and trends. Cancer Epid Biomarkers Prev. 2010:19: 1893-1907.
- 92. Ito Y, Ioka A, Tanaka M, Nakayama T, Tsukuma H. Trends in cancer incidence and mortality in Osaka, Japan: evaluation of cancer control activities. Cancer Sci. 2009;100: 2390-2395.

- 93. Allemani C, Weir HK, Carreira H, et al. Global surveillance of cancer survival 1995-2009: analysis of individual data for 25,676,887 patients from 279 population-based registries in 67 countries (CONCORD-2). Lancet, 2014.
- 94. Shulman LN, Willett W, Sievers A, Knaul FM. Breast cancer in developing countries: opportunities for improved survival. $JOncol.\ 2010; 2010:$ 595167.
- 95. Espinosa de Los Monteros K, Gallo LC. The relevance of fatalism in the study of Latinas' cancer screening behavior: a systematic review of the literature. Int J Behav Med. 2011;18: 310-318.
- 96. Azaiza F, Cohen M, Daoud F, Awad M. Traditional-Westernizing continuum of change in screening behaviors: comparison between Arab women in Israel and the West Bank. Breast Cancer Res Treat. 2011;128: 219-227.
- 97. De Ver Dye T, Bogale S, Hobden C, et al. A mixed-method assessment of beliefs and practice around breast cancer in Ethiopia: implications for public health programming and cancer control. Glob Public Health. 2011;6: 719-731.
- 98. Anderson BO, Cazap E, El Saghir NS, et al. Optimisation of breast cancer management in low-resource and middle-resourcecountries: executive summary of the Breast Health Global Initiative consensus, 2010. Lancet Oncol. 2011:12: 387-398.
- 99. Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N Engl IMed. 2002;347: 1233-1241.
- 100. Veronesi U, Cascinelli N, Mariani L, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. N Engl J Med. 2002;347: 1227-1232.
- 101. Litiere S, Werutsky G, Fentiman IS, et al. Breast conserving therapy versus mastectomy for stage I-II breast cancer: 20 year follow-up of the EORTC 10801 phase 3 randomised trial. Lancet Oncol. 2012;13: 412-419.
- 102. Division of Programme of Action for Cancer Therapy. International Atomic Energy Agency. AGaRT: Advisory Group on increasing access to Radiotherapy Technology Available from URL: http://cancer.iaea.org/ agart.asp. Accessed October 31, 2014.
- 103. International Atomic Energy Agency. Comprehensive audits of radiotherapy practices: a tool for quality improvement. Available from URL: http://www-pub.iaea.org/MTCD/Publications/PDF/Pub1297_web. pdf. Accessed November 19, 2014.
- 104. Eniu A, Carlson RW, El Saghir NS, et al. Guideline implementation for breast healthcare in low- and middle-income countries: treatment resource allocation. Cancer. 2008:113: 2269-2281.

The Global 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. Cancer is an enormous global health burden, touching every region and socioeconomic group. Tobacco use is a major cause of the increasing global burden of cancer as the number of smokers worldwide continues to grow.

Worldwide Tobacco Use

Tobacco-related diseases are the most preventable cause of death worldwide, responsible for the deaths of approximately half of all long-term tobacco users.

- Each year, tobacco use is responsible for almost 6 million premature deaths, 80% of which are in low- and middle-income countries; by 2030, this number is expected to increase to 8 million.
- Between 2002 and 2030, tobacco-attributable deaths are expected to decrease by 9% in high-income countries, while increasing by 100% (from 3.4 million to 6.8 million) in lowand middle-income countries.
- In addition to lung cancer, tobacco use causes cancers of the oral cavity and pharynx, esophagus, stomach, colorectum, liver, pancreas, larynx, uterine cervix, ovary, urinary bladder, kidney, and myeloid leukemia.

The first global public health treaty, the Framework Convention on Tobacco Control (FCTC), was unanimously adopted by the World Health Assembly on May 21, 2003, and subsequently entered into force as a legally binding accord for all ratifying states on February 27, 2005. The purpose of the treaty is to fight the devastating health and economic effects of tobacco on a global scale by requiring parties to adopt a comprehensive range of tobacco control measures. It features specific provisions to control both the global supply and demand for tobacco, including the regulation of tobacco product contents, packag-ing, labeling, advertising, promotion, sponsorship, taxation, illicit trade, youth access, exposure to secondhand tobacco smoke, and environmental and agricultural impacts. Parties to the treaty are expected to strengthen national legislation, enact effective tobacco control policies, and cooperate internationally to reduce global tobacco consumption. A number of major tobaccoproducing nations, including Argentina, Indonesia, Malawi, the United States, and Zimbabwe, have not ratified the treaty.

· As of October 2014, 179 out of 196 eligible countries have ratified or acceded to the treaty, representing approximately 89% of the world's population.

- · About one-third of the world's population was covered by at least one comprehensive tobacco control measure in 2012, up from about 15% in 2008.
- The WHO estimates that 16% of the world's population lives in smoke-free environments.
- · Although tobacco tax increases are among the most costeffective tobacco control strategies, less than 8% of the world population is covered by comprehensive tobacco tax policy.

The Role of the American Cancer Society

With more than a century of experience in cancer control, the American Cancer Society is uniquely positioned to help in leading the global fight against cancer and tobacco by assisting and empowering the world's cancer societies and anti-tobacco advocates. The Society's Global Health and Intramural Research departments are raising awareness about the growing global cancer burden and promoting evidence-based cancer and tobacco control programs.

The Society has established key focus areas to help reduce the global burden of cancer, including global grassroots policy and awareness, tobacco control, cancer screening and vaccination for breast and cervical cancers, access to pain relief, and the support of cancer registration in low- and middle-income countries.

Make cancer control a political and public health priority.

Noncommunicable diseases (NCDs) such as cancer, heart disease, and diabetes account for about 65% of the world's deaths. Although 67% of these deaths occur in low- and middle-income countries, less than 3% of private and public health funding is allocated to prevent and control NCDs in these areas. In September 2011, world leaders gathered at a special United Nations High-level Meeting and adopted a Political Declaration that elevates cancer and other NCDs on the global health and development agenda and includes key commitments to address these diseases. In 2012, the decision-making body of the World Health Organization (WHO) approved a resolution calling for a 25 percent reduction in premature deaths from NCDs by 2025 (also known as 25 by 25). This ambitious goal set the stage for the adoption of a comprehensive framework aimed at monitoring NCD risk factors (e.g., smoking prevalence) and indicators of increased access to breast and cervical cancer screening, palliative care, and vaccination coverage. To maintain the momentum for making cancer and other NCDS a global priority, the Society collaborates with key partners, including the NCD Alliance, the Union for International Cancer Control (UICC), the American Heart Association, and the American Diabetes Association. In addition to promoting cancer control as a global public health priority, the Society also partners with key stakeholders to build a global network to fight cancer through advocacy, capacity building, information sharing, and resource mobilization.

Develop cancer control capacity globally. Many governments in low- and middle-income countries are ill-prepared to adequately and appropriately address the increasing burden of cancer in their countries. In many cases, civil society actors (non-governmental organizations, institutions, and individuals) are also not yet fully engaged in effectively addressing cancer.

