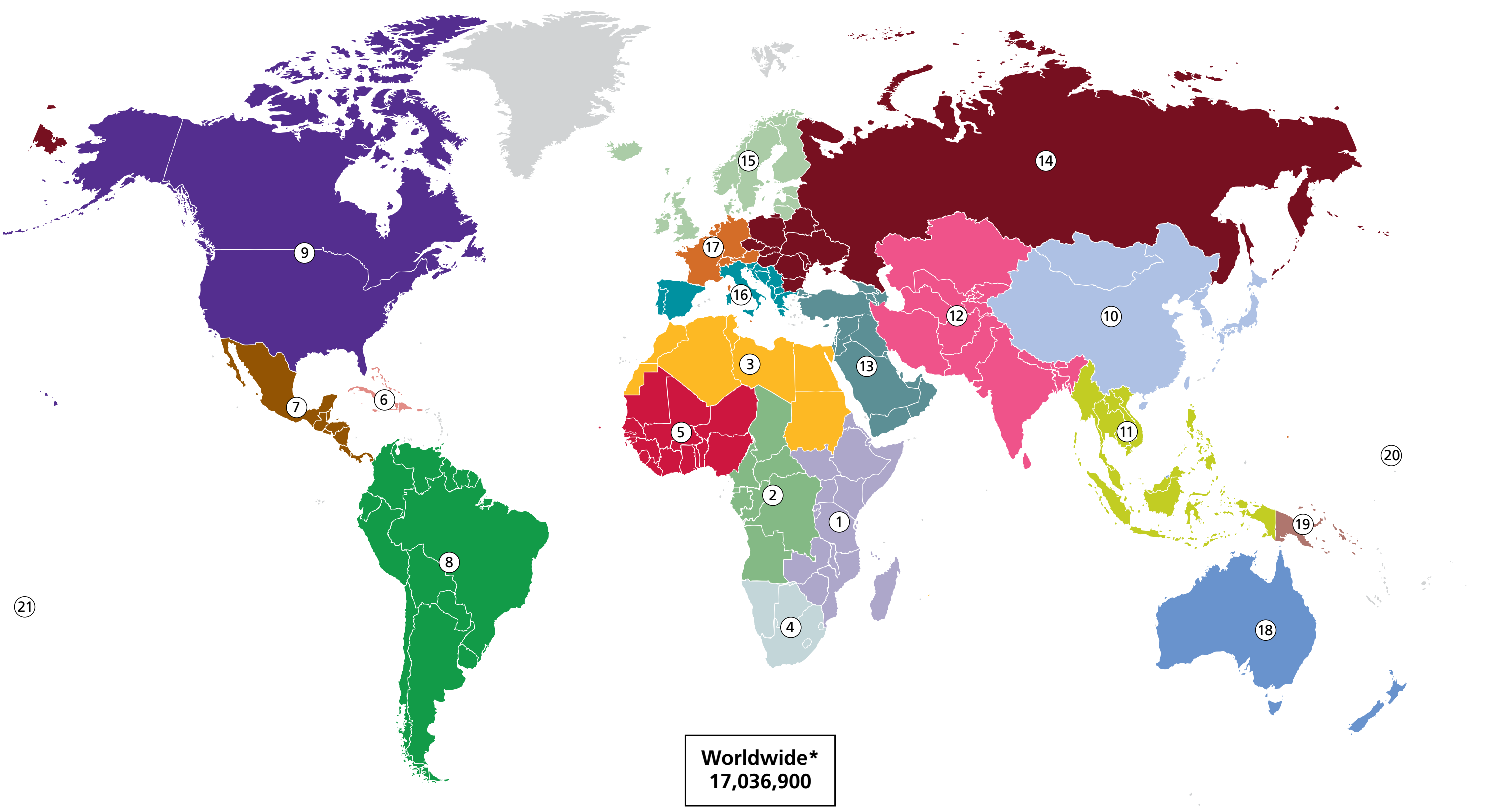
American Cancer Society®

Global Cancer Facts & Figures 4th Edition

Estimated Number of New Cancer Cases by World Area, 2018*



1 Eastern Africa (324,900)	**6** Caribbean (106,600)	**11** South-Eastern Asia (975,800)	**16** Southern Europe (872,200)
2 Middle Africa (94,000)	**7** Central America (245,500)	**12** South-Central Asia (1,719,200)	**17** Western Europe (1,212,700)
3 Northern Africa (279,100)	**8** South America (992,100)	**13** Western Asia (390,600)	**18** Australia/New Zealand (163,800)
4 Southern Africa (108,900)	**9** Northern America (1,896,100)	**14** Central and Eastern Europe (1,203,000)	**19** Melanesia (14,600)
5 Western Africa (224,200)	**10** Eastern Asia (5,587,800)	**15** Northern Europe (623,400)	**20** Micronesia (1,000)
			21 Polynesia (1,500)

*Region estimates do not sum to the worldwide estimate due to calculation method.
Source: GLOBOCAN 2018.

Special Section: The Obesity Epidemic

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Contents

International Agency for Research on Cancer

World Health Organization

This publication would not have been possible without the contributions of the International Agency for Research on Cancer and their work in producing GLOBOCAN 2018 (gco.iarc.fr) alongside the work of cancer registrars worldwide.

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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. Although the causes of cancer remain largely unknown, particularly for those that occur during childhood, there are many factors known to increase risk. Some of these are modifiable, such as tobacco use and excess body weight, while others are generally unmodifiable, such as inherited genetic mutations, hormones, and immune conditions. These risk factors may act simultaneously or in sequence to initiate and/or promote cancer growth.

How Many New Cancer Cases and Deaths Are Expected to Occur in 2018 Worldwide?

Cancer causes about 1 in every 6 deaths worldwide, more than AIDS, tuberculosis, and malaria combined. Today, it is the second-leading cause of death (following cardiovascular diseases) worldwide and in high- and very high Human Development Index (HDI) countries (Table 1; see page 3 for HDI definition).

According to estimates from the International Agency for Research on Cancer (IARC), there will be 17.0 million new cancer cases in 2018 worldwide, of which 657,000 will occur in countries with a low HDI, 2.8 million in medium-HDI countries, 6.4 million in high-HDI countries, and 7.2 million in very high-HDI countries. (Figure 1). These estimates do not include non-melanoma skin cancers, for which the majority are not tracked by cancer registries. The corresponding estimated cancer deaths in 2018 will be 9.5 million (about 26,000 cancer deaths a day) – 456,700 in low-HDI countries, 1.8 million in medium-HDI countries, 4.0 million in high-HDI countries, and 3.2 million in very high-HDI countries (Figure 1).

Table 1. Leading Causes of Death Worldwide by Human Development Index (HDI), 2016 (Millions)

	Worldwide			Low HDI			Medium HDI			High HDI			Very High HDI		
	Rank	Deaths	%	Rank	Deaths	%	Rank	Deaths	%	Rank	Deaths	%	Rank	Deaths	%
Cardiovascular diseases	1	17.9	31%	2	1.2	14%	1	5.2	28%	1	6.9	41%	1	4.4	35%
Malignant neoplasms	2	9.0	16%	6	0.5	6%	3	1.8	10%	2	3.5	20%	2	3.1	25%
Infectious and parasitic diseases	3	5.5	10%	1	2.4	29%	2	2.4	13%	11	0.4	2%	11	0.3	2%
Respiratory diseases	4	3.8	7%	12	0.2	2%	4	1.5	8%	3	1.3	7%	4	0.8	7%
Unintentional injuries	5	3.4	6%	5	0.7	8%	5	1.3	7%	4	1.0	6%	7	0.5	4%
Respiratory infections	6	3.0	5%	4	0.9	10%	7	1.1	6%	8	0.5	3%	6	0.5	4%
Neurological conditions	7	2.5	4%	14	0.1	1%	12	0.5	3%	5	0.9	5%	3	1.0	8%
Digestive diseases	8	2.5	4%	7	0.3	4%	8	1.0	6%	6	0.6	4%	5	0.5	4%
Neonatal conditions	9	2.2	4%	3	0.9	11%	6	1.1	6%	12	0.2	1%	17	0.04	0.3%
Diabetes mellitus	10	1.6	3%	13	0.1	2%	9	0.7	4%	7	0.5	3%	9	0.3	2%
Intentional injuries	11	1.5	3%	8	0.3	3%	11	0.5	3%	10	0.4	2%	10	0.3	2%
Genitourinary diseases	12	1.4	3%	15	0.1	1%	10	0.6	3%	9	0.4	3%	8	0.3	3%
Congenital anomalies	13	0.6	1%	11	0.2	2%	13	0.2	1%	13	0.1	1%	16	0.05	0.4%
Nutritional deficiencies	14	0.5	1%	9	0.2	3%	14	0.2	1%	17	0.05	0.3%	18	0.03	0.2%
Endocrine, blood, immune disorders	15	0.4	1%	16	0.1	1%	16	0.1	0.4%	15	0.1	0.4%	13	0.1	1%
All causes		56.9			8.4			18.4			17.0			12.5	

Estimates may not sum to worldwide total due to rounding

Source: Global Health Estimates 2016: Deaths by Cause, Age, Sex, by Country and by Region, 2000-2016. Geneva, World Health Organization; 2018; Human Development Report 2016. New York, United Nations Development Programme; 2016.

Figure 1. Estimated New Cancer Cases* and Deaths Worldwide for Leading Cancer Sites by Human Development Index, 2018

WORLD

Cases: Males		Cases: Females		Deaths: Males		Deaths: Females	
All sites	8,818,700	All sites	8,218,200	All sites	5,347,300	All sites	4,142,600
Lung, bronchus & trachea	1,368,500	Breast	2,088,800	Lung, bronchus & trachea	1,184,900	Breast	626,700
Prostate	1,276,100	Colon, rectum & anus	823,300	Liver	548,400	Lung, bronchus & trachea	576,100
Colon, rectum & anus	1,026,200	Lung, bronchus & trachea	725,400	Stomach	513,600	Colon, rectum & anus	396,600
Stomach	683,800	Uterine cervix	569,800	Colon, rectum & anus	484,200	Uterine cervix	311,400
Liver	596,600	Thyroid	436,300	Prostate	359,000	Stomach	269,100
Urinary bladder	424,100	Uterine corpus	382,100	Esophagus	357,200	Liver	233,300
Esophagus	399,700	Stomach	349,900	Pancreas	226,900	Pancreas	205,300
Non-Hodgkin lymphoma	284,700	Ovary	295,400	Leukemia	179,500	Ovary	184,800
Kidney	254,500	Liver	244,500	Urinary bladder	148,300	Esophagus	151,400
Leukemia	249,500	Non-Hodgkin lymphoma	224,900	Non-Hodgkin lymphoma	146,000	Leukemia	129,500

VERY HIGH HUMAN DEVELOPMENT INDEX

Cases: Males		Cases: Females		Deaths: Males		Deaths: Females	
All sites	3,790,100	All sites	3,384,900	All sites	1,764,000	All sites	1,418,900
Prostate	802,300	Breast	912,500	Lung, bronchus & trachea	431,000	Lung, bronchus & trachea	240,700
Lung, bronchus & trachea	545,000	Colon, rectum & anus	407,800	Colon, rectum & anus	202,900	Breast	205,600
Colon, rectum & anus	491,000	Lung, bronchus & trachea	339,300	Prostate	158,300	Colon, rectum & anus	177,600
Bladder	256,900	Uterine corpus	202,700	Pancreas	114,700	Pancreas	111,600
Stomach	203,900	Thyroid	169,800	Liver	110,400	Ovary	66,800
Kidney	152,500	Pancreas	119,200	Stomach	105,400	Stomach	65,500
Liver	134,400	Stomach	113,000	Bladder	72,000	Liver	56,600
Non-Hodgkin lymphoma	133,700	Melanoma of the skin	112,100	Esophagus	63,400	Leukemia	44,400
Melanoma of the skin	127,600	Non-Hodgkin lymphoma	110,200	Leukemia	58,800	Uterine corpus	44,200
Pancreas	123,500	Ovary	107,700	Kidney	53,500	Non-Hodgkin lymphoma	40,600

HIGH HUMAN DEVELOPMENT INDEX

Cases: Males		Cases: Females		Deaths: Males		Deaths: Females	
All sites	3,417,500	All sites	2,988,500	All sites	2,413,600	All sites	1,585,600
Lung, bronchus & trachea	659,300	Breast	666,700	Lung, bronchus & trachea	601,800	Lung, bronchus & trachea	270,600
Colon, rectum & anus	414,700	Colon, rectum & anus	323,200	Stomach	325,500	Breast	184,000
Stomach	386,700	Lung, bronchus & trachea	315,300	Liver	318,100	Colon, rectum & anus	159,600
Liver	339,200	Thyroid	214,100	Esophagus	219,400	Stomach	154,200
Prostate	324,700	Stomach	181,400	Colon, rectum & anus	201,100	Liver	124,500
Esophagus	240,000	Uterine cervix	180,900	Prostate	120,200	Esophagus	93,200
Urinary bladder	116,800	Liver	129,800	Pancreas	89,100	Uterine cervix	85,400
Pancreas	95,600	Uterine corpus	128,200	Leukemia	66,000	Pancreas	73,800
Non-Hodgkin lymphoma	82,700	Esophagus	103,600	Brain, central nervous system	57,600	Ovary	55,500
Leukemia	81,000	Ovary	95,300	Urinary bladder	48,900	Brain, central nervous system	47,100

MEDIUM HUMAN DEVELOPMENT INDEX

Cases: Males		Cases: Females		Deaths: Males		Deaths: Females	
All sites	1,344,200	All sites	1,446,700	All sites	975,400	All sites	871,700
Lung, bronchus & trachea	154,500	Breast	402,800	Lung, bronchus & trachea	142,900	Breast	183,800
Lip, oral cavity	125,900	Uterine cervix	206,100	Liver	98,900	Uterine cervix	122,800
Colon, rectum & anus	101,600	Ovary	77,600	Lip, oral cavity	71,200	Lung, bronchus & trachea	58,800
Liver	101,600	Colon, rectum & anus	72,400	Stomach	70,900	Ovary	50,700
Prostate	94,100	Lung, bronchus & trachea	64,400	Colon, rectum & anus	66,400	Colon, rectum & anus	45,400
Stomach	80,500	Lip, oral cavity	45,900	Esophagus	63,800	Liver	40,100
Esophagus	67,900	Thyroid	45,300	Prostate	49,000	Stomach	39,500
Leukemia	57,100	Stomach	45,200	Leukemia	44,800	Lip, oral cavity	33,700
Non-Hodgkin lymphoma	51,400	Uterine corpus	42,500	Non-Hodgkin lymphoma	36,400	Leukemia	32,800
Larynx	46,600	Liver	41,700	Brain, central nervous system	30,400	Esophagus	31,700

LOW HUMAN DEVELOPMENT INDEX

Cases: Males		Cases: Females		Deaths: Males		Deaths: Females	
All sites	262,700	All sites	394,300	All sites	192,100	All sites	264,600
Prostate	53,900	Breast	105,600	Prostate	31,100	Uterine cervix	65,600
Liver	21,100	Uterine cervix	89,900	Liver	20,800	Breast	52,800
Colon, rectum & anus	18,500	Colon, rectum & anus	19,600	Colon, rectum & anus	13,600	Colon, rectum & anus	13,800
Non-Hodgkin lymphoma	16,800	Ovary	14,700	Non-Hodgkin lymphoma	12,900	Liver	11,900
Kaposi sarcoma	16,700	Non-Hodgkin lymphoma	12,400	Stomach	11,700	Ovary	11,700
Stomach	12,500	Liver	12,300	Esophagus	10,400	Stomach	9,900
Leukemia	11,100	Stomach	10,200	Leukemia	9,800	Esophagus	9,000
Esophagus	10,700	Leukemia	9,800	Kaposi sarcoma	9,600	Leukemia	8,700
Lung, bronchus & trachea	9,000	Esophagus	9,200	Lung, bronchus & trachea	8,900	Non-Hodgkin lymphoma	7,900
Urinary bladder	7,500	Kaposi sarcoma	9,100	Lip, oral cavity	4,500	Lung, bronchus & trachea	5,700

*Excluding non-melanoma skin cancers. Estimates may not sum to worldwide total due to rounding.
Source: GLOBOCAN 2018.

Human Development Index

The Human Development Index (HDI) is a measure of development that considers not only standard of living, but also health and education. The health component of HDI is measured by life expectancy at birth. Education includes average years of schooling for adults 25 years of age and older and expected years of schooling for children. Standard of living is measured by gross national income per capita. These scores are used to create a composite measure that can be grouped into levels: low, medium, high, and very high HDI.