The Society's Global Capacity Development program is intended to strengthen the civil society response to cancer in focus countries around the world, taking advantage of more than 100 years of institutional experience and expertise in cancer control. This program provides intensive and culturally appropriate technical assistance to targeted organizations in low- and middle-income countries. The program's areas of intervention include the basic elements of organizational capacity development, such as governance, financial management, fundraising, program design and management, and monitoring and evaluation. In 2015, the Global Capacity Development program will focus the majority of its staffing and resources on strengthening the cancer response in Ethiopia, Kenya, and Uganda in the key areas of patient support for which the Society has adaptable and effective models for transportation, lodging, and patient navigation.

Make effective pain treatment available to all in need. Untreated moderate to severe pain that grows worse each day, which is experienced by about 80% of people with advanced cancer, is a consistent feature of cancer care in resource-limited settings. Improved access to essential pain medicines is not the only thing that cancer patients in low- and middle-income countries need, but it is arguably the easiest and least expensive need to meet, would do the most to relieve suffering, and recent data suggest it may also extend survival. In Nigeria, the Society partnered with the government to make morphine available for the first time in several years and set up a local production system in 22 teaching hospitals that lowered the price for patients by 81%. The Society has awarded a grant to Hospice Africa Uganda (HAU) to fund upgrades that will allow them to automate some

aspects of oral morphine production in their national production facility. These facility upgrades will allow HAU to handle the increasing demand for pain relief with lower costs. The Society is also partnering with Kenyatta National Hospital in Nairobi, Kenya; Black Lion hospital in Addis Ababa, Ethiopia; and Mbabane Government Hospital in Mbabane, Swaziland, to implement the Pain-Free Hospital Initiative, a one-year hospital-wide quality improvement initiative designed to change clinical practice by integrating effective, high-quality pain treatment into hospital-based services.

Reduce tobacco use, with a particular focus on sub-Saharan Africa. Through an \$8 million (US) grant received from the Bill & Melinda Gates Foundation in 2010, the Society and its partners, the Africa Tobacco Control Alliance, the Framework Convention Alliance, the Campaign for Tobacco-Free Kids, and the International Union Against Tuberculosis and Lung Disease, support and assist national governments and civil society in Africa to implement tobacco control policies such as advertising bans, tobacco tax increases, graphic warning labels, and the promotion of smoke-free environments.

Increase awareness about the global cancer burden. The Society continues to work with global partners to increase awareness about the growing global cancer and tobacco burdens and their impact on low- and middle-income countries. In addition to print publications, the Society website, cancer.org, provides cancer information to millions of individuals throughout the world. In 2014, 40% of visits to the website came from outside the United States. Information is currently available in English, Spanish, Chinese, Bengali, Hindi, Korean, Urdu, and Vietnamese. For more information on the global cancer burden, visit the Society's Global Health program website at cancer.org/international and global.cancer.org and visit cancer.org and tobaccoatlas.org to see the following Intramural Research program publications:

The Tobacco Atlas, Fourth Edition
The Cancer Atlas, Second Edition

Sources of Statistics

Incidence and mortality rates: Cancer incidence is the number of newly diagnosed cancer cases in a population during a specific time period, expressed herein as a rate per 100,000 persons. Cancer mortality is the number of cancer deaths in a population during a given time period and is also as a rate per 100,000 persons. Cancer mortality rates reflect both incidence and survival. Incidence and mortality numbers and rates for 2012 were obtained from GLOBOCAN 2012 (globocan.iarc.fr/), published by the International Agency for Research on Cancer (IARC).

GLOBOCAN estimates cancer incidence and mortality rates in each country of the world using different methods depending on the accuracy and availability of data. ¹⁴³ Coverage of population-based cancer registries ranges from 1% in Africa, 6% in Asia, and 8% in Latin America to 42% in Europe, 78% in Oceania, and 95% in Northern America. ¹⁴⁴ Mortality data are available for about one-third of the world population, and are generally of higher quality in high-income countries. ¹⁴⁵ IARC also makes available historic incidence and mortality data in its Cancer Incidence in

Five Continents database (ci5.iarc.fr/) 144 and World Health Organization Cancer Mortality Database (www-dep.iarc.fr/WHOdb/WHOdb.htm). 146

For countries where complete national incidence data were not available, data from the below listed regional registries were used.

Country	Regional registries representing countries
Algeria	Setif
Australia	New South Wales, Queensland, South, Tasmania, Victoria and Western
Austria	Tyrol and Vorarlberg
Brazil	Goiania
Canada	Manitoba, Nova Scotia and Sasketchewan
China	Hong-Kong, Jiashan County and Shanghai
Colombia	Cali
Ecuador	Quito
France	Bas-Rhin, Calvados, Doubs, Isere, Haut-Rhin, Herault, Somme and Tarn
Germany	Berlin, Brandenburg, Mecklenburg, Saxony, Saxony-Anhalt, Schleswig-Holstein and Thuringia
India	Chennai, Mumbay and Poona
Israel	Jews
Italy	Ferrara Province, Lombardy, Varese Province, Modena, Parma, Ragusa Province, Romagna, Sassari Province, Torino
Japan	Miyagi, Nagasaki and Osaka
Philippines	Manila
Poland	Cracow city, Kielce and Lower Silesia
Russian Federation	St Petersburg
Spain	Albacete, Cuenca, Girona, Granada, Murcia, Navarra and Tarragona
Switzerland	Geneva, Graubunden and Glarus, Neuchatel, St. Gall- Appenzell, Valais and Vaud
Thailand	Chiang Mai, Lampang and Songkhla
Uganda	Kyadondo
United Kingdom	England: Birmingham and West Midlands Region, Merseyside and Cheshire, North Western, Oxford, South and Western Regions, Yorkshire, East of England Region, Scotland and Northern Ireland
USA	SEER: states of Connecticut, Hawaii, Iowa, New Mexico, and Utah and metropolitan areas of San Francisco-Oakland (California), Detroit (Michigan), Seattle-PugetSound (Washington) and Atlanta (Georgia)
Zimbabwe	Harare: Africans

Source: Ferlay J, Bray F, Steliarova-Foucher E and Forman D. Cancer Incidence in Five Continents, CI5plus: IARC CancerBase No. 9 [Internet]. Lyon, France: International Agency for Research on Cancer; 2014. Available from: http://ci5.iarc.fr

Global incidence and mortality rates were age-standardized to the 1960 world standard population. Rates presented herein cannot be compared to rates standardized to a different population. Age-standardization controls for differences in age distribution, allowing for comparisons over time and across populations.

Survival: Cancer survival is the length of time a person lives following cancer diagnosis. The relative survival rate represents the percentage of cancer patients who are living after a specified time period since cancer diagnosis compared with the expected survival of a cancer-free population of the same age, race, and sex. Survival rates are usually presented for those who live five years after diagnosis. The large variation in survival rates across countries and regions reflects a combination of differences in the mix of cancer types, the prevalence of screening and diagnostic services, and/or the availability of effective and timely treatment. Methodological problems relating to incompleteness of registration and follow-up also contribute to apparent differences.

Developed vs. Developing Countries

A country's development may be classified according to one of several systems, including the United Nations dichotomy of more-developed and less-developed; World Bank income groups; or the United Nations Development Programme's Human Development Index ranking.

The United Nations

More-developed regions' rates have been estimated as the population-weighted average of all regions of Europe, plus Northern America, Australia/New Zealand, and Japan. Less-developed regions' rates have been estimated as the population-weighted average of all regions of Africa, Asia (excluding Japan), Latin America and the Caribbean, Melanesia, Micronesia, and Polynesia.

World Bank Income Group

Economies are divided according to 2013 gross national income (GNI) per capita in US Dollars, calculated using the World Bank Atlas method. The groups are: low income, \$1,045 or less; lower middle income, \$1,046 to \$4,125; upper middle income, \$4,126 to \$12,745 middle income, and high income, \$12,746 or more.

Low-income economies:

Afghanistan	Gambia, The	Nepal
Bangladesh	Guinea	Niger
Benin	Guinea-Bisau	Rwanda
Burkina Faso	Haiti	Sierra Leone
Burundi	Kenya	Somalia
Cambodia	Korea, Dem Rep.	Tajikistan
Central African Republic	Liberia	Tanzania
Chad	Madagascar	Togo
Comoros	Malawi	Uganda
Congo, Dem. Rep	Mali	Zimbabwe
Eritrea	Mozambique	
Ethiopia	Myanmar	

Lower-middle-income economies:

Armenia	Kiribati	São Tomé and Principe
Bhutan	Kosovo	Senegal
Bolivia	Kyrgyz Republic	Solomon Islands
Cameroon	Lao PDR	South Sudan
Cabo Verde	Lesotho	Sri Lanka
Congo, Rep.	Mauritania	Sudan
Côte d'Ivoire	Micronesia, Fed. Sts.	Swaziland
Djibouti	Moldova	Syrian Arab Republic
Egypt, Arab Rep.	Mongolia	Timor-Leste
El Salvador	Morocco	Ukraine
Georgia	Nicaragua	Uzbekistan
Ghana	Nigeria	Vanuatu
Guatemala	Pakistan	Vietnam
Guyana	Papua New Guinea	West Bank and Gaza
Honduras	Paraguay	Yemen, Rep.
Indonesia	Philippines	Zambia
India	Samoa	

Upper-middle-income economies:

opper-illidate-illic	office economies.	
Angola	Fiji	Palau
Albania	Gabon	Panama
Algeria	Grenada	Peru
American Samoa	Hungary	Romania
Argentina	Iran, Islamic Rep.	Serbia
Azerbaijan	Iraq	Seychelles
Belarus	Jamaica	South Africa
Belize	Jordan	St. Lucia
Bosnia and Herzegovina	Kazakhstan	St. Vincent and the Grenadines
Botswana	Lebanon	Suriname
Brazil	Libya	Thailand
Bulgaria	Macedonia, FYR	Tonga
China	Malaysia	Tunisia
Colombia	Maldives	Turkey
Costa Rica	Marshall Islands	Turkmenistan
Cuba	Mauritius	Tuvalu
Dominica	Mexico	Venezuela, RB
Dominican Republic	Montenegro	
Ecuador	Namibia	

High-income economies:

_		
Andorra	French Polynesia	Norway
Antigua and Barbuda	Germany	Oman
Aruba	Greece	Poland
Australia	Greenland	Portugal
Austria	Guam	Puerto Rico
Bahamas, The	Hong Kong SAR, China	Qatar
Bahrain	Iceland	Russian Federation

High-income economies: (continued)

Barbados	Ireland	San Marino
Belgium	Isle of Man	Saudi Arabia
Bermuda	Israel	Singapore
Brunei Darussalam	Italy	Sint Maarten
Canada	Japan	Slovak Republic
Cayman Islands	Korea, Rep.	Slovenia
Channel Islands	Kuwait	Spain
Chile	Latvia	St. Kitts and Nevis
Croatia	Liechtenstein	St. Martin
Curaçao	Lithuania	Sweden
Cyprus	Luxembourg	Switzerland
Czech Republic	Macao SAR, China	Trinidad and Tobago
Denmark	Malta	Turks and Caicos Islands
Estonia	Monaco	United Arab Emirates
Equatorial Guinea	Netherlands	United Kingdom
Faeroe Islands	New Caledonia	United States
Finland	New Zealand	Uruguay
France	Northern Mariana Islands	Virgin Islands (US)

Human Development Index

The United Nations Development Programme's Human Devel $opment\ Index\ is\ a\ composite\ measure\ of\ educational\ attainment$ and life expectancy, as well as level of income. It can be used as a ranking or in categories of very high, high, medium, and low. The 2014 groups are:

Very high:

Andorra	Germany	New Zealand
Argentina	Greece	Norway
Australia	Hong Kong, China (SAR)	Poland
Austria	Hungary	Portugal
Bahrain	Iceland	Qatar
Belgium	Ireland	Saudi Arabia
Brunei Darussalam	Israel	Singapore
Canada	Italy	Slovakia
Chile	Japan	Slovenia
Croatia	Korea (Republic of)	Spain
Cuba	Kuwait	Sweden
Cyprus	Latvia	Switzerland
Czech Republic	Liechtenstein	United Arab Emirates
Denmark	Lithuania	United Kingdom
Estonia	Luxembourg	United States
Finland	Malta	
France	Netherlands	

High:

riigii.		
Albania	Fiji	Russian Federation
Algeria	Georgia	Saint Kitts and Nevis
Antigua and Barbuda	Grenada	Saint Lucia
Armenia	Iran (Islamic Republic of)	Saint Vincent and the Grenadines
Azerbaijan	Jamaica	Serbia
Bahamas	Jordan	Seychelles
Barbados	Kazakhstan	Sri Lanka
Belarus	Lebanon	Suriname
Belize	Libya	Thailand
Bosnia and Herzegovina	Malaysia	The former Yugoslav Republic of Macedonia
Brazil	Mauritius	Tonga
Bulgaria	Mexico	Trinidad and Tobago
China	Montenegro	Tunisia
Colombia	Oman	Turkey
Costa Rica	Palau	Ukraine
Dominica	Panama	Uruguay
Dominican Republic	Peru	Venezuela (Bolivarian Republic of)
Ecuador	Romania	

Medium:

Bangladesh	Honduras	Palestine, State of
Bhutan	India	Paraguay
Bolivia (Plurinational State of)	Indonesia	Philippines
Botswana	Iraq	Samoa
Cambodia	Kiribati	Sao Tome and Principe
Cape Verde	Kyrgyzstan	South Africa
Congo	Lao People's Democratic Republic	Syrian Arab Republic
Egypt	Maldives	Tajikistan
El Salvador	Micronesia (Federated States of)	Timor-Leste
Equatorial Guinea	Moldova (Republic of)	Turkmenistan
Gabon	Mongolia	Uzbekistan
Ghana	Morocco	Vanuatu
Guatemala	Namibia	Viet Nam
Guyana	Nicaragua	Zambia

Low:

Afghanistan	Guinea	Pakistan
Angola	Guinea-Bissau	Papua New Guinea
Benin	Haiti	Rwanda
Burkina Faso	Kenya	Senegal
Burundi	Lesotho	Sierra Leone
Cameroon	Liberia	Solomon Islands

Low: (continued)

Central African Republic	Madagascar	Sudan
Chad	Malawi	Swaziland
Comoros	Mali	Tanzania (United Republic of)
Congo (Democratic Republic of the)	Mauritania	Togo
Côte d'Ivoire	Mozambique	Uganda
Djibouti	Myanmar	Yemen
Eritrea	Nepal	Zimbabwe
Ethiopia	Niger	
Gambia	Nigeria	