World population by HDI level:

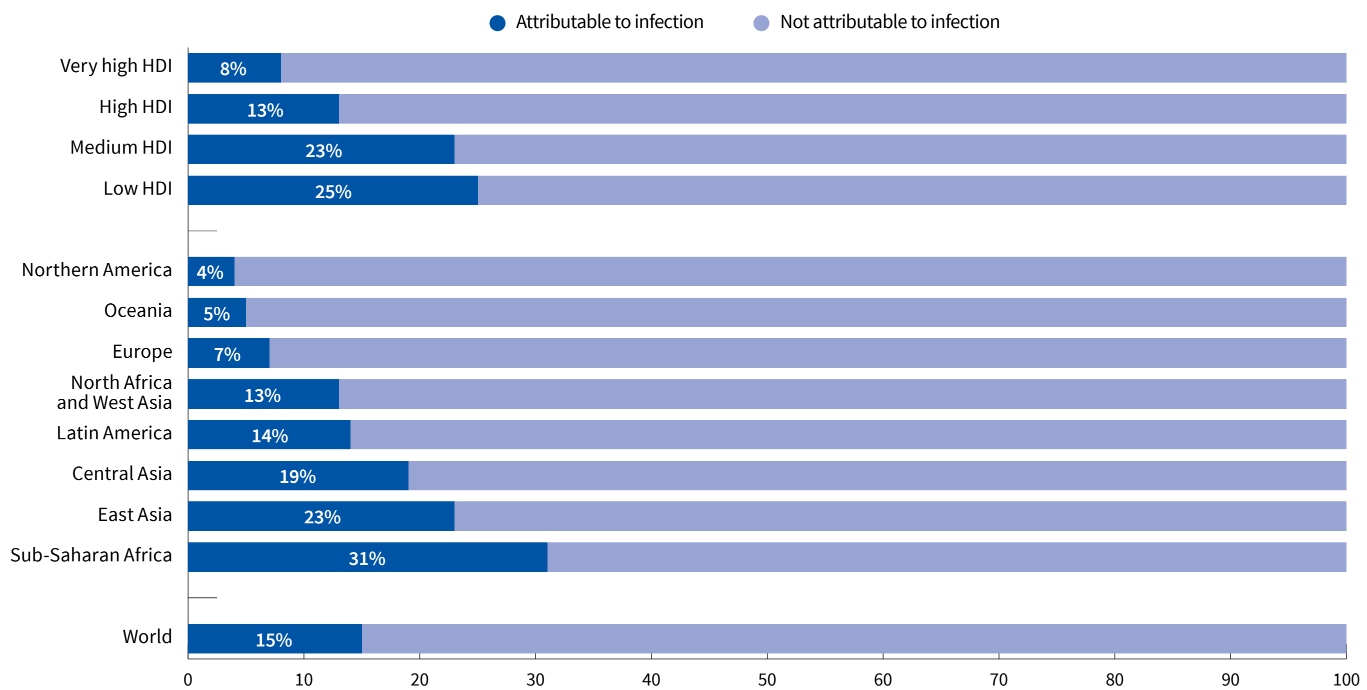
Low 1.0 billion	Medium 2.8 billion
High 2.5 billion	Very high 1.4 billion

By 2040, the global burden is expected to grow to 27.5 million new cancer cases and 16.3 million cancer deaths simply due to the growth and aging of the population.[1] However, the future cancer burden will probably be considerably larger due to increasing prevalence of factors that increase risk, such as smoking, unhealthy diet, physical inactivity, and fewer pregnancies. Cancers related to these factors, such as lung, breast, and colorectal cancers, are already on the rise in economically transitioning countries, a trend that will continue if preventive measures are not widely applied.

How Does Cancer Occurrence Vary Globally?

Factors that contribute to differences in cancer incidence and mortality across countries include variations in age structure; prevalence of risk factors; and availability and use of preventive services, early detection tests (e.g., mammography), and high-quality treatment (mortality). Many of these factors are strongly influenced by level of development. For example, cancers associated with infection are more common in lower-HDI countries because of a higher prevalence of cancer-causing infections, such as *Helicobacter pylori (H. pylori)*. While approximately 15% of all incident cancers worldwide are attributed to infections, the percentage is about three times higher in low- (25%) and medium- (23%) HDI countries than in very

Figure 2. Proportion of Cancers Attributable to Infection by Human Development Index and World Region, 2012



HDI = Human Development Index.

Source: Plummer M, de Martel C, Vignat J, Ferlay J, Bray F, Franceschi S. Global burden of cancers attributable to infections in 2012: a synthetic analysis. *Lancet Glob Health*. 2016;4:e609-616.

high-HDI (8%) countries (Figure 2).[2] Stomach cancer continues to be the most common infection-related cancer worldwide, followed by liver and cervical cancers.

The greatest number of new cancer cases in 2018 will be in Eastern Asia (5.6 million), followed by Northern America (1.9 million) and South-Central Asia (1.7 million; Table 2). The greatest number of deaths will be in Eastern Asia (3.4 million), followed by South-Central Asia (1.2 million) and Northern America (693,000). These numbers reflect the size of the population, as well as cancer occurrence and survival.

In males, the two most commonly diagnosed cancers in 2018 will be prostate and lung in very high-HDI countries; lung and colorectum in high-HDI countries; lung and lip/oral cavity for medium-HDI countries; and prostate and liver in low-HDI countries (Figure 1). In females, the two most common cancers will be breast and colorectum in very high- and high-HDI countries and breast and cervix uteri in medium- and low-HDI countries (Figure 1).

Lung cancer will be the leading cause of cancer death for males in 2018 in all except low-HDI countries (prostate cancer) and for females except in medium- and low-HDI countries, where breast and cervical cancer, respectively, will rank first (Figure 1). The second-leading cause of cancer death in males will be colorectal (very high-HDI countries); stomach (high-HDI countries); and liver cancer (medium- and low-HDI countries). Among females, it will be breast cancer in all except medium-HDI countries, where cervical cancer will rank second.

Table 3 lists the most common types of cancer cases and deaths in 2018 by geographic region, and Figure 3 shows the most commonly diagnosed cancer in each country, illustrating the larger diversity in males than in females. The most common cancers in men other than lung and prostate include liver in Egypt, Mongolia, and several countries in Western Africa (Burkina Faso, Guinea, Guinea-Bissau, Mauritania, Niger, The Gambia) and South-Eastern Asia (Cambodia, Laos, Thailand, Vietnam); colorectum in Slovakia, Japan, the Republic of Korea (South Korea), and several countries in Western Asia (Bahrain, Oman, Qatar,

Table 2. Estimated Number of New Cancer Cases and Deaths by World Area, 2018*

	Cases			Deaths		
	Male	Female	Overall	Male	Female	Overall
Eastern Africa	126,400	198,400	324,900	92,900	134,400	227,300
Middle Africa	40,500	53,500	94,000	30,200	37,600	67,800
Northern Africa	132,300	146,800	279,100	95,600	81,000	176,600
Southern Africa	47,400	61,500	108,900	29,700	31,300	61,000
Western Africa	87,200	136,900	224,200	62,100	88,300	150,400
Caribbean	54,900	51,700	106,600	34,000	28,500	62,400
Central America	109,900	135,600	245,500	56,800	60,800	117,600
South America	480,600	511,400	992,100	250,900	234,800	485,600
Northern America	970,100	926,000	1,896,100	363,900	329,100	693,000
Eastern Asia	3,090,600	2,497,300	5,587,800	2,129,600	1,315,100	3,444,700
South-Eastern Asia	470,900	504,900	975,800	342,400	283,400	625,800
South-Central Asia	848,200	871,000	1,719,200	614,600	545,000	1,159,600
Western Asia	204,400	186,200	390,600	128,900	90,800	219,700
Eastern Europe	595,200	607,800	1,203,000	381,700	310,800	692,500
Northern Europe	326,600	296,800	623,400	145,400	126,800	272,200
Southern Europe	479,200	393,000	872,200	244,900	174,300	419,300
Western Europe	658,700	554,100	1,212,700	305,900	239,800	545,800
Australia/New Zealand	87,700	76,100	163,800	32,700	25,600	58,300
Melanesia	6,400	8,200	14,600	4,200	4,700	8,900
Micronesia	500	500	1,000	400	300	600
Polynesia	800	700	1,500	500	400	800

*Excludes non-melanoma skin cancer. Estimates by sex may not sum to overall total due to rounding.

Source: GLOBOCAN 2018.

Table 3. Most Common Types of New Cancer Cases and Deaths by World Area, 2018

Cancer Cases

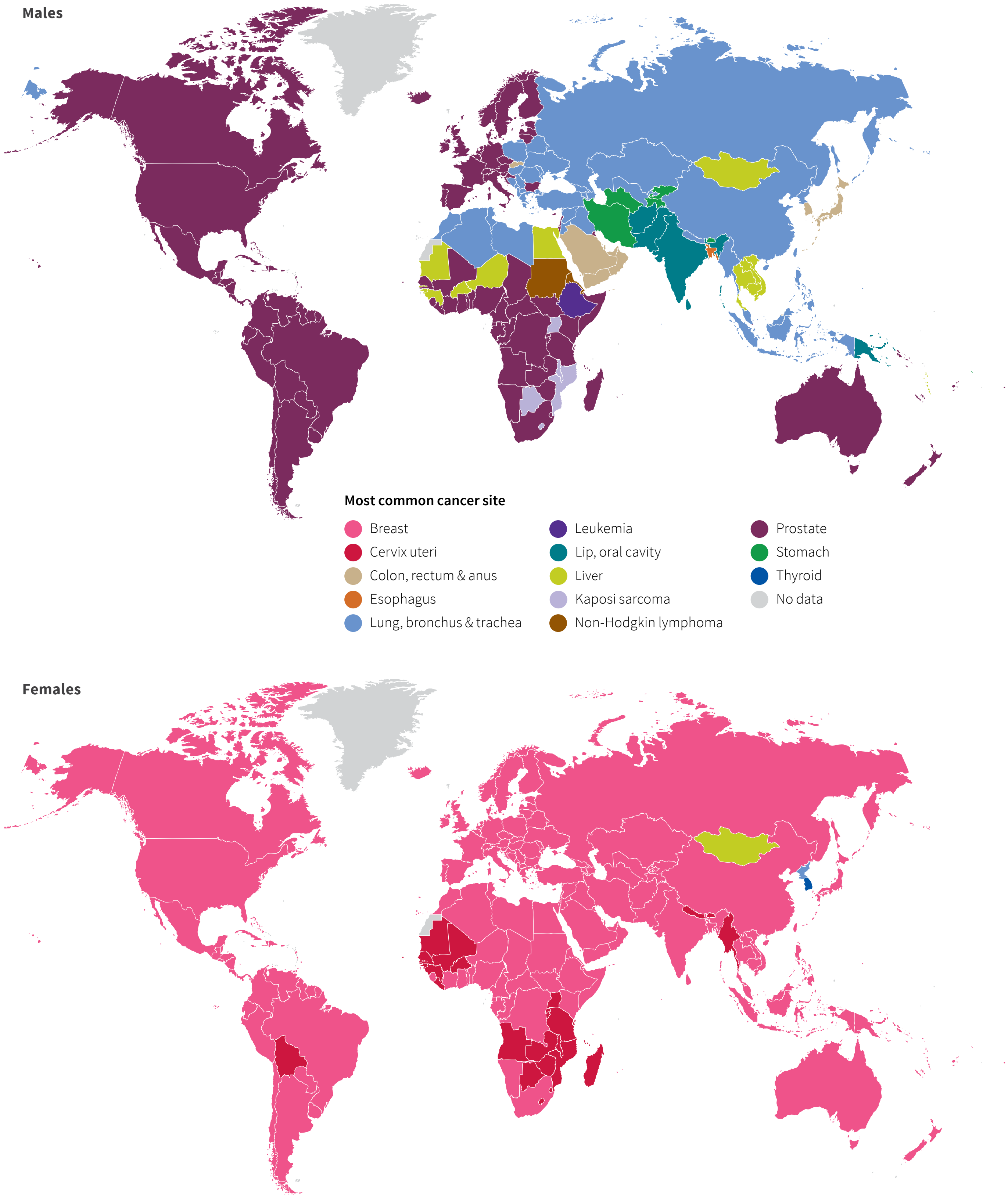
	Males				Females			
	First	**%**	**Second**	**%**	**First**	**%**	**Second**	**%**
Eastern Africa	Prostate	16%	Kaposi sarcoma	12%	Cervix uteri	27%	Breast	20%
Middle Africa	Prostate	29%	Liver	10%	Breast	27%	Cervix uteri	24%
Northern Africa	Liver	15%	Lung	12%	Breast	37%	Colorectum	6%
Southern Africa	Prostate	27%	Lung	12%	Breast	24%	Cervix uteri	23%
Western Africa	Prostate	27%	Liver	12%	Breast	33%	Cervix uteri	23%
Caribbean	Prostate	32%	Lung	12%	Breast	27%	Colorectum	11%
Central America	Prostate	31%	Colorectum	9%	Breast	26%	Cervix uteri	9%
South America	Prostate	29%	Colorectum	10%	Breast	29%	Colorectum	10%
Northern America	Prostate	24%	Lung	14%	Breast	28%	Lung	13%
Eastern Asia	Lung	20%	Stomach	14%	Breast	19%	Lung	13%
South-Eastern Asia	Lung	17%	Liver	14%	Breast	27%	Cervix uteri	12%
South-Central Asia	Lip, oral cavity	14%	Lung	9%	Breast	28%	Cervix uteri	14%
Western Asia	Lung	20%	Prostate	13%	Breast	30%	Colorectum	9%
Eastern Europe	Lung	18%	Prostate	16%	Breast	25%	Colorectum	13%
Northern Europe	Prostate	28%	Colorectum	13%	Breast	28%	Lung	12%
Southern Europe	Prostate	21%	Lung	15%	Breast	30%	Colorectum	13%
Western Europe	Prostate	24%	Lung	14%	Breast	31%	Colorectum	11%
Australia/New Zealand	Prostate	25%	Colorectum	13%	Breast	29%	Colorectum	13%
Melanesia	Prostate	17%	Lip, oral cavity	11%	Breast	26%	Cervix uteri	15%
Micronesia	Lung	26%	Prostate	20%	Breast	27%	Lung	15%
Polynesia	Prostate	27%	Lung	21%	Breast	34%	Lung	12%

Cancer Deaths

	Males				Females			
	First	**%**	**Second**	**%**	**First**	**%**	**Second**	**%**
Eastern Africa	Prostate	14%	Esophagus	10%	Cervix uteri	28%	Breast	15%
Middle Africa	Prostate	24%	Liver	13%	Cervix uteri	25%	Breast	21%
Northern Africa	Liver	20%	Lung	16%	Breast	25%	Liver	10%
Southern Africa	Lung	18%	Prostate	16%	Cervix uteri	21%	Breast	16%
Western Africa	Prostate	20%	Liver	17%	Cervix uteri	27%	Breast	24%
Caribbean	Prostate	25%	Lung	17%	Breast	19%	Lung	13%
Central America	Prostate	17%	Stomach	10%	Breast	19%	Cervix uteri	13%
South America	Lung	15%	Prostate	14%	Breast	16%	Lung	11%
Northern America	Lung	25%	Colorectum	9%	Lung	25%	Breast	14%
Eastern Asia	Lung	26%	Liver	15%	Lung	20%	Stomach	11%
South-Eastern Asia	Lung	21%	Liver	19%	Breast	18%	Cervix uteri	13%
South-Central Asia	Lung	12%	Lip, oral cavity	11%	Breast	23%	Cervix uteri	14%
Western Asia	Lung	31%	Colorectum	9%	Breast	19%	Colorectum	10%
Eastern Europe	Lung	26%	Colorectum	13%	Breast	16%	Colorectum	15%
Northern Europe	Lung	21%	Prostate	15%	Lung	20%	Breast	14%
Southern Europe	Lung	26%	Colorectum	13%	Breast	16%	Colorectum	13%
Western Europe	Lung	24%	Colorectum	11%	Breast	17%	Lung	17%
Australia/New Zealand	Lung	18%	Prostate	12%	Lung	18%	Breast	14%
Melanesia	Lung	13%	Liver	12%	Breast	22%	Cervix uteri	17%
Micronesia	Lung	35%	Liver	15%	Lung	24%	Breast	18%
Polynesia	Lung	31%	Prostate	14%	Breast	21%	Lung	17%

Source: GLOBOCAN 2018.

Figure 3. Most Commonly Diagnosed Cancers Worldwide by Sex, 2018



Source: GLOBOCAN 2018.

Saudi Arabia, United Arab Emirates, Yemen); stomach in five South-Central Asian countries (Bhutan, Iran, Kyrgyzstan, Tajikistan, Turkmenistan); lip and oral cavity in Papua New Guinea, Afghanistan, India, Pakistan, and Sri Lanka; Kaposi sarcoma in Malawi, Mozambique, Uganda, Botswana, and Lesotho; non-Hodgkin lymphoma in Djibouti, Eritrea, and Sudan; leukemia in Ethiopia; and esophagus in Bangladesh. In women, the most common cancer other than breast and cervix is limited to liver in Mongolia, lung in the Democratic People's Republic of Korea (North Korea), and thyroid in South Korea.

Who Is at Risk of Developing Cancer?

Approximately 21 out of 100 men and 18 out of 100 women globally will develop cancer by the age of 75.[1] However, these probabilities are estimated based on cancer occurrence in the general population and over- or underestimate individual risk because of differences in exposures, family history, and/or genetic susceptibility. For example, many behaviors that increase cancer risk, such as smoking, unhealthy eating, and a sedentary lifestyle, are more common in higher-HDI countries and contribute to higher cancer rates (Table 4).[3,4]

Cancer risk increases with age; an estimated 80% of all cancers in the world are diagnosed in people 50 years of age or older.[1] In very high-HDI countries, 60% of all newly diagnosed cancer cases occur at 65 years of age and older, compared with 46% in high-HDI countries and about 30% in medium- and low-HDI countries.[1] This difference is largely due to the younger age distribution of developing countries (Figure 4).