World Regions

UN Areas

Eastern Africa: Burundi, Comoros, Djibouti, Eritrea, Ethiopia, Kenya, La Reunion (France), Madagascar, Malawi, Mauritius, Mozambique, Rwanda, Somalia, Tanzania, Uganda, Zambia, and Zimbabwe. Middle Africa: Angola, Cameroon, Central African Republic, Chad, Democratic Republic of Congo, Republic of Congo, Equatorial Guinea, and Gabon. Northern Africa: Algeria, Egypt, Libya, Morocco, Sudan, Tunisia, and Western Sahara. Southern Africa: Botswana, Lesotho, Namibia, South African Republic, and Swaziland. Western Africa: Benin, Burkina Faso, Cape Verde, Cote d'Ivoire, Gambia, Ghana, Guinea-Bissau, Guinea, Liberia, Mali, Mauritania, Niger, Nigeria, Senegal, Sierra Leone, and Togo. Caribbean: Bahamas, Barbados, Cuba, Dominican Republic, Guadeloupe (France), Haiti, Jamaica, Martinique (France), Puerto Rico, and Trinidad and Tobago. Central America: Belize, Costa Rica, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, and Panama. Southern America: Argentina, Bolivia, Brazil, Chile, Colombia, Ecuador, French Guyana, Guyana, Paraguay, Peru, Suriname, Uruguay, and Venezuela. Northern America: Canada, United States of America Eastern Asia: China, Japan, Democratic People's Republic of Korea, Republic of Korea, Mongolia, Taiwan Southeast Asia: Brunei Darussalam, Cambodia, Indonesia, Lao People Democratic Republic, Malaysia, Myanmar, Philippines, Singapore, Thailand, and Vietnam. South-Central Asia: Afghanistan, Bangladesh, Bhutan, India, Islamic Republic of Iran, Kazakhstan, Kyrgyzstan, Nepal, Pakistan, Sri Lanka, Tajikistan, Turkmenistan, and Uzbekistan. Western Asia: Armenia, Azerbaijan, Bahrain, Gaza Strip and West Bank (Palestine), Georgia, Iraq, Israel, Jordan, Kuwait, Lebanon, Oman, Qatar, Saudi Arabia, Syrian Arab Republic, Turkey, United Arab Emirates, and Yemen. Central and Eastern Europe: Belarus, Bulgaria, Czech Republic, Hungary, Republic of Moldova, Poland, Romania, Russian Federation, Slovakia, and Ukraine. Northern Europe: Denmark, Estonia, Finland, Iceland, Ireland, Latvia, Lithuania, Norway, Sweden, and United Kingdom. Southern Europe: Albania, Bosnia and Herzegovina, Croatia, Cyprus, Greece, Italy, Former Yugoslav Republic of Macedonia, Montenegro, Malta, Portugal, Serbia, Slovenia, Spain Western Europe: Austria, Belgium, France, Germany, Luxembourg, The Netherlands, Switzerland. Australia/New Zealand: Australia, and New Zealand. Melanesia: Fiji, New Caledonia, Papua New Guinea, Solomon Islands, and Vanuatu. Micronesia: Guam. Polynesia: French Polynesia and Samoa.

WHO Regions

African Region: Algeria, Angola, Benin, Botswana, Burkina Faso, Burundi, Cameroon, Cape Verde, Central African Republic, Chad, Comoros, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Equatorial Guinea, Eritrea, Ethiopia, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Kenya, Lesotho, Liberia, Madagascar, Malawi, Mali, Mauritania, Mauritius, Mozambique, Namibia, Niger, Nigeria, Rwanda, Sao Tome and Principe, Senegal, Seychelles, Sierra Leone, South Africa, Swaziland, Togo, Uganda, United Republic of Tanzania, Zambia, and Zimbabwe. Region of the Americas: Antigua and Barbuda, Argentina, Bahamas, Barbados, Belize, Bolivia, Brazil, Canada, Chile, Colombia, Costa Rica, Cuba, Dominica, Dominican Republic, Ecuador, El Salvador, Grenada, Guatemala, Guyana, Haiti, Honduras, Jamaica, Mexico, Nicaragua, Panama, Paraguay, Peru, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, Suriname, Trinidad and Tobago, United States of America, Uruguay, and Venezuela. Eastern Mediterranean Region: Afghanistan, Bahrain, Djibouti, Egypt, Iran (Islamic Republic of), Iraq, Jordan, Kuwait, Lebanon, Libyan Arab Jamahiriya, Morocco, Oman, Pakistan, Oatar, Saudi Arabia, Somalia, Sudan, Syrian Arab Republic, Tunisia, United Arab Emirates, and Yemen. European Region: Albania, Andorra, Armenia, Austria, Azerbaijan, Belarus, Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Georgia, Germany, Greece, Hungary, Iceland, Ireland, Israel, Italy, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Luxembourg, Malta, Monaco, Montenegro, Netherlands, Norway, Poland, Portugal, Republic of Moldova, Romania, Russian Federation, San Marino, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Tajikistan, the former Yugoslav Republic of Macedonia, Turkey, Turkmenistan, Ukraine, United Kingdom, and Uzbekistan. Southeast Asia Region: Bangladesh, Bhutan, Democratic People's Republic of Korea, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand, and Timor-Leste. Western Pacific Region: Australia, Brunei Darussalam, Cambodia, China, Cook Islands, Fiji, Japan, Kiribati, Lao People's Democratic Republic, Malaysia, Marshall Islands, Micronesia (Federated States of), Mongolia, Nauru, New Zealand, Niue, Palau, Papua New Guinea, Philippines, Republic of Korea, Samoa, Singapore, Solomon Islands, Tonga, Tuvalu, Vanuatu, and Vietnam.

References

- 1. Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. http://globocan.iarc.fr. Accessed December 12, 2013.
- 2. de Martel C, Ferlay J, Franceschi S, et al. Global burden of cancers attributable to infections in 2008: a review and synthetic analysis. Lancet Oncol. 2012;13(6):607-615.
- 3. Institute for Health Metrics and Evaluation (IHME). GBD Cause Patterns. Seattle, WA: IHME, University of Washington, 2013. Available from http://vizhub.healthdata.org/gbd-cause-patterns/. (Accessed September 15, 2014).
- 4. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2013;380(9859):2095-2128.
- 5. World Cancer Research Fund International. Cancer preventability estimates for food, nutrition, body fatness, and physical activity. 2014; http://www.wcrf.org/int/cancer-facts-figures/preventability-estimates/cancer-preventability-estimates-food-nutrition. Accessed September 16, 2014.
- 6. Clerc-Urmès I, Grzebyk M, Hédelin G. Net survival estimation with stns. Stata Journal. 2014;14(1):87-102.
- 7. International Agency for Research on Cancer. Global Initiative for Cancer Registry Development. http://gicr.iarc.fr/. Accessed 14 October, 2014.

- 8. Mackay J, Jemal A, Lee NC, Parkin DM. The Cancer Atlas, First Edition. Atlanta: American Cancer Society; 2006.
- 9. Agency for Healthcare Research and Quality. Total Expenses and Percent Distribution for Selected Conditions by Type of Service: United States, 2011. Medical Expenditure Panel Survey Household Component Data. Generated interactively. (October 02, 2014).
- 10. Hanly P, Soerjomataram I, Sharp L. Measuring the societal burden of cancer: The cost of lost productivity due to premature cancer-related mortality in Europe. Int J Cancer. 2014:doi 10.
- 11. Elkin EB, Bach PB. Cancer's next frontier: addressing high and increasing costs. JAMA. 2010;303(11):1086-1087.
- 12. Union for International Cancer Control. World Cancer Declaration. 2013; http://www.uicc.org/world-cancer-declaration. Accessed September 18, 2014.
- 13. Sener FS. Disease without borders. CA Cancer J Clin. 2005;55:7-9.
- 14. World Health Organization. National Cancer Control Programmes. Geneva: World Health Organization; 2002.
- 15. World Health Organization. Discussion paper: Prevention and control of NCDs: Priorities for investment. First Global Ministerial Conference on Healthy Lifestyles and Noncommunicable Disease Control Moscow 2011.
- 16. Framework Convention Alliance. Latest ratifications. 2014; http:// www.fctc.org/about-fca/tobacco-control-treaty/latest-ratifications.

- 17. World Health Organization. Global Strategy on Diet, Physical Activity, and Health 2004.
- 18. Vainio H, Bianchini F, eds. Breast Cancer Screening (volume 7). Lyon: IARC Press; 2002. IARC Handbooks of Cancer Prevention, ed.
- 19. Institute of Medicine (U.S.). Cancer control opportunities in low- and middle- income countries. Washington DC: The National Academies Press; 2007.
- 20. World Health Organization. Comprehensive Cervical Cancer Control: A guide to essential practice. Switzerland: World Health Organization;
- 21. Wright TC, Jr., Kuhn L. Alternative approaches to cervical cancer screening for developing countries. Best Pract Res Clin Obstet Gynaecol. 2012;26(2):197-208.
- 22. Jeronimo J, Bansil P, Lim J, et al. A multicountry evaluation of careHPV testing, visual inspection with acetic acid, and papanicolaou testing for the detection of cervical cancer. Int J Gynecol Cancer. 2014;24(3):576-585.
- 23. Goldie SJ, Gaffikin L, Goldhaber-Fiebert JD, et al. Cost-effectiveness of cervical-cancer screening in five developing countries. New Engl J Med. 2005;353(20):2158-2168.
- 24. World Health Organization. WHO's cancer pain ladder for adults. 2014; http://www.who.int/cancer/palliative/painladder/en/. Accessed September 22, 2014.
- 25. World Health Organization. Access to Controlled Medications Programme Geneva: WHO; 2007.
- 26. Cherny NI, Baselga J, de Conno F, Radbruch L. Formulary availability and regulatory barriers to accessibility of opioids for cancer pain in Europe: a report from the ESMO/EAPC Opioid Policy Initiative. Ann Oncol. 2010;21(3):615-626.
- 27. Bansal M, Patel FD, Mohanti BK, Sharma SC. Setting up a palliative care clinic within a radiotherapy department: a model for developing countries. Support Care Cancer. 2003;11(6):343-347.
- 28. Sharma K, Mohanti BK, Rath GK, Bhatnagar S. Pattern of palliative care, pain management and referral trends in patients receiving radiotherapy at a tertiary cancer center. Indian J Palliat Care. 2009;15(2):148-
- 29. Burton A. The UICC My Child Matters initiative awards:combating cancer in children in the developing world. Lancet. 2006;7:13-14.
- 30. Barr RD, Antillon Klussmann F, Baez F, et al. Asociacion de Hemato-Oncologia Pediatrica de Centro America (AHOPCA): a model for sustainable development in pediatric oncology. Pediatr Blood Cancer. 2014;61(2):345-354.
- 31. Magrath I, Steliarova-Foucher E, Epelman S, et al. Paediatric cancer in low-income and middle-income countries. Lancet Oncol. 2013;2013 Feb 19:doi 10.
- 32. Chatenoud L, Bertuccio P, Bosetti C, Levi F, Negri E, La Vecchia C. Childhood cancer mortality in America, Asia, and Oceania, 1970 through 2007. Cancer. 2010;116(21):5063-5074.
- 33. Howlader N, Noone AM, Krapcho M, Garshell J, Miller D, Altekruse SF, Kosary CL, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER Cancer Statistics Review, 1975-2011, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/ $csr/1975_2011/, based \ on \ November \ 2013 \ SEER \ data \ submission, posted$ to the SEER web site, April 2014.
- 34. Howard SC, Metzger ML, Wilimas JA, et al. Childhood cancer epidemiology in low-income countries. Cancer. 2008;112(3):461-472.
- 35. Ward E, DeSantis C, Robbins A, Kohler B, Jemal A. Childhood and adolescent cancer statistics, 2014. CA Cancer J Clin. 2014;64(2):83-103.

- 36. Sullivan R, Kowalczyk JR, Agarwal B, et al. New policies to address the global burden of childhood cancers. Lancet Oncol. 2013;2013 Feb
- 37. Ribeiro RC, Steliarova-Foucher E, Magrath I, et al. Baseline status of paediatric oncology care in ten low-income or mid-income countries receiving My Child Matters support: a descriptive study. Lancet Oncol. 2008;9(8):721-729.
- 38. Swaminathan R, Rama R, Shanta V. Childhood cancers in Chennai, India, 1990-2001: incidence and survival. Int J Cancer. 2008;122(11):2607-
- 39. Wiangnon S, Veerakul G, Nuchprayoon I, et al. Childhood cancer incidence and survival 2003-2005, Thailand: study from the Thai Pediatric Oncology Group. Asian Pac J Cancer Prev. 2011;12(9):2215-2220.
- 40. Bao PP, Zheng Y, Wu CX, et al. Population-based survival for childhood cancer patients diagnosed during 2002-2005 in Shanghai, China. Pediatr Blood Cancer. 2012;59(4):657-661.
- 41. Center MM, Jemal A, Ward E. International trends in colorectal cancer incidence rates. Cancer Epidemiol Biomarkers Prev. 2009;18(6):1688-
- 42. Edwards BK, Ward E, Kohler BA, et al. Annual report to the nation on the status of cancer, 1975-2006, featuring colorectal cancer trends and impact of interventions (risk factors, screening, and treatment) to reduce future rates. Cancer. 2010;116(3):544-573.
- 43. Martin JJ, Hernandez LS, Gonzalez MG, Mendez CP, Rey Galan C, Guerrero SM. Trends in childhood and adolescent obesity prevalence in Oviedo (Asturias, Spain) 1992-2006. Acta Paediatr. 2008;97(7):955-958.
- 44. Salcedo V, Gutierrez-Fisac JL, Guallar-Castillon P, Rodriguez-Artalejo FCINIJOD, Pmid. Trends in overweight and misperceived overweight in Spain from 1987 to 2007. Int J Obes. 2010;34(12):1759-1765.
- 45. Center MM, Jemal A, Smith RA, Ward E. Worldwide variations in colorectal cancer. CA Cancer J Clin. 2009;59(6):366-378.
- 46. Winawer SJ. The multidisciplinary management of gastrointestinal cancer. Colorectal cancer screening. Best Pract Res Clin Gastroenterol. 2007;21(6):1031-1048.
- 47. National Cancer Institute. International Cancer Screening Network: Inventory of Colorectal Cancer Screening Activities in ICSN Countries, May 2008. 2009; http://appliedresearch.cancer.gov/icsn/colorectal/ screening.html. Accessed February 27, 2013.
- 48. Atkin WS, Edwards R, Kralj-Hans I, et al. Once-only flexible sigmoidoscopy screening in prevention of colorectal cancer: a multicentre randomised controlled trial. Lancet. 2010;375(9726):1624-1633.
- 49. Maringe C, Walters S, Rachet B, et al. Stage at diagnosis and colorectal cancer survival in six high-income countries: a population-based study of patients diagnosed during 2000-2007. Acta Oncol. 2013;52(5):919-932.
- 50. Islami F, Kamangar F, Aghcheli K, et al. Epidemiologic features of upper gastrointestinal tract cancers in Northeastern Iran. Br J Cancer. 2004;90(7):1402-1406.
- 51. Tran GD, Sun XD, Abnet CC, et al. Prospective study of risk factors for esophageal and gastric cancers in the Linxian general population trial cohort in China. Int J Cancer. 2005;113(3):456-463.
- 52. Blot WJ, McLaughlin JK, Fraumeni Jr JF. Esophageal Cancer. In: Schottenfeld D, Fraumeni Jr J, eds. Cancer Epidemiology and Prevention. 3rd ed. New York: Oxford University Press; 2006:697-706.
- 53. Lu CL, Lang HC, Luo JC, et al. Increasing trend of the incidence of esophageal squamous cell carcinoma, but not adenocarcinoma, in Taiwan. Cancer Causes Control. 2010;21:269-274.