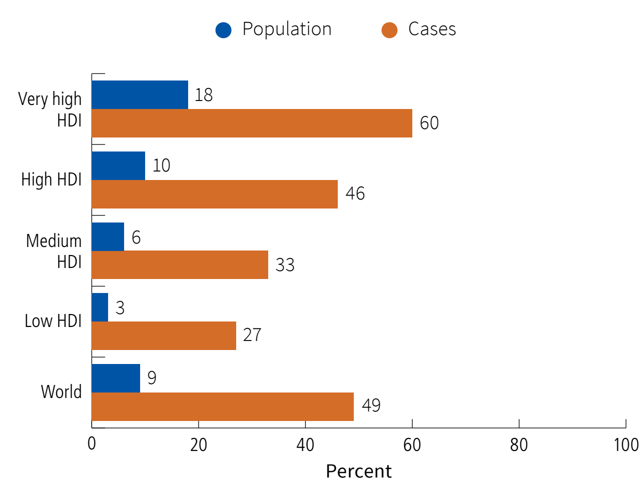
What Percentage of People Survive Cancer?

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 remaining evidence of cancer and those who have relapsed or are still in treatment. While 5-year survival is useful in monitoring progress against 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 experience of cancer patients in a given population, it does not predict individual prognosis.

Cancer survival in a population is affected by a number of factors, including the types of cancer that occur, the stages at which they are diagnosed, the prevalence of screening/early detection services, and whether treatment is available (Table 5). For cancers that are more amenable to screening and/or treatment, such as female breast, colorectal, and certain childhood cancers, there are large survival differences by HDI level. For example, the 5-year survival rate for breast cancer in 2010-2014 was 90% in the US and Australia, compared with 65% in Malaysia (Table 5). There can also be survival differences within a country that reflect differences in access to screening and treatment; 5-year survival for cervical cancer in the United States in 2004-2009 was 64% among whites and 56% among blacks.[5] In contrast, for cancer sites without early detection or effective treatment, such as liver, lung, or pancreas, survival rates vary less. In addition to differences in screening and treatment, international differences in cancer survival rates are also affected by disease awareness and data quality.

Calculation of cancer survival requires an established high-quality cancer registration system and complete

Figure 4. Adults 65 Years of Age and Older as Proportions (%) of Population versus Cancer Cases by Human Development Index, 2018



Source: GLOBOCAN 2018.

Table 4. Estimated Incidence and Mortality Rates* by Sex, Cancer Site, and Human Development Index, 2018

Males

	Very high HDI		High HDI		Medium HDI		Low HDI	
	Incidence	Mortality	Incidence	Mortality	Incidence	Mortality	Incidence	Mortality
Bladder	18.1	4.3	7.1	2.9	3.7	2.0	3.1	2.0
Brain, central nervous system	5.8	3.9	4.5	3.7	2.7	2.4	1.4	1.3
Colorectum	37.2	13.9	25.2	12.0	8.6	5.7	7.5	5.7
Esophagus	6.3	4.8	14.6	13.3	5.8	5.4	4.5	4.4
Gallbladder	2.7	1.7	2.3	1.8	1.5	1.1	0.4	0.3
Hodgkin lymphoma	2.3	0.3	0.9	0.3	0.9	0.5	0.9	0.5
Hypopharynx	1.9	0.9	0.7	0.4	2.8	1.1	0.3	0.2
Kaposi sarcoma	0.4	0.0	0.2	0.0	0.3	0.2	4.3	2.4
Kidney	12.8	3.9	4.7	2.7	1.8	1.2	1.2	1.0
Larynx	4.2	1.6	3.2	1.8	4.0	2.4	1.9	1.6
Leukemia	9.3	4.3	6.0	4.5	4.4	3.4	3.1	2.9
Lip, oral cavity	6.4	2.0	2.5	1.2	10.0	5.7	2.2	1.8
Liver	10.6	8.1	20.8	19.4	8.6	8.3	7.9	7.9
Lung	40.4	30.8	40.0	36.4	13.4	12.4	3.9	3.9
Melanoma of skin	10.7	1.8	1.0	0.4	0.4	0.3	0.8	0.6
Mesothelioma	1.1	0.9	0.2	0.2	0.1	0.1	0.1	0.1
Multiple myeloma	3.7	1.9	1.4	1.0	1.3	1.0	0.9	0.8
Nasopharynx	0.8	0.4	3.3	1.7	2.3	1.6	1.1	1.0
Non-Hodgkin lymphoma	11.2	3.5	5.3	2.8	4.1	3.0	5.0	4.3
Oropharynx	3.2	1.2	0.9	0.5	2.0	1.6	0.5	0.4
Pancreas	9.1	8.3	5.8	5.4	1.6	1.6	1.9	1.9
Penis	0.7	0.2	0.6	0.2	1.2	0.7	0.8	0.4
Prostate	61.1	8.9	19.6	7.0	8.6	4.5	26.1	15.9
Salivary glands	0.9	0.3	0.6	0.2	0.6	0.4	0.8	0.6
Stomach	15.0	7.3	23.5	19.7	6.9	6.1	5.1	4.9
Testis	5.3	0.3	1.6	0.2	0.7	0.3	0.3	0.2
Thyroid	5.2	0.3	4.0	0.3	1.2	0.4	0.9	0.3
All sites†	299.6	124.2	211.1	146.9	112.4	82.6	98.9	76.2

Females

	Very high HDI		High HDI		Medium HDI		Low HDI	
	Incidence	Mortality	Incidence	Mortality	Incidence	Mortality	Incidence	Mortality
Bladder	4.2	1.1	1.8	0.8	1.0	0.5	1.8	1.3
Brain, central nervous system	4.3	2.7	3.9	2.9	1.8	1.5	1.2	1.1
Breast	75.2	13.1	40.1	10.3	30.7	14.3	32.8	17.1
Cervix uteri	9.4	3.0	11.1	4.9	15.6	9.5	29.8	23.0
Colorectum	25.0	8.9	17.8	8.3	5.7	3.5	7.0	5.1
Corpus uteri	15.7	2.6	7.6	1.5	3.3	1.2	3.1	1.6
Esophagus	1.3	0.9	5.7	5.0	2.9	2.5	3.4	3.4
Gallbladder	2.2	1.5	2.5	2.0	2.4	1.8	0.7	0.6
Hodgkin lymphoma	1.8	0.2	0.7	0.2	0.6	0.3	0.6	0.4
Hypopharynx	0.2	0.1	0.1	0.0	0.6	0.2	0.2	0.2
Kaposi sarcoma	0.1	0.0	0.0	0.0	0.2	0.1	2.1	1.2
Kidney	6.3	1.5	2.6	1.2	1.1	0.6	1.1	0.8
Larynx	0.6	0.2	0.4	0.3	0.5	0.4	0.4	0.3
Leukemia	6.3	2.6	4.6	2.9	3.2	2.5	2.7	2.5
Lip, oral cavity	2.3	0.6	1.3	0.5	3.6	2.7	1.7	1.3
Liver	3.5	2.9	7.2	6.8	3.3	3.2	4.3	4.2
Lung	21.4	14.0	17.4	14.6	5.1	4.7	2.2	2.1
Melanoma of skin	9.6	1.0	1.0	0.3	0.4	0.2	0.9	0.7
Mesothelioma	0.3	0.2	0.1	0.1	0.1	0.1	0.1	0.1
Multiple myeloma	2.4	1.3	1.0	0.7	0.7	0.6	0.8	0.7
Nasopharynx	0.3	0.1	1.2	0.5	0.8	0.5	0.5	0.4
Non-Hodgkin lymphoma	7.7	2.0	4.0	1.8	2.7	1.7	3.4	2.4
Oropharynx	0.8	0.2	0.2	0.1	0.4	0.3	0.2	0.2
Ovary	8.6	4.3	5.8	3.2	5.9	4.0	4.6	4.0
Pancreas	6.5	5.7	4.0	3.9	1.3	1.3	1.6	1.6
Salivary glands	0.6	0.1	0.4	0.1	0.6	0.3	0.5	0.4
Stomach	6.6	3.3	10.1	8.3	3.5	3.1	3.7	3.7
Thyroid	18.2	0.4	13.8	0.5	3.3	0.5	2.2	0.6
Vagina	0.3	0.1	0.2	0.1	0.6	0.3	0.5	0.3
Vulva	1.5	0.4	0.5	0.2	0.7	0.3	0.9	0.3
All sites†	252.9	80.7	175.8	87.3	111.5	68.1	126.0	89.8

*Per 100,000, age standardized to the world standard population. †Excludes non-melanoma skin cancer.

Source: GLOBOCAN 2018.

Table 5. Five-year Net Survival Rates* (%) among Adults 15 Years of Age and Older in Select Countries by Cancer Site, 2010-2014

	Esophagus	Stomach	Colon	Rectum	Liver	Lung	Female Breast	Cervix	Prostate
Asia									
Chinese registries	30	36	58	57	14	20	83	68	69
Indian registries	4	9	39	30	6†	4	66	59	44
Israel	26	32	72	68	19†	27	88	67	96
Kuwait	25†	22	59	58	19	13	75	57	84
Malaysia (Penang)	14†	30	56	58	10†	10	65†	57†	88
South Korea	31	69	72	71	27	25	87	77	90
Thai registries	7	13	47	44	7	9	69†	54†	68
Turkish registries	19	25	55	53	16	15	82	61	84
Northern America									
Canada	16	30	67	67	19	21	88	67	94
US registries	20	33	65	64	17	21	90	63	97
Central and Southern America									
Brazilian registries	10†	21†	48†	42†	11†	9	75†	60	92
Chilean registries	9	17	44†	33†	4†	5†	76†	57†	82†
Colombian registries	11†	17†	35†	38†	5†	9†	72†	49†	80†
Costa Rica	21†	41	60	54	24†	20†	87	78†	93
Europe									
Austria	19	35	64	64	15†	20	85	64	90
Belgium	24	38	68	67	21	18	86	65	94
Czech Republic	10	21	56	52	7	11	81	61	85
Denmark	14	20	62	65	8	17	86	70	86
Estonia	5	29	58	55	4	17	77	67	86
German registries	21	34	65	62	13	18	86	65	92
Italian registries	14	31	64	61	20	16	86	67	90
Polish registries	9	21	53	48	11	14	77	55	78
Slovenia	9	29	62	60	7	15	84	66	85
Spanish registries	13	28	63	60	17	14	85	65	90
UK registries	16	21	60	63	13	13	86	64	89
Oceania									
Australian registries	24	32	71	71	19	19	90	66	95
New Zealand	15	26	64	66	19	15	88	67	90

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

Source: Allemani C, Matsuda T, Di Carlo V, et al. Global surveillance of trends in cancer survival 2000-14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. *Lancet*. Jan 30 2018. doi: 10.1016/S0140-6736(17)33326-3.

and accurate follow-up of patients for several years to ascertain vital status. For this reason, cancer survival statistics are generally more often available for higher-resource countries. However, efforts are underway at the International Agency for Research on Cancer (IARC) to establish and strengthen cancer registries in lower-resource countries through the SURVCAN-3 project, which is providing assistance with follow-up in benchmarking survival in 80 registry populations, as part of the Global Initiative for Cancer Registry Development (GICR, http://gicr.iarc.fr).[8] Please see Sources of Statistics, page 70, for more information.

How Is Cancer Staged?

Although accurate stage assessment at the time of diagnosis is essential for optimizing therapy and assessing prognosis, it is not available in many parts of the world. For most cancers, 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 at the time of diagnosis. 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 tracking trends over time. According to this system, if cancer cells are present only in the layer of cells where they developed, 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 mainly use a different staging system. The TNM is the most commonly used staging system and assesses cancer growth and spread in 3 ways: extent of the primary tumor (T), absence or presence of regional lymph node involvement (N), and absence or presence of distant metastases (M). Once the T, N, and M 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 stage IV being the most advanced disease. Some cancers (e.g., lymphoma) have alternative staging systems. As the biology of cancer has become better understood, additional tumor-specific features have been incorporated into staging and/or treatment plans for some cancers.

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. 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.). The exact global cost of cancer is unknown, but 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 2015 was $80.2 billion.[9] The estimated annual health care expenditure for cancer in Europe in 2014 was €83 billion (about $110 billion).[10] In the major developing countries of Brazil, Russia, Indonesia, China, and South Africa, the total cost of lost productivity due to premature mortality from cancer was estimated to be $46.3 billion in 2012.[11] 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.[12]

Cancer Prevention and Control

A substantial proportion of cancers could be prevented, including all cancers caused by tobacco use and other unhealthy behaviors. In 2015, about 20% of cancer deaths in the world were caused by tobacco use.[1, 13] In addition, the World Cancer Research Fund estimates that about 15%-20% of cancers worldwide are related to excess body weight, physical inactivity, and/or poor nutrition, and thus could also be prevented.[14] Certain cancers caused by infectious agents, such as human papillomavirus (HPV), hepatitis B virus (HBV), hepatitis C virus (HCV), and *H. pylori*, which account for 15% of cancers worldwide, could be prevented through behavioral changes, vaccination, or treatment of the infection. Additionally, many cases of skin cancer could be prevented by protecting skin from excessive sun exposure and not using indoor tanning devices.

Screening can help prevent colorectal and cervical cancers by allowing for the detection and removal of precancerous lesions. Screening can also detect some cancers early, when treatment is often more successful, and reduces mortality for cancers of the breast, colorectum, cervix, and lung (among long-term current or former heavy smokers). In addition, a heightened awareness of changes in the breast, skin, mouth, eyes, or genitalia may also result in the early detection of cancer.[15]

A balanced approach to cancer control includes prevention, early detection, and effective treatment, including palliative care.[16] Successful national cancer control policies and programs raise awareness, reduce exposure to risk factors, 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.[17]

Prevention: The goal of prevention is to reduce or eliminate exposure to cancer-causing agents (or increase resistance to them), which includes factors related to tobacco use, unhealthy diet, physical inactivity, occupational exposures, other environmental factors, and infections. Primary prevention offers the greatest public health potential and the most cost-effective, long-term cancer control.

Approaches to primary prevention include application of effective tobacco control measures; avoidance of excess sun exposure and indoor tanning; immunization against, or treatment of, infectious agents that cause cancer; reduction of excessive alcohol consumption; maintenance of a healthy body weight and physically active lifestyles; and reduction in occupational exposure to carcinogens. The WHO has assessed public health interventions and declared the hepatitis B vaccination and cervical cancer screening to be "best buys" because they can potentially have a large public health impact while being cost-effective, inexpensive, and feasible to implement.[18]

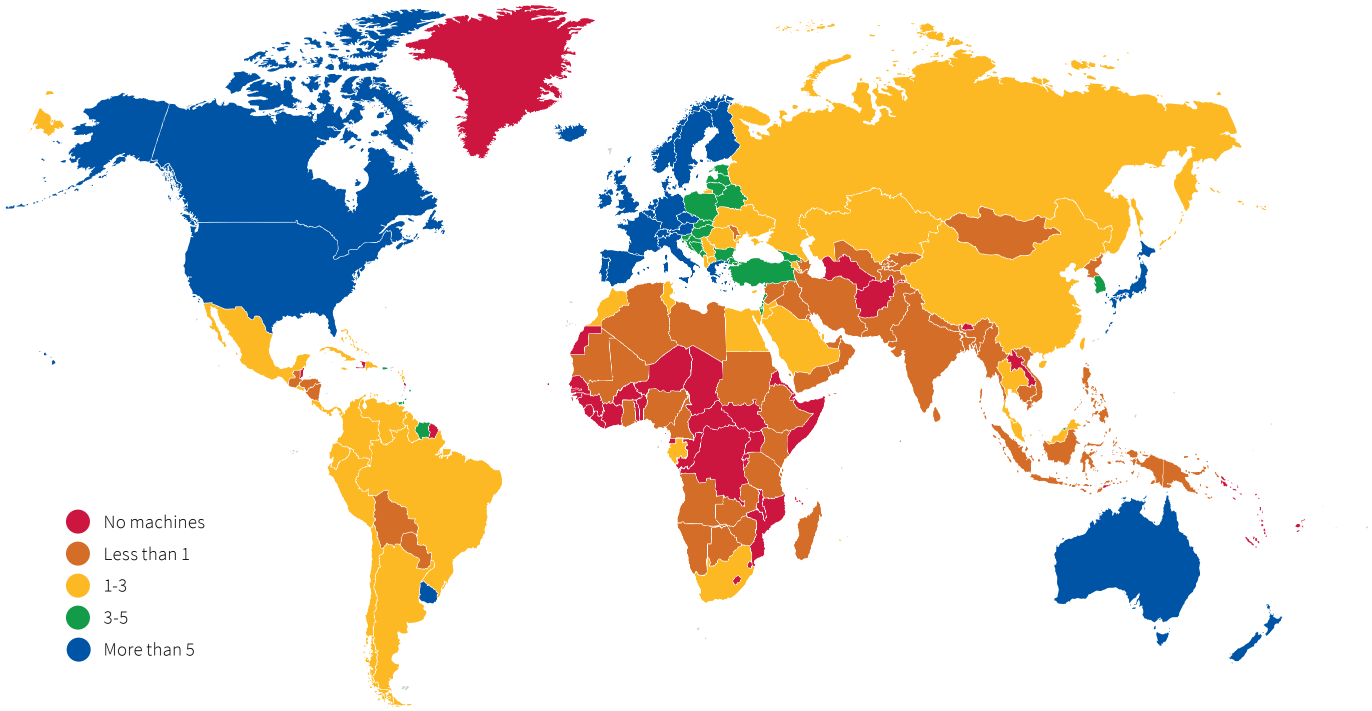
Early detection: The main objective of early detection is to diagnose precancerous lesions or early-stage cancers when they can be treated most effectively. Early detection is only valuable if it leads to timely diagnostic follow-up and effective treatment. Strategies include: 1) opportunistic screening 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.[19] Cancers with 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 high-resource countries. Lung cancer screening in particular is unlikely to be feasible in lower-resource countries in the near future due to the technical expertise and infrastructure required. Lower-HDI countries considering whether to institute screening for a specific cancer should consider the burden of the cancer in the population; the cost-effectiveness of the screening method; how well the test works in the population, including the number of individuals who must be screened in order to prevent one cancer death; and the availability of health care infrastructure that ensures timely treatment for all who test positive.[20] In some cases, the most feasible and cost-effective method may be raising awareness of cancer signs and symptoms.

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 treatment protocols. The primary modalities of cancer treatment are surgery, chemotherapy, radiotherapy, hormone therapy, immune therapy, and targeted therapy.

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 assists developing countries by integrating radiotherapy into sustainable comprehensive cancer control programs. Many countries, especially lower-HDI countries, do not have sufficient radiotherapy centers to provide treatment for all of the cancer patients in need, and about 60 countries do not have a single radiotherapy facility (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, is the use of inexpensive oral pain medications ranging from aspirin to opiates, depending on individual patient needs.[21] 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. Pain treatment administered according to the ladder is effective in 80%-90% of patients.[22] 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.[23] The WHO has played an important role in encouraging effective pain management and monitoring the availability of opioids internationally.[24] Surgery, chemotherapy, and radiotherapy are also important components of palliative care. Radiotherapy in particular is often used for pain relief without curative intent.[25, 26]

Figure 5. Number of Radiotherapy Machines per 1 Million People, 2017



Source: Directory of Radiotherapy Centers (DIRAC). International Atomic Energy Agency, 2017.

Selected Cancers

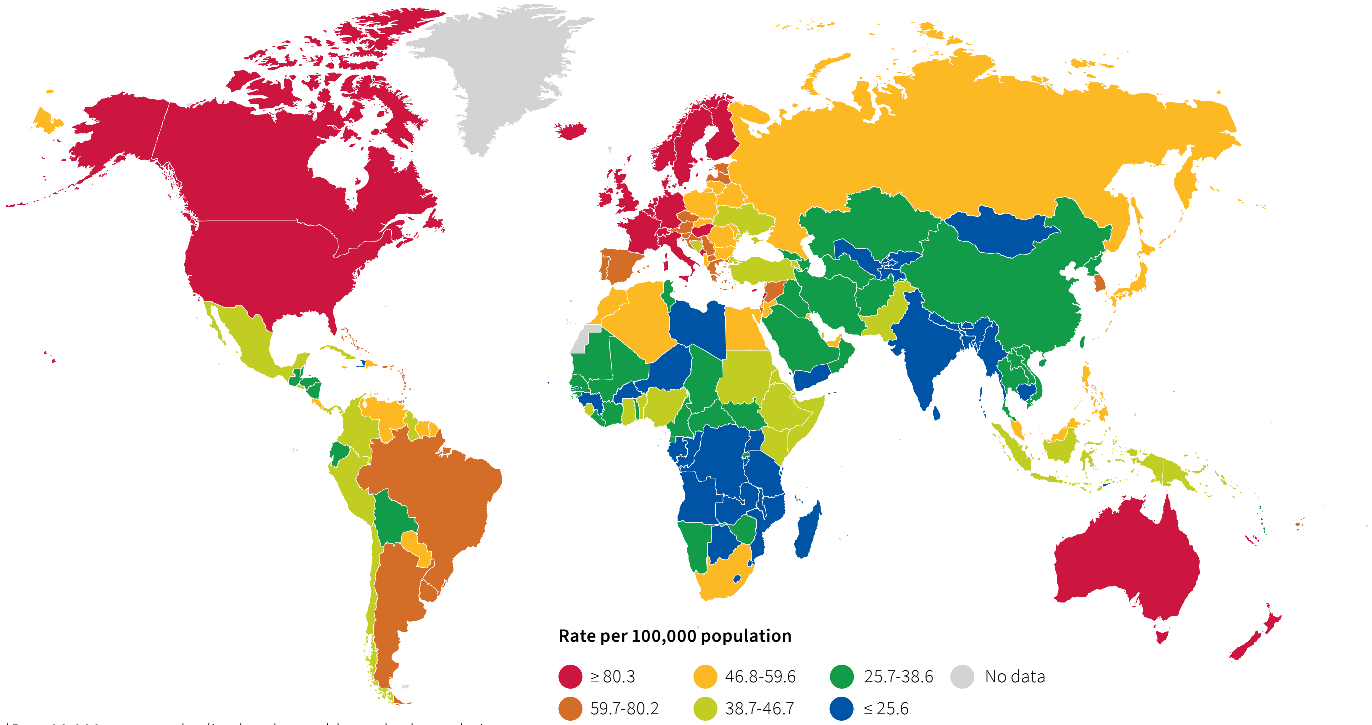
Breast Cancer

New cases: Breast cancer is the most frequently diagnosed cancer in women worldwide with more than 2 million new cases expected to be diagnosed in 2018, accounting for 25% of all new cancer cases in women. A little less than half (44%) of these cases will occur in very high-HDI countries, which represent about 19% of the world female population (Figure 6).

Deaths: An estimated 626,700 breast cancer deaths will occur in women in 2018. Breast cancer is the leading cause of cancer death among women worldwide and in medium-HDI countries and ranks second for other HDI levels.

Risk factors: Like most cancers, older age is the strongest risk factor for breast cancer. Many other factors that influence risk modify exposure of breast tissue to reproductive hormones.[27] Some of these are potentially modifiable, such as weight gain after the age of 18 and/or being overweight or obese (for postmenopausal breast cancer), postmenopausal hormone use (combined estrogen and progestin), physical inactivity, and alcohol consumption; breastfeeding decreases risk.[27, 28] Additional reproductive factors associated with increased risk include a long menstrual history (menstrual periods that start early and/or end later in life), never having children, having one's first child after age 30, high natural levels of female sex hormones, and recent use of oral contraceptives.[29] Factors related to medical history that increase risk include a personal or family history of breast or ovarian cancer; inherited mutations (genetic alterations) in *BRCA1*, *BRCA2*, or other breast cancer susceptibility genes; certain benign breast conditions, such as atypical hyperplasia; a history of

Figure 6. International Variation in Breast Cancer Incidence Rates*, 2018



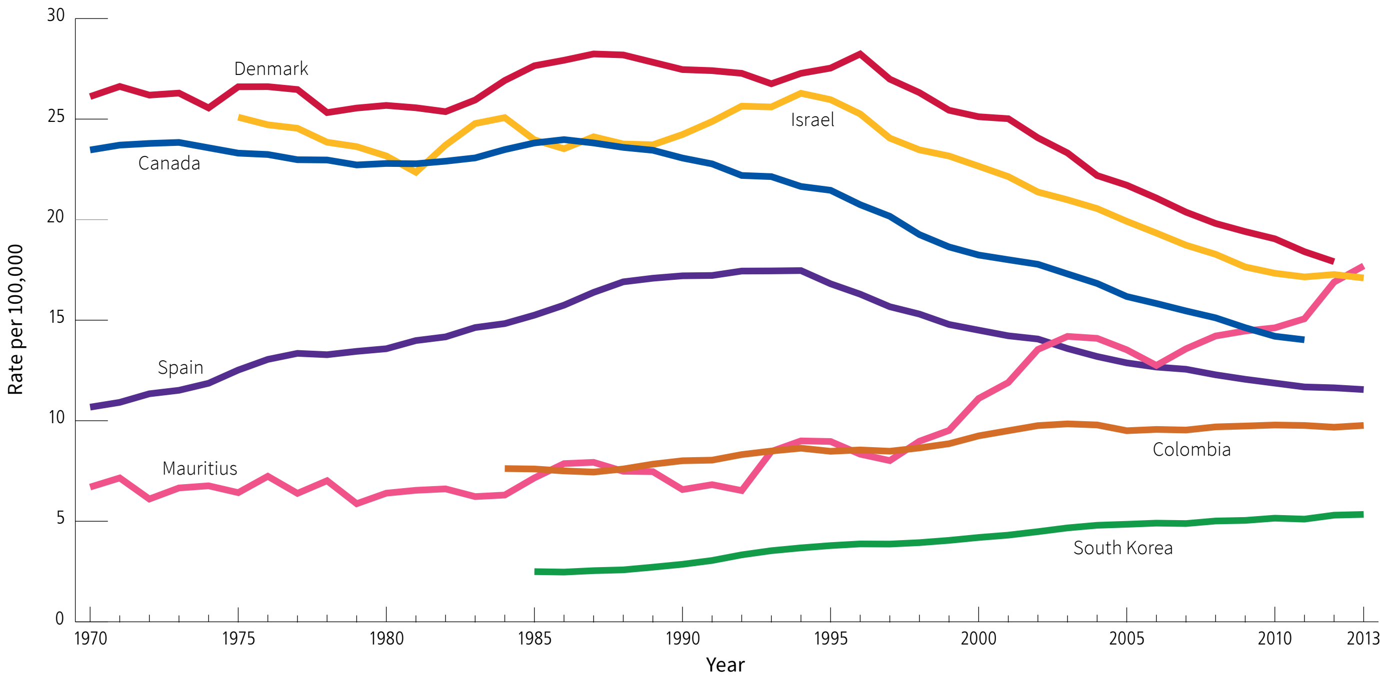
*Per 100,000, age standardized to the world standard population.
Source: GLOBOCAN 2018.

ductal or lobular carcinoma in situ; high-dose radiation to the chest at a young age (e.g., for treatment of lymphoma); high breast tissue density (the amount of glandular tissue relative to fatty tissue measured on a mammogram); and type 2 diabetes (independent of obesity).[27, 30] Mutations in the cancer susceptibility genes *BRCA1* and *BRCA2* are more common in women of Ashkenazi (Eastern European) Jewish descent (about 2% versus less than 1% in the general population).[31, 32]

Global trends: 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 postmenopausal hormone use.[33, 34] Since the early 2000s, incidence has declined or stabilized in many of these countries, including Canada, the United Kingdom, France, the United States, and Australia, due to declines in postmenopausal hormone use following the publication of a major study linking it to increased breast cancer risk,[35-39] and perhaps plateaus in mammographic screening prevalence.[40] In contrast, breast cancer incidence rates have been rising rapidly in historically lower-risk areas, such as countries of Latin America, Africa, and Asia. This trend likely reflects increased obesity and physical inactivity, delayed childbearing, fewer childbirths, earlier age at menarche, and shorter duration of breastfeeding, as well as increases in breast cancer screening and awareness.[41]

Breast cancer mortality has been decreasing since the 1990s in the US, Canada, and many European countries. 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.[33, 42-44] In contrast, mortality rates continue to increase in many countries in Asia, Africa, and Latin America, reflecting increasing incidence trends (Figure 7).[45-48] For example, death rates have increased continuously in Japan (1.1% per year from 1997 to 2011) and in South Korea (2.1% per year from 1994 to 2011).[40] Notably, these are both high-income countries where

Figure 7. Trends in Breast Cancer Death Rates*, Select Countries, 1970-2013



*Per 100,000, age standardized to the world standard population. Rates have been smoothed using 3-year averages.
Source: WHO Cancer Mortality Database.

cancer treatment is available, although mammography screening has not been widely embraced.

Signs and symptoms: The most common sign is a lump or mass in the breast. Other symptoms include persistent changes to the breast, such as thickening, swelling, distortion, tenderness, skin irritation, redness, scaliness, and nipple abnormalities or spontaneous nipple discharge. Early breast cancer usually has no symptoms and is most often diagnosed through mammography screening.

Early detection: Mammography is a low-dose x-ray procedure used to detect breast cancer at an early stage. Early detection with mammography can allow for less extensive treatment and has been shown to reduce breast cancer mortality. However, like any screening tool, mammography is not perfect; it can miss cancer (false negative) and can also appear abnormal in the absence of cancer (false positive). Mammography also detects cancers and in situ lesions (e.g., ductal carcinoma in situ) that would never have progressed and caused harm (i.e., overdiagnoses).

Mammography screening is recommended in countries with high incidence rates and good health care infrastructure that can afford long-term screening programs and access to diagnostic and treatment services.[49] A number of countries, primarily in Europe, have implemented organized, population-based mammography screening programs.[40] Countries with limited resources, where mammography screening is neither cost-effective nor feasible, should prioritize increasing public awareness and access to prompt and effective diagnosis for women with symptomatic breast cancer. Clinical breast examination may be an effective, low-cost screening option for these settings. Although it has not demonstrated a mortality benefit in randomized clinical trials, clinical breast examination has been shown to detect tumors at an earlier stage.[50] A simulation study using data from India predicted that annual clinical breast exams from ages 40 to 60 could lower the breast cancer death rate by 23%.[51] Programs to raise public awareness and promote clinical breast examination have been successfully implemented in some low-income countries. For example, a program in

Table 6. Stage Distribution (%) for Breast Cancer in Selected Countries, Population-based Data

<table>
<tr><th>Country</th><th>Stage I</th><th>Stage II</th><th>Stage III</th><th>Stage IV</th></tr>
<tr><td>Brazil, 2000-2009[54]</td><td>20</td><td>41</td><td>30</td><td>9</td></tr>
<tr><td>Côte d'Ivoire, 2008-2009[55]</td><td colspan="2">26</td><td>45</td><td>29</td></tr>
<tr><td>Egypt, 1999-2006[56]</td><td>4</td><td>34</td><td>46</td><td>16</td></tr>
<tr><td>England, 2012[57]</td><td>44</td><td>39</td><td>10</td><td>7</td></tr>
<tr><td>Republic of Congo, 2008-2009[55]</td><td colspan="2">19</td><td>35</td><td>47</td></tr>
<tr><td>Sweden (Sweden-born), 2004-2009[58]</td><td>47</td><td>44</td><td>5</td><td>4</td></tr>
<tr><td>United States (SEER 18 registries), 2007-2013[59]</td><td>49</td><td>34</td><td>11</td><td>6</td></tr>
</table>

Percentages corrected to exclude stage 0 and unknown stage. Percentages may not sum to 100 due to rounding.

rural villages in Sudan increased early-stage breast cancer detection through in-home breast examination conducted by trained female volunteers.[52] In an urban cohort in Mumbai, India, the proportion of early-stage breast cancers increased from 74% in 2005-2013 (preintervention) to 81% in 2013-2016 (postintervention), following the implementation of a program to increase breast cancer awareness.[53] Table 6 illustrates the wide geographic variation in stage at diagnosis for breast cancer. About 15% or more women diagnosed with this cancer in Egypt, Côte d'Ivoire, and the Republic of Congo had stage IV disease, compared with 10% or fewer in Brazil, England, Sweden, and the US.