- 54. Castro C, Bosetti C, Malvezzi M, et al. Patterns and trends in esophageal cancer mortality and incidence in Europe (1980-2011) and predictions to 2015. Ann Oncol. 2014;25(1):283-290.
- 55. Otterstatter MC, Brierley JD, De P, et al. Esophageal cancer in Canada: trends according to morphology and anatomical location. Can J Gastroenterol. 2012;26(10):723-727.
- 56. Cook MB, Chow WH, Devesa SS. Oesophageal cancer incidence in the United States by race, sex, and histologic type, 1977-2005. Br J Cancer. 2009;101(5):855-859.
- 57. Pennathur A, Gibson MK, Jobe BA, Luketich JD. Oesophageal carcinoma. Lancet. 2013;381(9864):400-412.
- 58. Islami F, Kamangar F. Helicobacter pylori and esophageal cancer risk: a meta-analysis. Cancer Prev Res (Phila). 2008;1(5):329-338.
- 59. Xie FJ, Zhang YP, Zheng QQ, et al. Helicobacter pylori infection and esophageal cancer risk: an updated meta-analysis. World J Gastroenterol. 2013;19(36):6098-6107.
- 60. Lagergren J, Lagergren P. Recent developments in esophageal adenocarcinoma. CA Cancer J Clin. 2013.
- 61. Islami F, Boffetta P, Ren JS, Pedoeim L, Khatib D, Kamangar F. Hightemperature beverages and foods and esophageal cancer risk--a systematic review. Int J Cancer. 2009;125(3):491-524.
- 62. Islami F, Pourshams A, Nasrollahzadeh D, et al. Tea drinking habits and oesophageal cancer in a high risk area in northern Iran: population based case-control study. BMJ. 2009;338:b929.
- 63. Rasool S, B AG, Syed Sameer A, Masood A. Esophageal cancer: associated factors with special reference to the Kashmir Valley. *Tumori*. 2012;98(2):191-203.
- 64. Wu M, Liu AM, Kampman E, et al. Green tea drinking, high tea temperature and esophageal cancer in high- and low-risk areas of Jiangsu Province, China: a population-based case-control study. Int J Cancer. 2009;124(8):1907-1913.
- 65. Liyanage SS, Rahman B, Ridda I, et al. The aetiological role of human papillomavirus in oesophageal squamous cell carcinoma: a meta-analysis. PloS One. 2013;8(7):e69238.
- 66. Petrick JL, Wyss AB, Butler AM, et al. Prevalence of human papillomavirus among oesophageal squamous cell carcinoma cases: systematic review and meta-analysis. Br J Cancer. 2014;110(9):2369-2377.
- 67. Yong F, Xudong N, Lijie T. Human papillomavirus types 16 and 18 in esophagus squamous cell carcinoma: a meta-analysis. Ann Epidemiol. 2013;23(11):726-734.
- 68. Sitas F, Egger S, Urban MI, et al. InterSCOPE study: Associations between esophageal squamous cell carcinoma and human papillomavirus serological markers. J Natl Cancer Inst. 2012;104(2):147-158.
- 69. Spechler SJ. Barrett esophagus and risk of esophageal cancer: a clinical review. JAMA. 2013;310(6):627-636.
- 70. Ballester V, Cruz-Correa M. Endoscopic surveillance of gastrointestinal premalignant lesions: current knowledge and future directions. Curr Opin Gastroenterol. 2014;30(5):477-483.
- 71. Verbeek RE, Leenders M, Ten Kate FJ, et al. Surveillance of Barrett's Esophagus and Mortality from Esophageal Adenocarcinoma: A Population-Based Cohort Study. Am J Gastroenterol. 2014;109(8):1215-1222.
- 72. De Angelis R, Sant M, Coleman MP, et al. Cancer survival in Europe 1999-2007 by country and age: results of EUROCARE--5-a populationbased study. Lancet Oncol. 2014;15(1):23-34.
- 73. London WT, McGlynn KA. Liver Cancer. In: Schottenfeld D, Fraumeni Jr. J, eds. Cancer Epidemiology and Prevention. 3rd ed. New York: Oxford University Press; 2006:763-786.