Survival: Five-year net survival for breast cancer is higher than for most other cancers, with at least two-thirds of women in countries shown in Table 5, surviving at least five years after diagnosis, and rates of 85% or higher in the US, Canada, Australia, Israel, South Korea, Costa Rica, and many Northern and Western European countries.[6]

Table 7. Five-year Net Survival Rates* (%) for Selected Cancers among Children 0-14 Years of Age in Select Countries, 2010-2014

	Brain	Acute Lymphoblastic Leukemia	Lymphoma
Africa			
Algerian registries	54†		78†
Asia			
Chinese registries	41	58	61
Israel	78	88	92
Kuwait		88	96
Malaysia (Penang)	63†	82†	85†
South Korea	60	84	91
Thai registries	45†	66†	74†
Turkish registries	63	81	83
Northern America			
Canada	73	93	93
US registries	78	90	94
Central and Southern America			
Argentine registries	63†	76†	83
Brazilian registries	29	66	88
Colombian registries	47†	69†	
Costa Rica	70	80	94
Ecuadorian registries	48	50	67
Europe			
Belarus	69	87	85
Belgium	75	91	95
Czech Republic	70	88	90
Denmark	80	94	94
Estonia	65	88	88
German registries	70	91	97
Italian registries	75	88	92
Polish registries	63	87	93
Slovenia	60	70	100
Spanish registries	66	85	93
UK registries	72	92	92
Oceania			
Australian registries	67	91	92
New Zealand	58	91	97

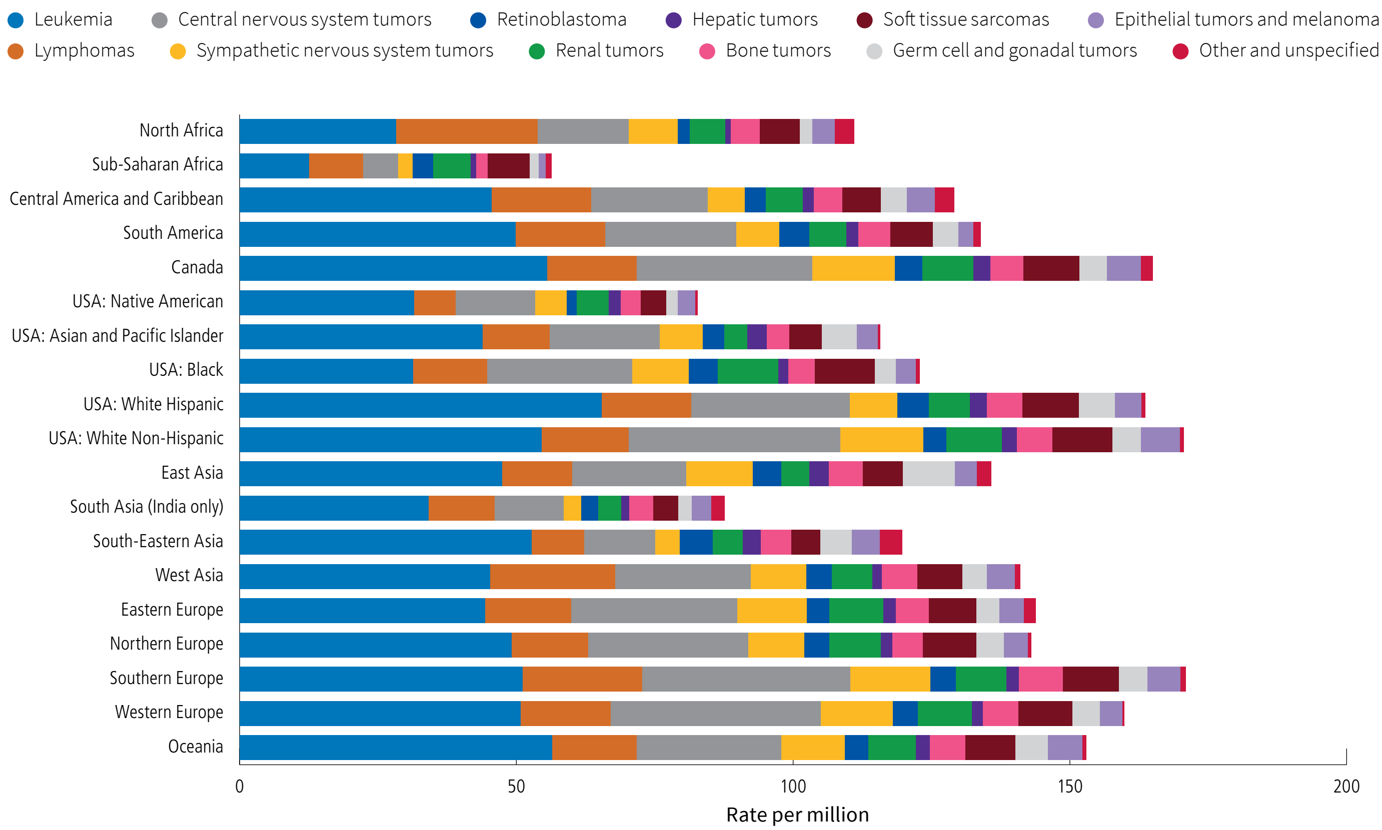
*Survival rates are age-standardized. †Data are subject to limitations. Please see source.

Source: Allemani C, Matsuda T, Di Carlo V, et al. Global surveillance of trends in cancer survival 2000-14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. *Lancet*. Jan 30 2018. doi: 10.1016/S0140-6736(17)33326-3.

Childhood Cancer

New cases: An estimated 198,700 new cancer cases will occur among children ages 0-14 in 2018.[1] Although incidence rates are generally higher in higher-HDI countries, 82% of children diagnosed with cancer live in lower-HDI countries.[1] It is more difficult to measure childhood cancer incidence accurately in lower-HDI countries because cancer registries cover a very small percentage of the population[60] and cases are often undiagnosed due to the greater frequency of death from infectious diseases and malnutrition.[61] Leukemia is the most common form of cancer among children in most

Figure 8. Distribution of Cancer in Children 0-14 Years of Age by Region, 2001-2010, Age-standardized Incidence Rates per Million



Source: Steliarova-Foucher E, Colombet M, Ries LAG, et al. International incidence of childhood cancer, 2001-10: a population-based registry study. *Lancet Oncol.* Jun 2017;18(6):719-731.

parts of the world, accounting for 32% of all childhood cancers.[60] In Africa, however, lymphomas (including Burkitt lymphoma) have the highest rates (Figure 8). Other common childhood cancers include brain and other central nervous system tumors (20%) and lymphomas (12%).

Deaths: Worldwide, an estimated 74,800 children will die from cancer in 2018.[1] Mortality rates are lowest in very high-HDI countries, despite higher incidence rates, because of the availability of high-quality diagnosis and treatment.[61,62] Cancer is emerging as a major cause of childhood death in Asia, Central and South America, North Africa, and the Middle East because fewer children are dying from preventable infectious diseases.[63]

Risk factors: There are few known risk factors for childhood cancer. Exposure to ionizing radiation increases the risk of childhood leukemia and possibly other cancers. Infection-related cancers are the most common childhood cancers in some developing countries, but account for a very small proportion of cases in Western countries. 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).

Global trends: Childhood cancer incidence rates have been increasing worldwide since the 1980s, except in sub-Saharan Africa, where they are decreasing.[60] Reasons for increasing trends are largely unknown, but may include improved diagnosis and reporting. In sub-Saharan Africa, the decreasing trend may be influenced by the declining incidence of Kaposi sarcoma due to improved management of HIV with antiretroviral therapy.[60, 64] In contrast, mortality rates for childhood cancer in general, and 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.[65] In developing countries, incidence and mortality trends for childhood cancers are often more difficult to analyze due to inadequate coverage by cancer registries, lack of vital statistics reporting, and competing causes of death.[65, 66]

Early detection: The early diagnosis of childhood cancer is often hampered by nonspecific symptoms shared by common childhood conditions. Parents should ensure that children have regular medical checkups and be alert to any unusual, persistent symptoms, including 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. The My Child Matters program of the Union for International Cancer Control funds projects aimed at improving early diagnosis of childhood cancers.[67]

Survival: Childhood cancer survival largely depends on timely diagnosis, cancer type, and the availability of effective treatment, and varies considerably by HDI level. For example, 5-year survival rates for brain cancer range from 80% in Denmark to 29% in Brazil among countries presented in Table 7. Among patients who survive, late effects of treatment may reduce quality of life, as childhood cancer therapy can have significant lifelong neurologic, developmental, and reproductive effects.[68]

Colon and Rectum

New cases: Colorectal cancer is the third most common cancer in men and the second in women. Worldwide, an estimated 1.8 million cases of colorectal cancer will occur in 2018. The highest incidence rates are expected in Northern America, Australia, New Zealand, Europe, South Korea, and Japan and the lowest in Africa and South-Central Asia (Figure 9).

Deaths: About 880,800 deaths from colorectal cancer will occur in 2018 worldwide, accounting for 9% of all cancer deaths.

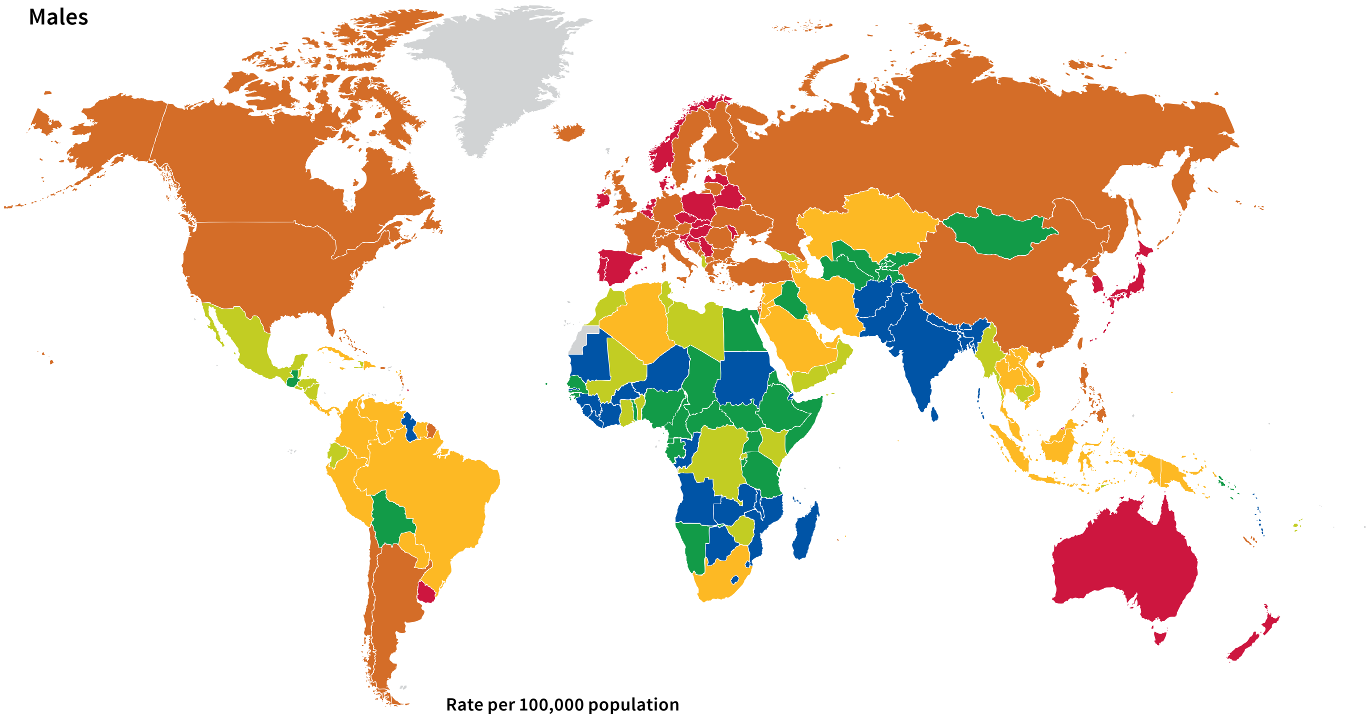
Risk factors: Modifiable factors that increase risk include obesity, physical inactivity, long-term smoking, a high consumption of red or processed meat, low calcium intake, moderate to heavy alcohol consumption, and a very low intake of fruits and vegetables and whole-grain fiber. Hereditary and medical factors that increase risk include a personal or family history of colorectal cancer and/or polyps (adenomatous), certain inherited genetic conditions (e.g., Lynch syndrome and familial adenomatous polyposis), a personal history of chronic inflammatory bowel disease (ulcerative colitis or Crohn's disease), and type 2 diabetes.

Regular long-term use of nonsteroidal anti-inflammatory drugs, such as aspirin, reduces risk, but these drugs can have serious adverse health effects, such as stomach bleeding. Decisions about aspirin use should be discussed with a health care provider.

Global trends: Colorectal cancer trends vary substantially worldwide, even within levels of HDI. Incidence rates are decreasing in some very high-HDI countries, such as the US, Israel, and Japan.[69] These countries have had widespread uptake of screening programs and early-detection programs since the 1990s, which resulted not only in decreasing mortality, but also in decreasing incidence due to the detection and removal of precancerous lesions. In other very high-HDI countries with decreasing incidence and no longstanding screening programs, such as Australia, New Zealand, and some European countries, decreasing incidence is likely due to favorably changing risk factors.[69] In contrast, incidence rates are increasing in other very high-HDI countries including Sweden, Italy, and Slovenia, as well as several lower-HDI countries undergoing rapid human development transition, likely due to increased prevalence of risk factors such as unhealthy diet, obesity, and smoking.[69] The most rapid increases of about 3% or more annually over the past 10 years are in high-HDI countries such as Costa Rica (men); Brazil (women); and Colombia and Bulgaria (both sexes).[69] In contrast to the

Figure 9. International Variation in Colorectal Cancer Incidence Rates*, 2018

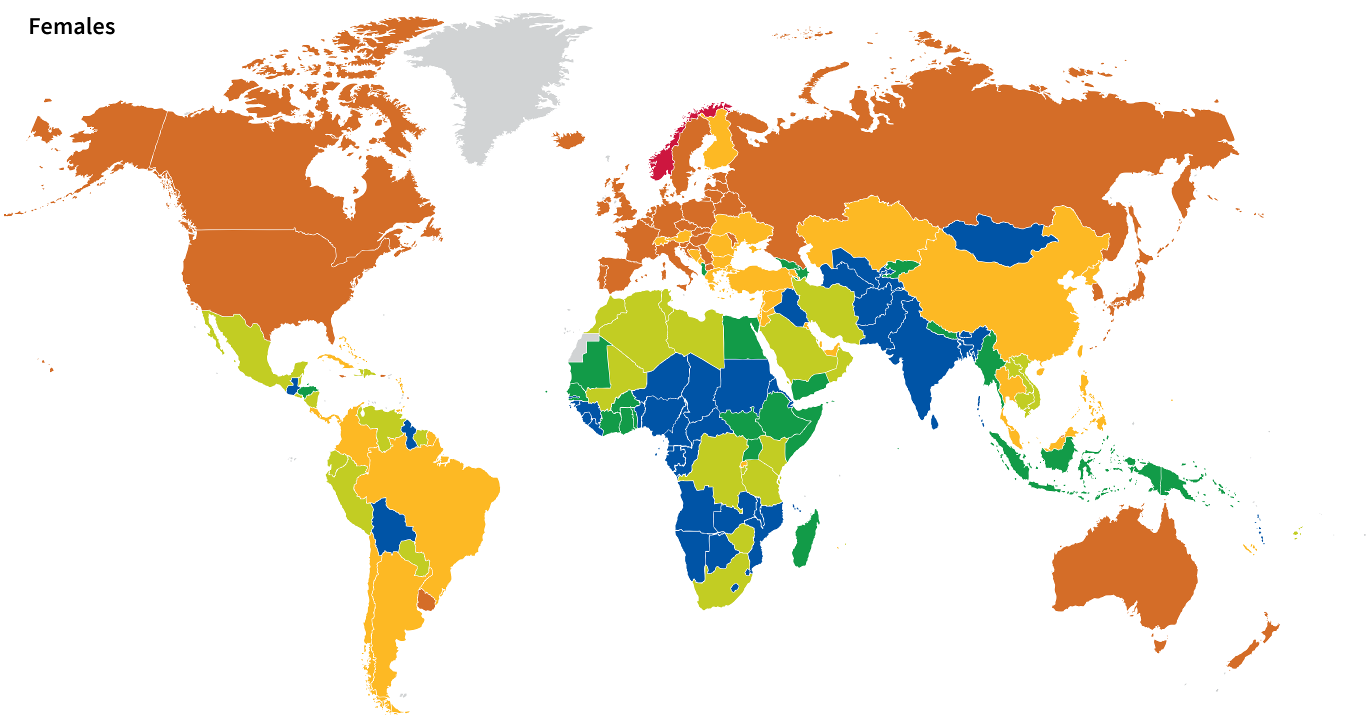
Males



Rate per 100,000 population

≥ 38.8
22.1-38.7
13.4-22.0
8.8-13.3
6.4-8.7
≤ 6.3
No data

Females



*Per 100,000, age standardized to the world standard population.

Source: GLOBOCAN 2018.

wide variation in incidence trends, colorectal cancer mortality rates have been decreasing in many countries worldwide, particularly very high-HDI countries, likely due to improvements in treatment and early detection. However, mortality rates are increasing in several of the high-HDI countries with the greatest increases in incidence.

Signs and symptoms: Symptoms 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, abdominal cramping or pain, decreased appetite, and weight loss. In some cases, the cancer causes blood loss that leads to anemia (low number of red blood cells), resulting in symptoms such as weakness and fatigue. Timely evaluation of symptoms consistent with colorectal cancer is essential for adults of any age. Early-stage colorectal cancer typically does not have symptoms, which is why screening is usually necessary to detect this cancer early.

Prevention and early detection: Aside from avoiding risk factors (page 17), colorectal cancer risk can be reduced through screening, which allows for the detection and removal of precancerous growths. Screening tests can also detect cancer at an early stage, when treatment is usually less extensive and more successful. The International Agency for Research on Cancer (IARC) has concluded that the benefits of screening with currently established stool-based tests (guaiac fecal occult blood test or fecal immunochemical test) or endoscopic exams (sigmoidoscopy or colonoscopy) outweigh the harms.[70] While colonoscopy is highly sensitive, it requires a skilled examiner, is more costly and less convenient, and has more potential harms compared with stool tests.[71] Therefore, stool tests, which are inexpensive and easy to perform, are more practical in many areas of the world.[72] Country-specific colorectal cancer screening programs, recommendations, and guidelines vary greatly worldwide. Most countries recommend beginning screening at age 50 for individuals at average risk and younger for those at higher risk because of their medical or family history. Some countries have implemented national screening programs (e.g., Finland, France, Slovenia, Japan, South Korea, Australia), but the majority of initiatives consist of recommendations and/or guidelines with opportunistic screening.[72] However, ongoing regional research and/or pilot studies have taken place in many countries, including Canada, Chile, and Thailand, to evaluate the potential for the implementation of organized screening.[72] Screening programs are not recommended in many lower-HDI countries with low incidence,[73] so these initiatives are scarce in Africa, Asia, and South America.

Survival: In Northern America, Australia/New Zealand, and many countries of Europe, colon and rectum cancer 5-year net survival is about 65% to 70% (Table 5). Among countries in Table 5, 5-year colon cancer survival rates are highest (72%) in Israel and South Korea and lowest in India (39%) (Table 5). Survival is much higher when colorectal cancer is detected at an early stage; however, fewer than half of cases are diagnosed early, even in developed countries, mainly due to suboptimal screening rates. For example, only about 40% of colorectal cancers are diagnosed at an early stage in Canada, Denmark, and the United Kingdom.[74]

Esophagus

New cases: An estimated 572,000 new cases will occur in 2018 worldwide. Esophageal cancer incidence varies by up to 20-fold, with the highest rates in Asia and Eastern and Southern Africa and the lowest in Western Africa, Northern America, and parts of Europe and South America (Figure 10). The distribution of the two main types of esophageal cancer, squamous cell carcinoma and adenocarcinoma, also varies dramatically worldwide. Squamous cell carcinoma accounts for over 90% of esophageal cancers in Eastern and South-Eastern Asia, sub-Saharan Africa, and Central Asia, compared with only 40% to 50% in Northern America, Oceania, and Northern and Western Europe.[75] Squamous cell carcinoma predominates in the high-risk area known as the "esophageal cancer belt," which stretches from Northern Iran through the Central Asian republics to North-Central China. Esophageal cancer is generally three to four times more common among men than women.

Deaths: About 508,600 people are expected to die from esophageal cancer in 2018. More than 60% of those deaths will occur in high-HDI countries, which make up 32% of the world population.

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.[76] These risk factors account for a smaller proportion in high-risk areas in Asia and Africa. For example, in South Africa, about 60% of squamous cell carcinomas are attributable to alcohol and tobacco combined.[77] Other risk factors are not well understood, but are thought to include poor nutritional status, low intake of fruits and vegetables, drinking beverages at extremely high temperatures, and exposure to polycyclic aromatic hydrocarbons.[78] Based on a review of the evidence, the IARC recently concluded that drinking very hot beverages, particularly maté, a beverage commonly consumed in South America, probably causes esophageal cancer.[79]

The main known risk factors for esophageal adenocarcinoma are excess body weight and chronic gastroesophageal reflux disease (GERD). Risk among people with obesity (BMI 30-39.9) is roughly double that of those with a normal BMI (18.5≤BMI<25).[80] GERD is a digestive disorder, most common in those who are overweight, in which acid from the stomach enters the lower section of the esophagus and irritates the esophageal lining. Over time, this can lead to Barrett's esophagus, a condition in which normal esophageal cells are replaced with cells similar to the lining of the small intestine. In a small proportion of cases, this change leads to adenocarcinoma. Smoking and low fruit and vegetable consumption are also risk factors for adenocarcinoma of the esophagus. *H. pylori* infection appears to be associated with reduced risk of esophageal adenocarcinoma.[81-83]

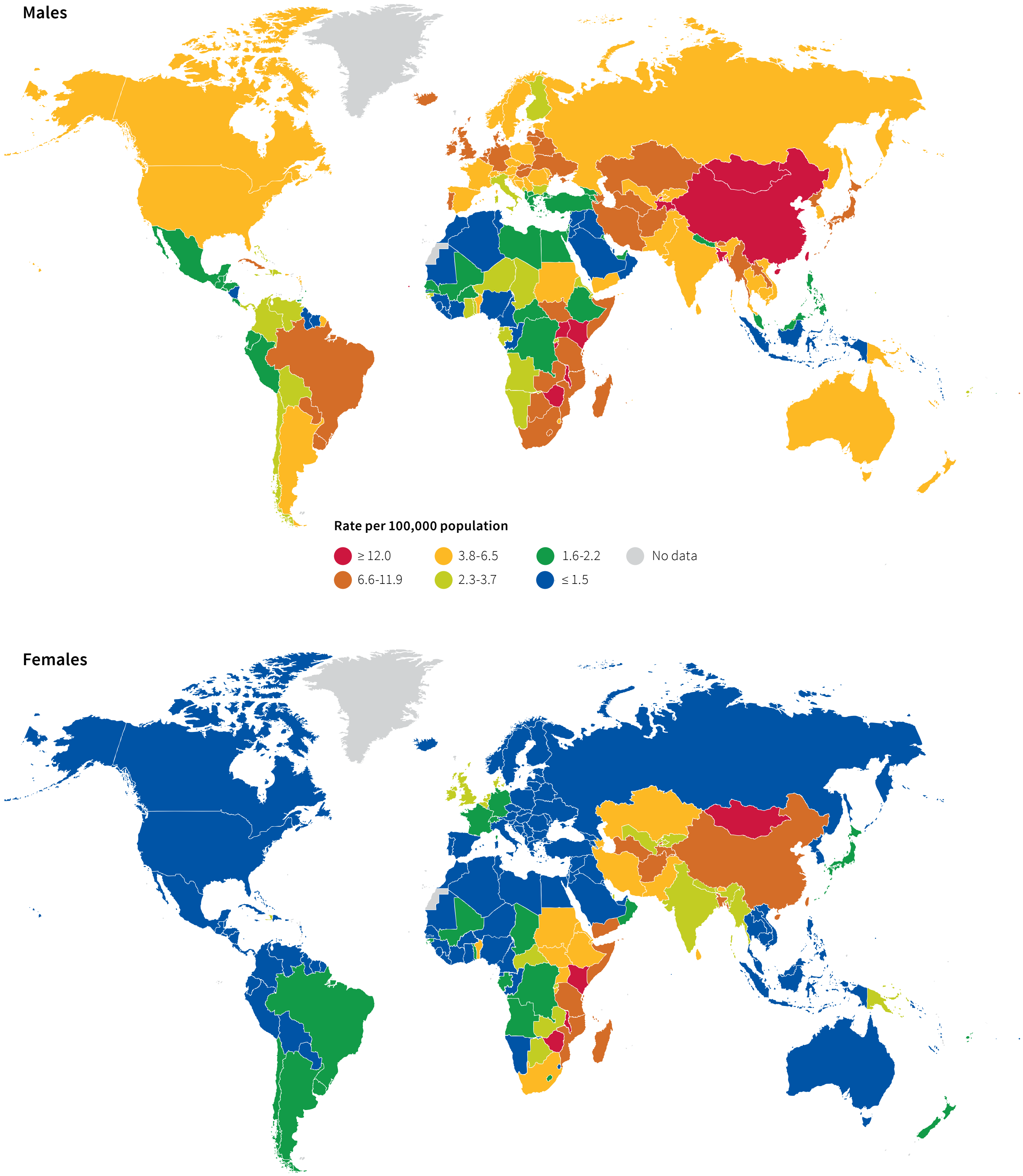
Global trends: In Western countries, such as the United States, Australia, France, and the United Kingdom, the incidence of esophageal squamous cell carcinoma has been steadily declining, primarily due to reductions in tobacco use, whereas adenocarcinoma has been increasing.[84] This trend is most likely due to increases in obesity and waist circumference, as well as increasing GERD.[80, 84, 85] The increases may also be related to declining prevalence of *H. pylori* infection.[86] In Asia, esophageal squamous cell carcinoma incidence decreased from 1988 to 2007 in Hong Kong, China, an urban area that experienced earlier uptake and subsequent decline of smoking, while adenocarcinoma rates have generally remained stable.[87] Overall esophageal cancer mortality rates have also decreased in high-risk areas of China since the 1970s for reasons that are poorly understood, but may partly reflect changes in mortality recording practices.[88] Overall esophageal cancer incidence and mortality rates have also decreased among men and women in many Central and South American countries, likely due to declines in the prevalence of smoking and alcohol consumption.[89]

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

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 adenocarcinoma mortality.[90] Treating gastric reflux with proton pump inhibitor drugs may prevent Barrett's esophagus, or esophageal adenocarcinoma once Barrett's esophagus has already developed, although clinical trials are lacking.[85, 91] Screening using endoscopy to detect and treat precancerous esophageal squamous dysplasia has been shown to reduce esophageal squamous cell carcinoma incidence and mortality in a very high-incidence region of China;[92] however, the use of this method for population screening is likely not feasible in most high-risk areas due to cost and infrastructure requirements.[76]

Survival: Most people with esophageal cancer eventually die of the disease because it is usually diagnosed at a late stage. Five-year net survival is about 20% to 30% for most very high-HDI countries and as low as 5% to 10% in some lower-resource countries (Table 5).

Figure 10. International Variation in Esophageal Cancer Incidence Rates*, 2018



*Per 100,000, age standardized to the world standard population.

Source: GLOBOCAN 2018.

Liver

New cases: Liver cancer is the fifth most common cancer in men and the ninth in women. An estimated 841,100 new liver cancer cases will be diagnosed during 2018, with China alone accounting for almost 50% of the total. Rates are more than twice as high in men as in women. Liver cancer rates are the highest in Eastern and South-Eastern Asia, Micronesia, West and Central Africa, and Egypt (Figure 11). Most (80%) primary liver cancers occurring worldwide are hepatocellular carcinoma (HCC).[93]

Deaths: Worldwide, liver cancer is the second-leading cause of cancer death in men and the sixth-leading cause among women, with about 781,600 deaths expected in 2018.

Risk factors: HCC is strongly associated with chronic infection with 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. The underlying cause of the liver cancer burden varies substantially between regions. For example, the proportion of liver cancer deaths due to HBV ranges from 6% in southern Latin America to 45% in Andean Latin America and western sub-Saharan Africa.[94] Other risk factors for HCC include heavy alcohol drinking, excess body weight, type 2 diabetes, non-alcoholic fatty liver disease (associated with obesity), and smoking.[93]

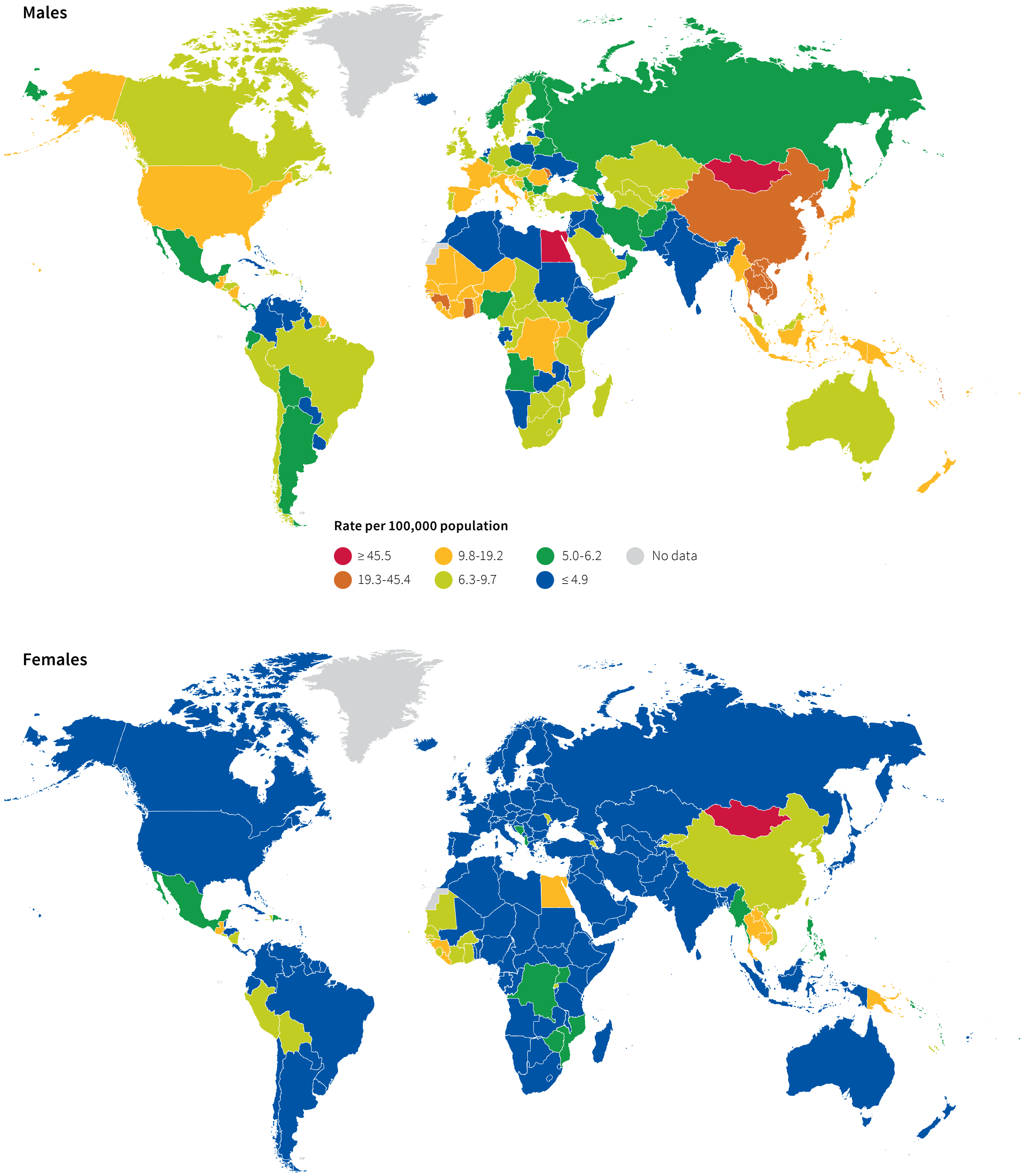
Additional risk factors for liver cancer, which are more prevalent in lower-HDI countries, include consumption of food contaminated with aflatoxin (a toxin produced by a fungus that infests grains, peanuts, soybeans, and corn that have been stored in warm, moist conditions) and infection with parasitic liver flukes, which causes cancer of the bile ducts (cholangiocarcinoma). A high prevalence of this infection contributes to high rates of cholangio-carcinoma in Thailand and other parts of Asia. In 2012, an estimated 73% of about 780,000 liver cancers worldwide were attributable to HBV, HCV, and liver fluke infection.[2]

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 2014.[95] This increase is primarily attributed to increases in chronic HCV infection during the 1960s and 1970s due to exposure to contaminated blood products or medical devices and injection drug abuse. Increases in the prevalence of obesity and diabetes mellitus in these countries may contribute to more recent liver cancer trends.[96] In contrast, liver cancer rates are decreasing in some historically high-risk areas, including China and Japan. These declines have been attributed to improved blood donation practices, policies discouraging intravenous drug abuse in Japan,[97] and programs for prevention of familial transmission of HBV and aflatoxin exposure in China.[98, 99] A more than 80% decline in liver cancer incidence rates among youth and young adults ages 5 to 29 in Taiwan has been reported as a result of a universal HBV childhood vaccination program begun in 1984.[100] 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: 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 clinical sign.

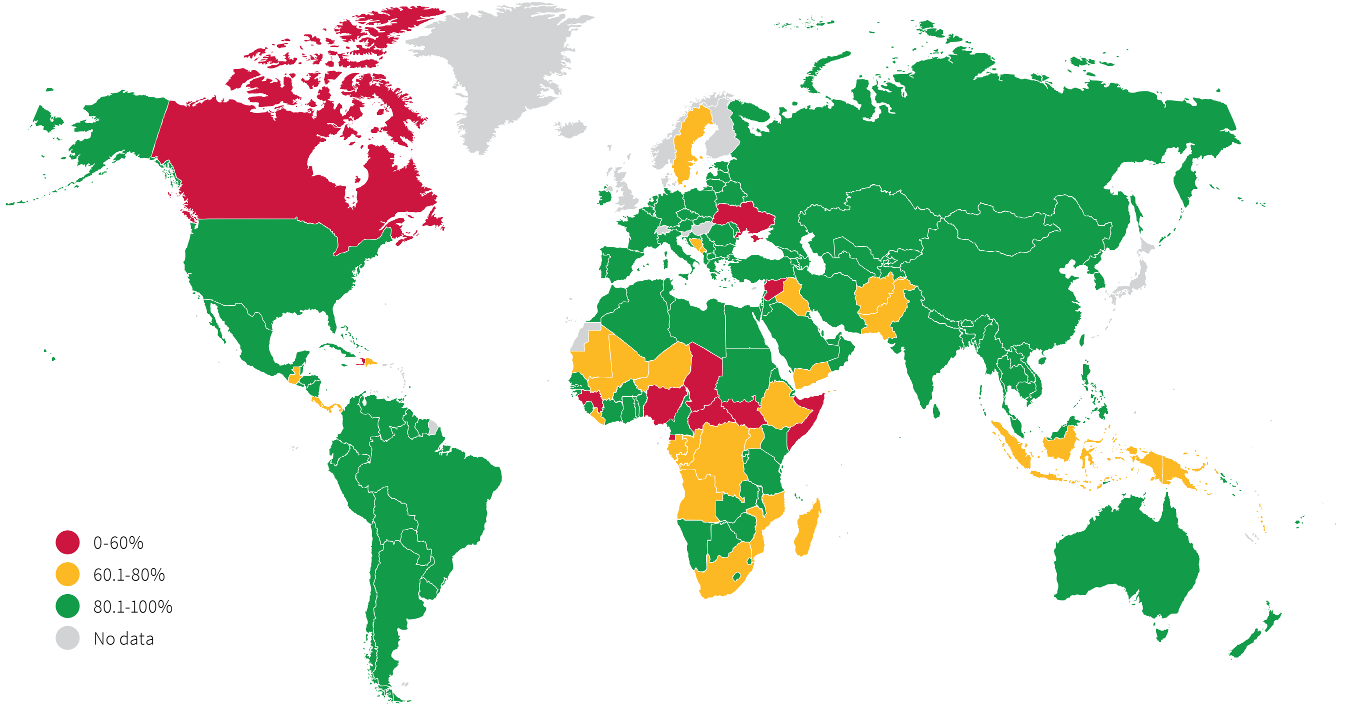
Prevention and early detection: A vaccine that protects against HBV has been available since 1982. The WHO recommends that all countries include the HBV vaccine in routine infant immunization programs. By the end of 2016, 186 countries had introduced the HBV vaccine into their national infant immunization schedules,[101] with most countries achieving more than 80% coverage for the full recommended dose (Figure 12). There is no vaccine available to prevent HCV infection. Antiviral therapies for HBV or HCV infection can substantially reduce cancer risk among those already infected.[102] However, these treatments may be costly and infeasible in many

Figure 11. International Variation in Liver Cancer Incidence Rates*, 2018



*Per 100,000, age standardized to the world standard population.
Source: GLOBOCAN 2018.