- 74. Altekruse SF, McGlynn KA, Reichman ME. Hepatocellular carcinoma incidence, mortality, and survival trends in the United States from 1975 to 2005. J Clin Oncol. 2009;27(9):1485-1491.
- 75. Mittal S, El-Serag HB. Epidemiology of Hepatocellular Carcinoma: Consider the Population. J Clin Gastroenterol. 2013.
- 76. Center MM, Jemal A. International trends in liver cancer incidence rates. Cancer Epidemiol Biomarkers Prev. 2011;20(11):2362-2368.
- 77. Chiang CJ, Yang YW, You SL, Lai MS, Chen CJ. Thirty-year outcomes of the national hepatitis B immunization program in Taiwan. JAMA. 2013:310(9):974-976.
- 78. El-Serag HB. Hepatocellular carcinoma. New Engl J Med. 2011;365 (12):1118-1127.
- 79. Trichopoulos D, Bamia C, Lagiou P, et al. Hepatocellular carcinoma risk factors and disease burden in a European cohort: a nested casecontrol study. J Natl Cancer Inst. 2011;103(22):1686-1695.
- 80. Lu T, Seto WK, Zhu RX, Lai CL, Yuen MF. Prevention of hepatocellular carcinoma in chronic viral hepatitis B and C infection. World J Gastroenterol. 2013;19(47):8887-8894.
- 81. Centers for Disease Control and Prevention. CDC Recommendations for the Identification of Chronic Hepatitis C Virus Infection among Persons Born During 1945-1965. 2014; http://www.cdc.gov/hepatitis/ HCV/1945-1965.htm. Accessed September 25, 2014.
- 82. Duangsong R, Promthet S, Thaewnongiew K. Development of a community-based approach to opisthorchiasis control. Asian Pac J Cancer Prev. 2013;14(11):7039-7043.
- 83. Sithithaworn P, Yongvanit P, Duenngai K, Kiatsopit N, Pairojkul C. Roles of liver fluke infection as risk factor for cholangiocarcinoma. J Hepatobiliary Pancreat Sci. 2014;21(5):301-308.
- 84. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Vol. 100E Personal Habits and Indoor Combustions 2012.
- 85. Bray FI, Weiderpass E. Lung cancer mortality trends in 36 European countries: secular trends and birth cohort patterns by sex and region 1970-2007. Int J Cancer. 2010;126(6):1454-1466.
- 86. Thun M, Peto R, Boreham J, Lopez AD. Stages of the cigarette epidemic on entering its second century. Tob Control. 2012;21(2):96-101.
- 87. Youlden DR, Cramb SM, Baade PD. The International Epidemiology of Lung Cancer: geographical distribution and secular trends. J Thorac Oncol. 2008;3(8):819-831.
- 88. Bosetti C, Malvezzi M, Rosso T, et al. Lung cancer mortality in European women: Trends and predictions. Lung Cancer. 2012;78(3):171-178.
- 89. Malvezzi M, Bosetti C, Rosso T, et al. Lung cancer mortality in European men: Trends and predictions. Lung Cancer. 0169;2013 Feb 20:doi 10.
- 90. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. CA Cancer J Clin. 2013;63(1):11-30.
- 91. Torre LA, Siegel RL, Ward EM, Jemal A. International variation in lung cancer mortality rates and trends among women. Cancer Epidemiol Biomarkers Prev. 2014;23(6):1025-1036.
- 92. Lam WK, White NW, Chan-Yeung MM. Lung cancer epidemiology and risk factors in Asia and Africa. Int J Tuberc Lung Dis. 2004;8(9):1045-
- 93. Jha P. Avoidable global cancer deaths and total deaths from smoking. Nat Rev Cancer. 2009;9(9):655-664.
- 94. Eriksen M, Mackay J, Ross H. The Tobacco Atlas. 4th edition Atlanta, GA: American Cancer Society; 2012.
- 95. El Ghissassi F, Baan R, Straif K, et al. A review of human carcinogens-part D: radiation. Lancet Oncol. 2009;10(8):751-752.

- 96. Danaei G, Vander Hoorn S, Lopez AD, Murray CJ, Ezzati M. Causes of cancer in the world: comparative risk assessment of nine behavioural and environmental risk factors. Lancet. 2005;366(9499):1784-1793.
- 97. Jemal A, Thun MJ, Ries LA, 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 Inst. 2008;100(23):1672-1694.
- 98. Centers for Disease Control and Prevention. State-specific trends in lung cancer incidence and smoking--United States, 1999-2008. MMWR Morb Mortal Wkly Rep. 2011;60(36):1243-1247.
- 99. Giovino GA, Mirza SA, Samet JM, et al. Tobacco use in 3 billion individuals from 16 countries: an analysis of nationally representative cross-sectional household surveys. Lancet. 2012;380(9842):668-679.
- 100. Aberle DR, Adams AM, Berg CD, et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. New Engl J Med. 2011;365(5):395-409.
- 101. Smith RA, Brooks D, Cokkinides V, Saslow D, Brawley OW. Cancer screening in the United States, 2013: A review of current american cancer society guidelines, current issues in cancer screening, and new guidance on cervical cancer screening and lung cancer screening. CA Cancer J Clin. 2013:doi 10.
- 102. World Health Organization. Early detection: screening for various cancers. 2013; http://www.who.int/cancer/detection/variouscancer/en/ index.html. Accessed February 28, 2013.
- 103. Jemal A, Simard EP, Dorell C, et al. Annual report to the nation on the status of cancer, 1975-2009, featuring the burden and trends in human papillomavirus (HPV)-associated cancers and HPV vaccination coverage levels. J Natl Cancer Inst. 2013;105(3):175-201.
- 104. Devesa SS, Fears T. Non-Hodgkin's lymphoma time trends: United States and international data. Cancer Res. 1992;52(19 Suppl):5432s-5440s.
- 105. Hartge P, Devesa SS. Quantification of the impact of known risk factors on time trends in non-Hodgkin's lymphoma incidence. Cancer Res. 1992;52(19 Suppl):5566s-5569s.
- 106. Eltom MA, Jemal A, Mbulaiteye SM, Devesa SS, Biggar RJ. Trends in Kaposi's sarcoma and non-Hodgkin's lymphoma incidence in the United States from 1973 through 1998. J Natl Cancer Inst. 2002;94(16):1204-1210.
- 107. Wabinga HR, Nambooze S, Amulen PM, Okello C, Mbus L, Parkin DM. Trends in the incidence of cancer in Kampala, Uganda 1991-2010. Int J Cancer. 2014;135(2):432-439.
- 108. Chokunonga E, Borok M, Chirenje Z, Nyakabau A, Parkin D. Trends in the incidence of cancer in the black population of harare, zimbabwe 1991-2010. Int J Cancer. 2013:doi 10.
- 109. Center MM, Jemal A, Lortet-Tieulent J, et al. International variation in prostate cancer incidence and mortality rates. Eur Urol. 2012;61(6):1079-1092.
- 110. Baade PD, Youlden DR, Krnjacki LJ. International epidemiology of prostate cancer: geographical distribution and secular trends. Mol Nutr Food Res. 2009;53(2):171-184.
- 111. Rebbeck TR, Devesa SS, Chang BL, et al. Global patterns of prostate cancer incidence, aggressiveness, and mortality in men of african descent. Prostate Cancer. 2013;2013:560857.
- 112. Islami F, Moreira DM, Boffetta P, Freedland SJ. A Systematic Review and Meta-analysis of Tobacco Use and Prostate Cancer Mortality and Incidence in Prospective Cohort Studies. Eur Urol. 0302;2014 Sep 18:doi 10.
- 113. Cuzick J, Thorat MA, Andriole G, et al. Prevention and early detection of prostate cancer. Lancet Oncol. 2014;15(11):e484-e492.