Figure 12. Percentage of 1-year-olds Who Received the Three-series Hepatitis B Vaccination*, 2016



*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, estimates by country, 1989-2016 [online database]. Available from: http://apps.who.int/gho/data/, accessed February 27, 2018.

low-resource countries.[103] Some companies that produce HCV antiviral therapies have negotiated donated or lower-cost drugs in several countries with a high burden of HCV, although challenges remain to reach all those infected.[104, 105] HCV 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 lower-HDI countries due to resource constraints. Globally, an estimated 95% of people living with chronic viral hepatitis are unaware of their status; in its Global Health Sector Strategy on Viral Hepatitis 2016-2021, the WHO recommends that all countries integrate hepatitis testing into their national policies and guidelines.[106] Although evidence of mortality benefits of screening for liver cancer are weak,[107] guidelines in the United States, Asia, and Europe recommend testing individuals at high risk (e.g., those with cirrhosis) with ultrasound or blood tests.[108]

Additional preventive strategies include avoiding smoking and limiting alcohol consumption. In lower-HDI 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 highly endemic areas in China.[109] Mass drug administration and public health campaigns may contribute to prevention of cholangiocarcinoma, a form of liver cancer caused by chronic infection by the liver fluke.[110]

Survival: Liver cancer is one of the most fatal cancers, with 5-year survival rates generally less than 20%, even in developed countries (Table 5). Higher survival in South Korea (27%) is likely due to established screening of high-risk individuals.[108, 111]

Lung and Bronchus

New cases: An estimated 2.1 million new cases will occur in 2018, accounting for about 12% of total cancer diagnoses. In males, the highest lung cancer incidence rates will be in Micronesia, Polynesia, Eastern and Western Europe, and Eastern Asia, and the lowest rates will be in sub-Saharan Africa (Figure 13). Among females, the highest lung cancer rates will be in Northern America, Northern and Western Europe, and Oceania, while the lowest will be in Africa and South-Central Asia (Figure 13). Lung cancer rates in Chinese females will be higher than rates among females in some European countries despite a lower prevalence of smoking, likely reflecting exposure to indoor air pollution from unventilated coal-fueled stoves and cooking fumes.[112]

Deaths: Worldwide, lung cancer is the leading cause of cancer death in men and the second-leading cause in women, with an estimated 1.8 million deaths expected in 2018 (1.2 million in men and 576,100 in women), accounting for 1 in 5 cancer deaths worldwide.

Risk factors: Cigarette smoking is by far the most important risk factor for lung cancer, accounting for about 75% of lung cancer deaths in men and 50% in women worldwide.[113] 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 thought to be the second-leading cause of lung cancer in Europe and Northern America (about 8%-15% of cases).[114, 115] 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 medium-HDI countries, is estimated to account for 9% of lung cancer deaths worldwide, while it accounts for 26% in South Asia and 33% in sub-Saharan Africa.[113] 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, and diesel exhaust. Some specific occupational exposures that increase risk include rubber manufacturing, paving, roofing, painting, and chimney sweeping. Risk is also probably increased among people with a history of tuberculosis.

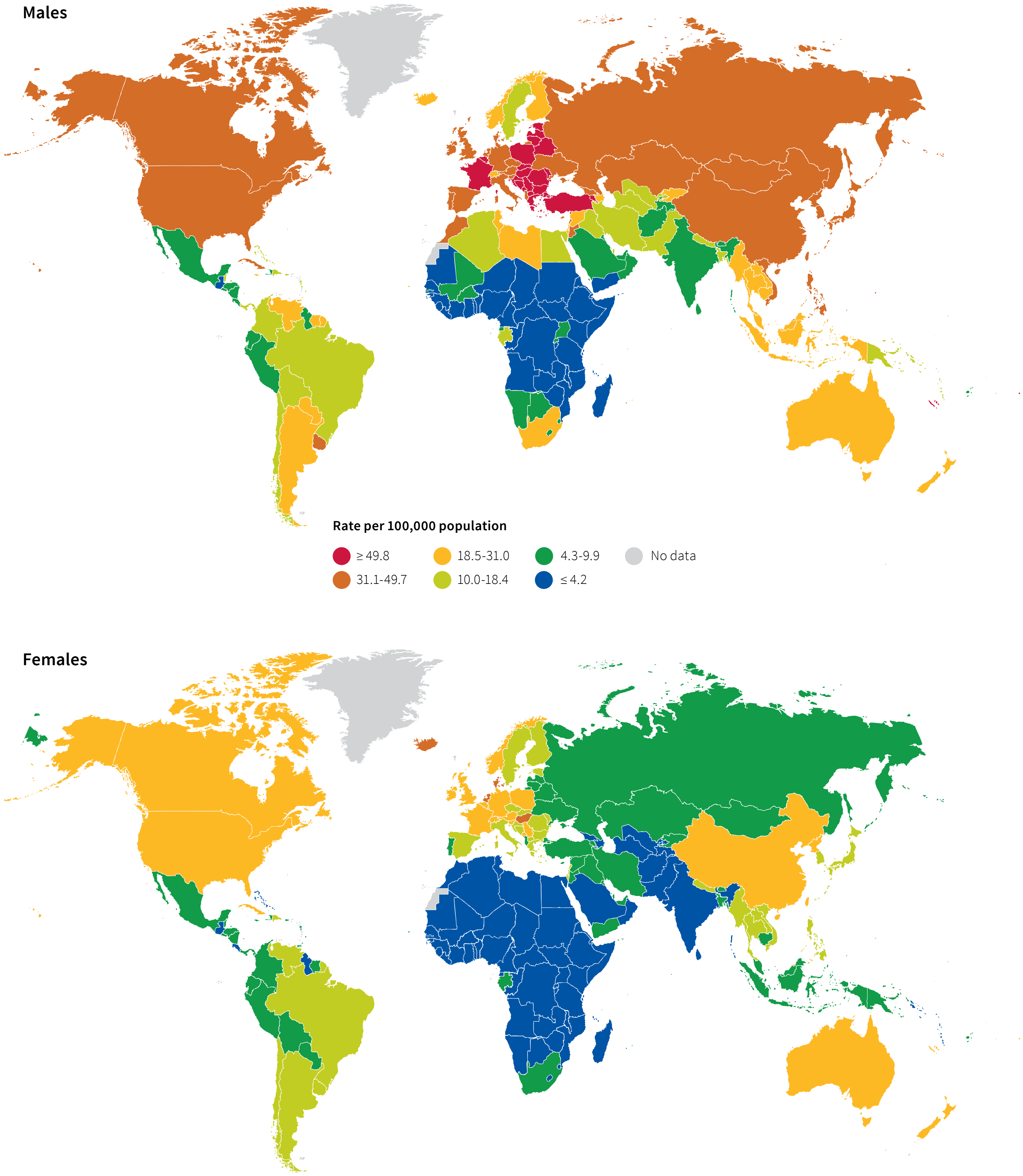
Global trends: Variations in lung cancer patterns largely reflect country-specific differences in the stage and degree of the tobacco epidemic.[116, 117] In several Western countries where the tobacco epidemic began earliest and peaked by the middle of the past century, such as the United Kingdom and Denmark, lung cancer mortality rates are decreasing in men and have plateaued or are decreasing in women.[118, 119] Rates are also decreasing in men, but continuing to increase in women, in countries where the tobacco epidemic peaked later, such as Spain, Hungary, and Brazil (Figure 14).[119] In countries where smoking has just peaked or continues to increase, such as China and several countries in Africa, lung cancer rates will likely continue to increase for at least the next several decades without large-scale interventions to accelerate smoking cessation and reduce initiation.[98, 120, 121]

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.

Prevention and early detection: 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 taxes, banning smoking in public places and tobacco sales to minors, restricting tobacco marketing, counteradvertising, and providing treatment and counseling for tobacco dependence. In the United States, state-level comprehensive tobacco control programs have markedly decreased smoking rates and accelerated the reduction in lung cancer occurrence, particularly in California.[122] In the developing world, many of the most populous countries, such as China, Indonesia, and Russia, already have substantial numbers of smokers.[123] If these and other developing countries take swift action to promote smoking cessation and prevent initiation, they can attenuate future lung cancer rates and the burden of smoking-related diseases.

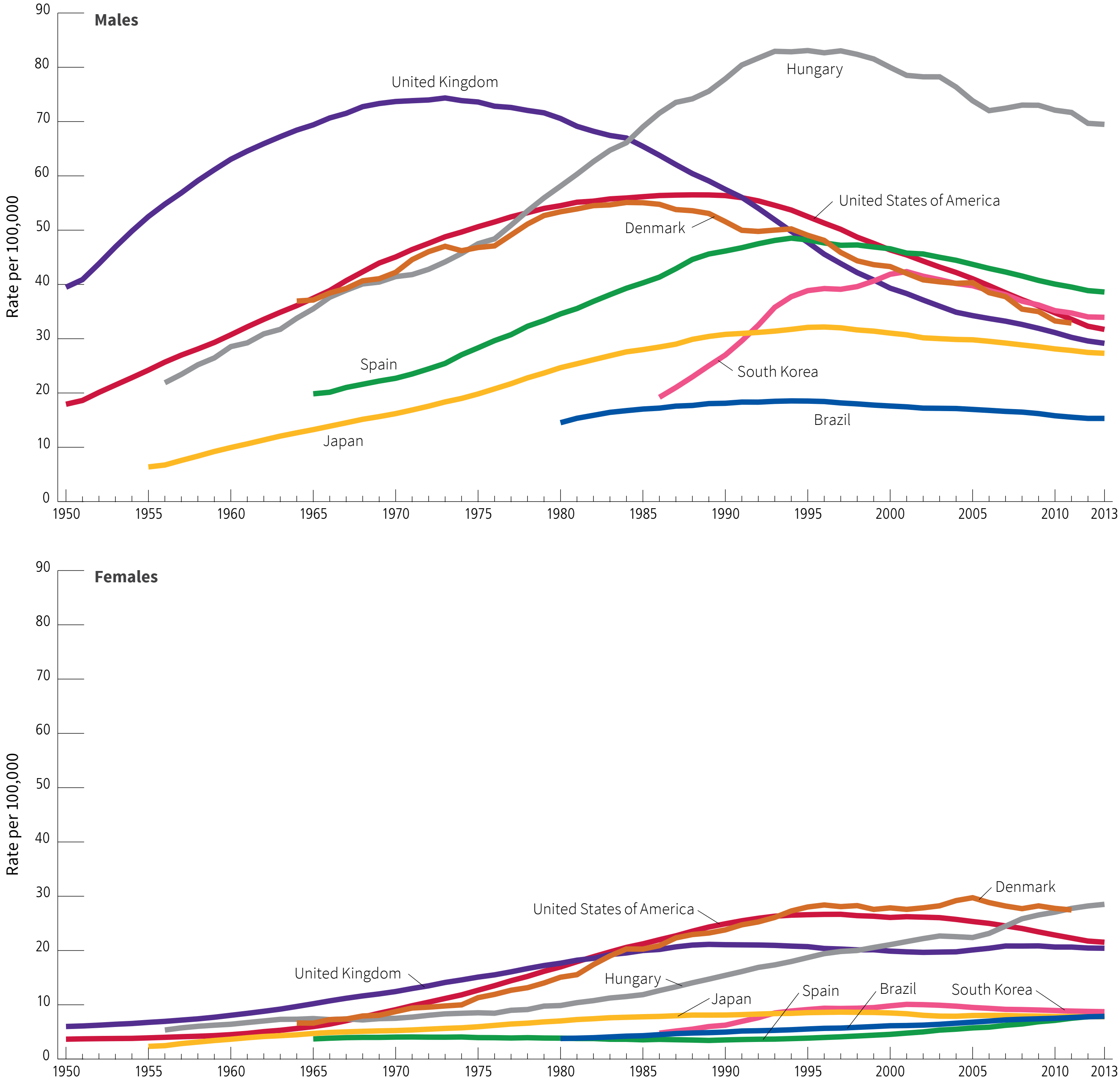
Results from the National Lung Screening Trial, a clinical trial in the United States designed to determine the effectiveness of lung cancer screening in high-risk

Figure 13. International Variation in Lung Cancer Incidence Rates*, 2018



*Per 100,000, age standardized to the world standard population.
Source: GLOBOCAN 2018.

Figure 14. Trends in Lung Cancer Death Rates*, Select Countries, 1950-2013



*Per 100,000, age standardized to the world standard population. Rates have been smoothed using 3-year averages.
Source: WHO Cancer Mortality Database.

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.[124] 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, may be substantially greater in settings that lack access to high-quality screening.[125] The WHO recommends that screening programs include access to effective treatment capable of reducing morbidity and mortality.[126] Thus, residents of countries with limited health care resources will not likely benefit from lung cancer screening in the near future.

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).

Non-Hodgkin Lymphoma

New cases: An estimated 509,600 new cases of non-Hodgkin lymphoma (NHL) will occur in 2018. NHL encompasses a wide variety of disease subtypes for which incidence patterns vary.[127] NHL is more common in higher-HDI countries, with incidence highest in Australia, Northern America, Western and Northern Europe, Israel, Lebanon, and Egypt and lowest in Central America and parts of Asia and Africa (Figure 15).

Deaths: An estimated 248,700 deaths from NHL will occur in 2018.

Risk factors: Most of the known risk factors are associated with severely altered immune function. For example, NHL risk is elevated in people who receive immune suppressants to prevent organ transplant rejection. Certain infections (e.g., Epstein Barr virus) increase the risk of NHL directly, whereas others increase risk indirectly by weakening (e.g., HIV) or continuously activating (e.g., *H. pylori* and HCV) the immune system. NHL is classified as an AIDS-defining illness among HIV-positive people, and the risk before the introduction of highly active antiretroviral therapy (HAART) was about 6 to 7 times greater among those with HIV compared with the general population.[128, 129] Some autoimmune disorders (e.g., Sjogren syndrome, lupus, and rheumatoid arthritis) are also associated with increased risk.[130] A family history of lymphoma increases risk for all NHL subtypes. Studies also suggest a role for certain personal risk factors (e.g., body weight) and environmental exposures for some subtypes.[130]

Global trends: The incidence of NHL increased in most developed countries through 1990 and leveled off thereafter.[95, 131, 132] While some of the increase may be due to improvements in diagnostic procedures and changes in classification, much of this trend reflects a true increase in disease occurrence.[133] In the United States, increased incidence of HIV infection contributed to some of the increase throughout the 1980s, particularly among white males, while the decline after 1990 likely reflects the declining incidence of HIV infection and the success of antiretroviral therapies.[134, 135] Since the introduction of HAART in the United States in 1996, NHL incidence rates have declined 30% to 50% among HIV-infected people.[136] The AIDS epidemic has also contributed to increased incidence of NHL in some developing countries,[137] such as those in sub-Saharan Africa, where antiretroviral therapy has had less influence on NHL trends.[138-140] For example, 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, perhaps reflecting the increasing availability of antiretroviral therapies since their introduction in the early 2000s.[141-143]

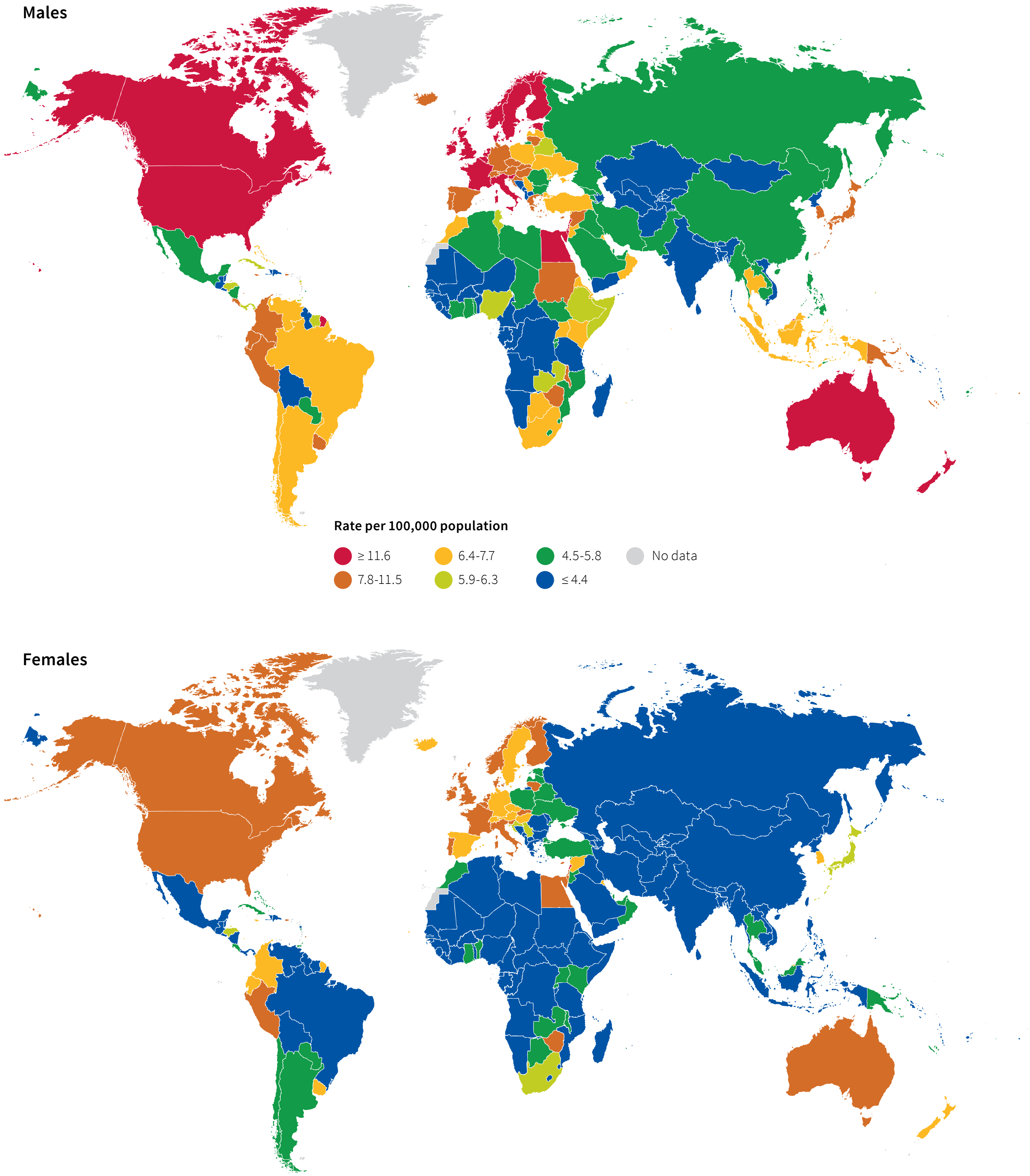
Signs and symptoms: Symptoms may include swollen lymph nodes or abdomen, feeling full after only a small amount of food, night sweats, fatigue, chest pain or pressure, unexplained weight loss, and fever.