- 114. Draisma G, Etzioni R, Tsodikov A, et al. Lead time and overdiagnosis in prostate-specific antigen screening: importance of methods and context. J Natl Cancer Inst. 2009;101(6):374-383.
- 115. Howson CP, Hiyama T, Wynder EL. The decline in gastric cancer: epidemiology of an unplanned triumph. Epidemiol Rev. 1986;8:1-27.
- 116. Malvezzi M, Bonifazi M, Bertuccio P, et al. An age-period-cohort analysis of gastric cancer mortality from 1950 to 2007 in Europe. Ann Epidemiol. 2010;20(12):898-905.
- 117. Bertuccio P, Chatenoud L, Levi F, et al. Recent patterns in gastric cancer: a global overview. Int J Cancer. 2009;125(3):666-673.
- 118. Parkin DM. The global health burden of infection-associated cancers in the year 2002. Int J Cancer. 2006;118(12):3030-3044.
- 119. Jemal A, Center MM, DeSantis C, Ward EM. Global patterns of cancer incidence and mortality rates and trends. Cancer Epidemiol Biomarkers Prev. 2010;19(8):1893-1907.
- 120. Shibata A, Parsonnet J. Stomach Cancer. In: Schottenfeld D, Fraumeni Jr. J, eds. Cancer Epidemiology and Prevention. 3rd ed. New York: Oxford University Press; 2006:707-720.
- 121. Carr JS, Zafar SF, Saba N, Khuri FR, El-Rayes BF. Risk factors for rising incidence of esophageal and gastric cardia adenocarcinoma. J Gastrointest Cancer. 2013;44(2):143-151.
- 122. Herrero R, Parsonnet J, Greenberg ER. Prevention of Gastric Cancer. JAMA. 2014;312(12):1197-1198.
- 123. Leung WK, Wu MS, Kakugawa Y, et al. Screening for gastric cancer in Asia: current evidence and practice. Lancet Oncology. 2008;9(3):279-287.
- 124. Tanaka M, Ma E, Tanaka H, Ioka A, Nakahara T, Takahashi H. Trends of stomach cancer mortality in Eastern Asia in 1950-2004: comparative study of Japan, Hong Kong and Singapore using age, period and cohort analysis. Int J Cancer. 2012;130(4):930-936.
- 125. Monitoring of cancer incidence in Japan-Survival 2003-2005 report, 2013: Center for Cancer Control and Information Services, National Cancer Center.
- 126. Allemani C, Weir HK, Carreira H, et al. Global surveillance of cancer survival 1995-2009: analysis of individual data for 25,676,887 patients from 279 population-based registries in 67 countries (CON-CORD-2). The Lancet. 2014.
- 127. Chavan S, Bray F, Lortet-Tieulent J, Goodman M, Jemal A. International variations in bladder cancer incidence and mortality. Eur Urol. 2014;66(1):59-73.
- 128. Bosetti C, Bertuccio P, Malvezzi M, et al. Cancer mortality in Europe, 2005-2009, and an overview of trends since 1980. Ann Oncol. 2013;24(10):2657-2671.
- 129. Guo P, Huang ZL, Yu P, Li K. Trends in cancer mortality in China: an update. Ann Oncol. 2012;23(10):2755-2762.
- 130. Parkin DM. The global burden of urinary bladder cancer. Scand J Urol Nephrol Suppl. 2008(218):12-20.
- 131. Brinkman M, Zeegers MP. Nutrition, total fluid and bladder cancer. Scand J Urol Nephrol Suppl. 2008(218):25-36.
- 132. Sant M, Allemani C, Santaquilani M, Knijn A, Marchesi F, Capocaccia R. EUROCARE-4. Survival of cancer patients diagnosed in 1995-1999. Results and commentary. Eur J Cancer. 2009;45(6):931-991.
- 133. Sankaranarayanan R, Swaminathan R, Brenner H, et al. Cancer survival in Africa, Asia, and Central America: a population-based study. Lancet Oncol. 2010;11:165-173.

- 134. Vaccarella S, Lortet-Tieulent J, Plummer M, Franceschi S, Bray F. Worldwide trends in cervical cancer incidence: Impact of screening against changes in disease risk factors. Eur J Cancer. 2013;0(0):0.
- 135. Bruni L, Diaz M, Castellsague X, Ferrer E, Bosch FX, de Sanjose S. Cervical human papillomavirus prevalence in 5 continents: meta-analysis of 1 million women with normal cytological findings. J Infect Dis. 2010;202(12):1789-1799.
- 136. Forman D, de Martel C, Lacey CJ, et al. Global burden of human papillomavirus and related diseases. Vaccine. 2012;30 Suppl 5:F12-23.
- 137. Engholm G, Ferlay J, Christensen N, Johannesen TB, Khan S., Køtlum JE, Milter MC, Ólafsdóttir E, Pukkala E, Storm HH. NORDCAN: Cancer Incidence, Mortality, Prevalence and Survival in the Nordic Countries, Version 6.1 (25.04.2014). Association of the Nordic Cancer Registries. Danish Cancer Society. Available from http://www.ancr.nu, accessed on 16/9/2014.
- 138. Bray F, Lortet-Tieulent J, Znaor A, Brotons M, Poljak M, Arbyn M. Patterns and trends in human papillomavirus-related diseases in Central and Eastern Europe and Central Asia. Vaccine. 2013;31 Suppl 7:H32-45.
- 139. Gustafsson L, Ponten J, Bergstrom R, Adami HO. International incidence rates of invasive cervical cancer before cytological screening. Int J Cancer. 1997;71(2):159-165.

- 140. GAVI. Millions of girls in developing countries to be protected against cervical cancer thanks to new HPV vaccine deals. 2013; http:// www.gavi.org/library/news/press-releases/2013/hpv-price-announcement/. Accessed September 12, 2014.
- 141. Sankaranarayanan R, Nene BM, Shastri SS, et al. HPV screening for cervical cancer in rural India. N Engl J Med. 2009;360(14):1385-1394.
- 142. Ye S, Yang J, Cao D, Lang J, Shen K. A systematic review of quality of life and sexual function of patients with cervical cancer after treatment. Int J Gynecol Cancer. 2014;24(7):1146-1157.
- 143. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int JCancer. 2010;127(12):2893-2917.
- 144. Forman D, Bray F, Brewster DH, Gombe Mbalawa C, Kohler B, Piñeros M, Steliarova-Foucher E, Swaminathan R, and Ferlay J, eds. Cancer Incidence in Five Continents, Vol. X (electronic version). 2013; http://ci5. iarc.fr. Accessed December 9, 2013.
- 145. Mathers CD, Fat DM, Inoue M, Rao C, Lopez AD. Counting the dead and what they died from: an assessment of the global status of cause of death data. Bull World Health Organ. 2005;83(3):171-177.
- 146. World Health Organization International Agency for Research on Cancer. Cancer Mortality Database. 2013; http://www-dep.iarc.fr/ WHOdb/WHOdb.htm. Accessed December 13, 2013.

Acknowledgments

We would like to acknowledge the contributions of the following individuals in the production of this report: Benjamin Anderson, MD, FACS; Tracie Bertaut, APR; Freddie Bray, PhD; Carol DeSantis, MPH; Stacey Fedewa, MPH; David Forman, PhD; Farhad Islami, MD, PhD; Joan Kramer, MD; Andrea Lancaster, MPH; Joannie Lortet-Tieulent, MSc; Ann McMikel; Kim Miller, MPH; Meg O'Brien, PhD; Max Parkin, MD; Anthony Piercy; Suleeporn Sangrajrang, PhD; Rengaswamy Sankaranarayanan, MD; Catherine Sauvaget, MD, PhD; Scott Simpson; Robert Smith, PhD; Eva Steliarova-Foucher, PhD; Richard Sullivan, MD, PhD; Dana Wagner; and Elizabeth Ward, PhD.

Global Cancer Facts & Figures 3rd Edition is a publication of the American Cancer Society, Atlanta, Georgia.



Thanks to the generous donations from corporate supporters and individuals like you, **we save lives** by helping people stay well and get well, by finding cures, and by fighting back.

cancer.org | 1.800.227.2345



The American Cancer Society, Inc. adheres to the Better Business Bureau's strong standards for charitable giving.