Survival: Survival varies widely by cell type, disease stage, and country. In the United States, the 5-year relative survival for non-Hodgkin lymphoma is 73%.[95] In Europe, the average 5-year relative survival is 59%, ranging from 44% in Poland to 74% in Iceland.[144]

Prostate

New cases: Prostate cancer is the second most frequently diagnosed cancer in men, with an estimated 1.3 million new cases expected in 2018. About two-thirds of these will be diagnosed in very high-HDI countries, where only 18% of the world's male population resides. Incidence rates vary by more than 100-fold worldwide, and are highest in some Caribbean islands, Australia/New Zealand, Northern and Western Europe, and Northern

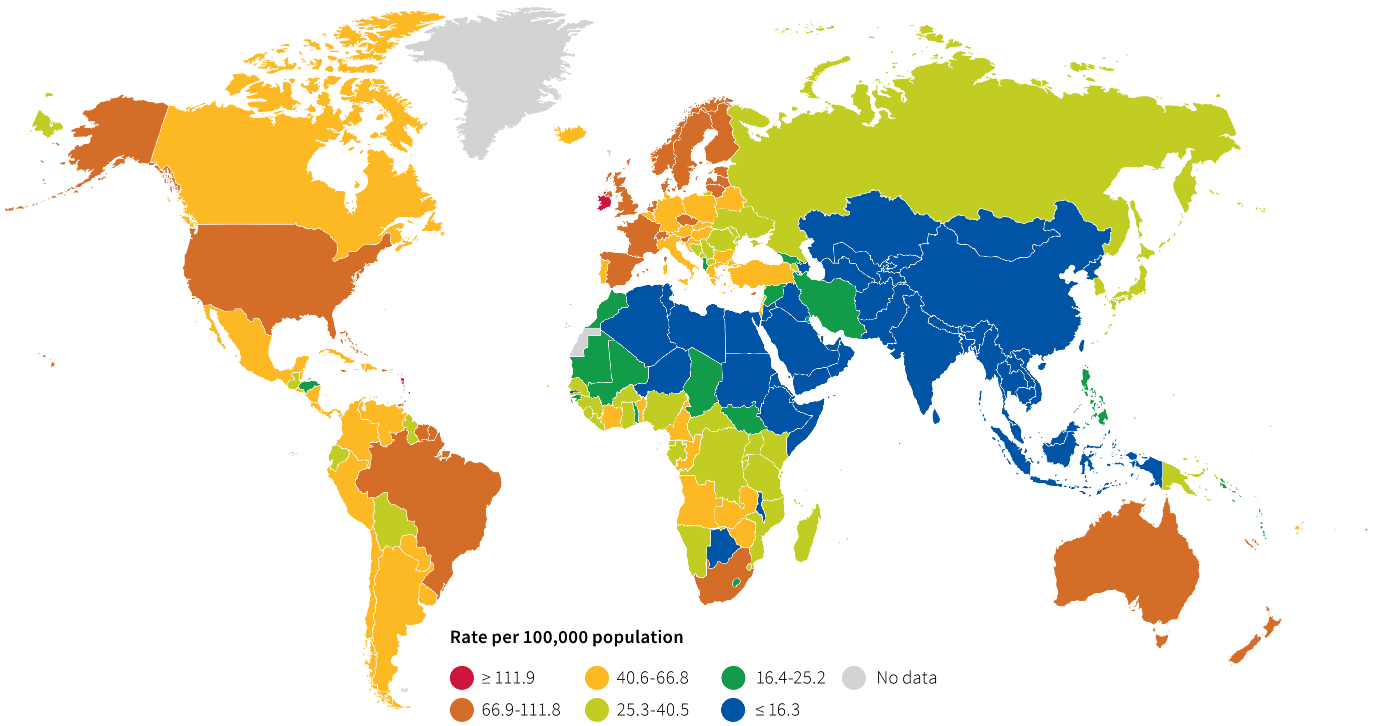
Figure 15. International Variation in Non-Hodgkin Lymphoma Incidence Rates*, 2018



*Per 100,000, age standardized to the world standard population.

Source: GLOBOCAN 2018.

Figure 16. International Variation in Prostate Cancer Incidence Rates*, 2018



*Per 100,000, age standardized to the world standard population.
Source: GLOBOCAN 2018.

America, and lowest in Asia (Figure 16). Much of the variation reflects differences in the use of prostate-specific antigen (PSA) testing.[145]

Deaths: With an estimated 359,000 deaths in 2018, prostate cancer will be the fifth-leading cause of cancer death in men worldwide. Men in Southern Africa and the Caribbean have the highest prostate cancer mortality rates in the world.[1]

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. Black men in the United States and Caribbean have the highest documented prostate cancer incidence rates in the world for reasons that are poorly understood, but may partly reflect genetic susceptibility.[146, 147] 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 and *BRCA1* and *BRCA2* mutations. Smoking appears to increase risk of fatal prostate cancer and obesity for aggressive prostate cancer.[148, 149]

Global trends: Incidence rates increased in many countries at various development levels throughout the past four decades.[145] Incidence trends in countries with a rapid uptake of PSA screening, such as Australia, Canada, and the United States, followed a consistent pattern with a rapid rise in incidence of prostate cancer in the early 1990s soon after the introduction of PSA testing, followed by a sharp decline as the pool of prevalent cases diminished.[145, 146] Prostate cancer incidence rates declined sharply in the US following the recommendation against the routine use of PSA testing by the United States Preventive Services Task Force in 2012.[150] In other high-income countries with more gradual adoption of PSA testing, such as many countries in Western Europe, the increase in incidence has been less dramatic.[145, 146] Rates also have been increasing in some countries where PSA testing began later or remains uncommon, such as the United Kingdom, Japan, Brazil, Costa Rica, Thailand, and sub-Saharan Africa.[141, 142, 145, 146, 151, 152]

Death rates for prostate cancer have been decreasing in many countries, including those in Northern America, Oceania, Northern and Western Europe, Latin America, and developed countries of Asia.[151, 153] This decrease has been attributed mainly to improved treatment and/or early detection, although the specific contribution of PSA testing is debated.[154] In contrast, mortality rates are rising in some Asian and Central and Eastern European countries, such as the Philippines, Singapore, Bulgaria, Belarus, and Russia.[153] The increase is thought to reflect changing risk factors in combination with limited access to appropriate treatment.[145, 153]

Signs and symptoms: Early prostate cancer usually has no symptoms. Men with more advanced disease may experience weak or interrupted urine flow; difficulty starting or stopping 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.

Early detection: Whether and how to use PSA screening to reduce deaths from prostate cancer while balancing potential harms remains controversial.[155] Routine PSA screening is not recommended in many European countries[156] for men at average risk because of concerns about the high rate of overdiagnosis (detecting disease that would have never caused symptoms), along with the significant potential for serious side effects associated with prostate cancer treatment. The United States Preventive Services Task Force recommends that average risk men ages 55-69 have a conversation with their health care provider about the benefits and limitations of PSA testing and make an informed decision about whether to be tested based on their personal values and preferences.[157] 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.[155, 158]

Survival: Over the past 30 years, the dramatic improvement in survival in high-income countries largely reflects lead-time bias attributable to the early diagnosis of asymptomatic prostate cancer (some of which would never have become clinically evident) through PSA testing. Thus, the 5-year net survival rate ranges from 95% or greater in the US and Australia to 44% in India (Table 5).

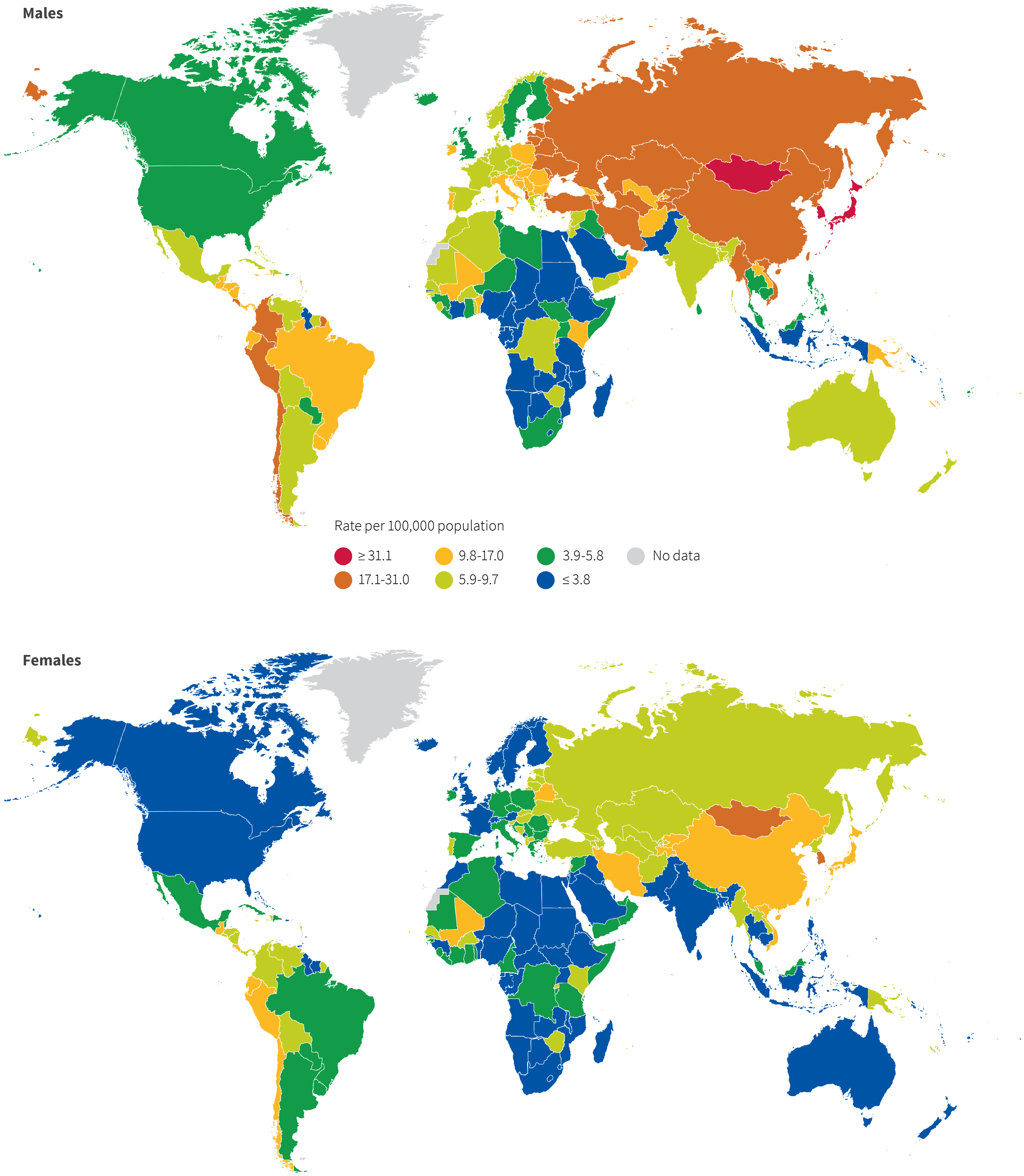
Stomach

New cases: Stomach cancer will be the fifth most common malignancy in the world in 2018, with an estimated 1 million new cases. Approximately 55% of cases occur in high-HDI countries, which make up 32% of the world population. Generally, stomach cancer rates are about twice as high in men as in women after the age of about 40. Stomach cancer incidence rates vary widely across countries, ranging in men from about 1 case (per 100,000) in Swaziland and Botswana to about 58 in South Korea and in women from less than 1 case in the Gambia and Indonesia to about 24 in South Korea (Figure 17). Incidence rates generally are highest in Asia (particularly Eastern Asia), Eastern Europe, and parts of Latin America, and lowest in Africa.

Deaths: Stomach cancer is the third- and fifth-leading cause of cancer death in men and women, respectively. About 782,700 people worldwide will die from stomach cancer in 2018.

Risk factors: Chronic infection with *H. pylori* is the strongest known risk factor for stomach cancer, with 89% of new non-cardia (the lower part of the stomach) gastric cancer cases worldwide attributed to this bacteria.[159] The most likely route of *H. pylori* transmission is from person to person through fecal-oral, gastro-oral, or oral-oral routes.[160] Possible environmental sources include water contaminated with human waste. Prevalence of *H. pylori* infection is higher in Africa, South America, and Western Asia (about 70%) than in Oceania (24%), Western Europe (34%), and Northern America (37%).[161] Although less than 5% of chronically infected individuals will develop stomach cancer,[162] rates are surprisingly low in Africa relative to the high prevalence of *H. pylori* infection. This phenomenon, sometimes referred to as the "African enigma," remains unexplained, but may be related to evolutionary or environmental factors, such as coinfection with other bacteria and/or parasites that neutralize the harmful effects of *H. pylori*.[163, 164] Other risk factors for stomach cancer include smoking[165] and

Figure 17. International Variation in Stomach Cancer Incidence Rates*, 2018



*Per 100,000, age standardized to the world standard population.
Source: GLOBOCAN 2018.

probably high consumption of alcohol, foods preserved by salting, and processed meat.[166] Smokers have a 50% to 60% increased risk for stomach cancer compared with nonsmokers.[112] Obesity is associated with increased risk of adenocarcinoma of the gastric cardia, possibly due to gastro-esophageal reflux disease or chronic inflammation.[166, 167]

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.[168, 169] Similar decreasing trends have been noted in more recent years in areas with historically high rates, including several countries in Asia (Japan, China), Latin America (Brazil, Costa Rica), and Europe (Latvia).[170] Factors thought to have contributed to these declines include the proliferation of home refrigerators and decreased reliance on salted and preserved foods and the reduction in chronic *H. pylori* infection due to sanitation and antibiotics.[170, 171] In developed countries, decreases in smoking prevalence may also account for some of the decline.[170] 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, perhaps due to increased obesity and/or improvements in classification.[48, 172]

Signs and symptoms: Stomach cancer has very few symptoms in the early stages, but may include indigestion, a bloated sensation after eating, feeling full after eating a small amount, 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.

Prevention and early detection: The primary prevention strategies for stomach cancer include reducing intake of alcohol, foods preserved by salting, and processed meat; 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.[173, 174] While this approach requires further study in community settings, it represents a promising intervention for stomach cancer prevention in the future. However, there are also concerns about whether this approach to *H. pylori* eradication would result in antibiotic resistance, microbiome imbalance, and/or other negative consequences.[173, 174] It is estimated that endoscopic screening results in a 40% reduction in stomach cancer mortality in high-risk populations of East Asia.[175] National stomach cancer screening programs are available in Japan and South Korea, where they have resulted in the detection of many cancers at an earlier, more treatable stage.[176, 177] Population screening is not recommended in low-incidence countries.

Survival: In Japan and South Korea, because about half of stomach cancers are diagnosed at an early stage due to screening, the 5-year net survival rate is 60% or more (Table 5).[6, 177, 178] In contrast, the 5-year survival is 33% in the US, where only about 25% of cases are diagnosed at an early stage.[179] In lower-HDI countries, survival rates are generally below 25%.

Urinary Bladder

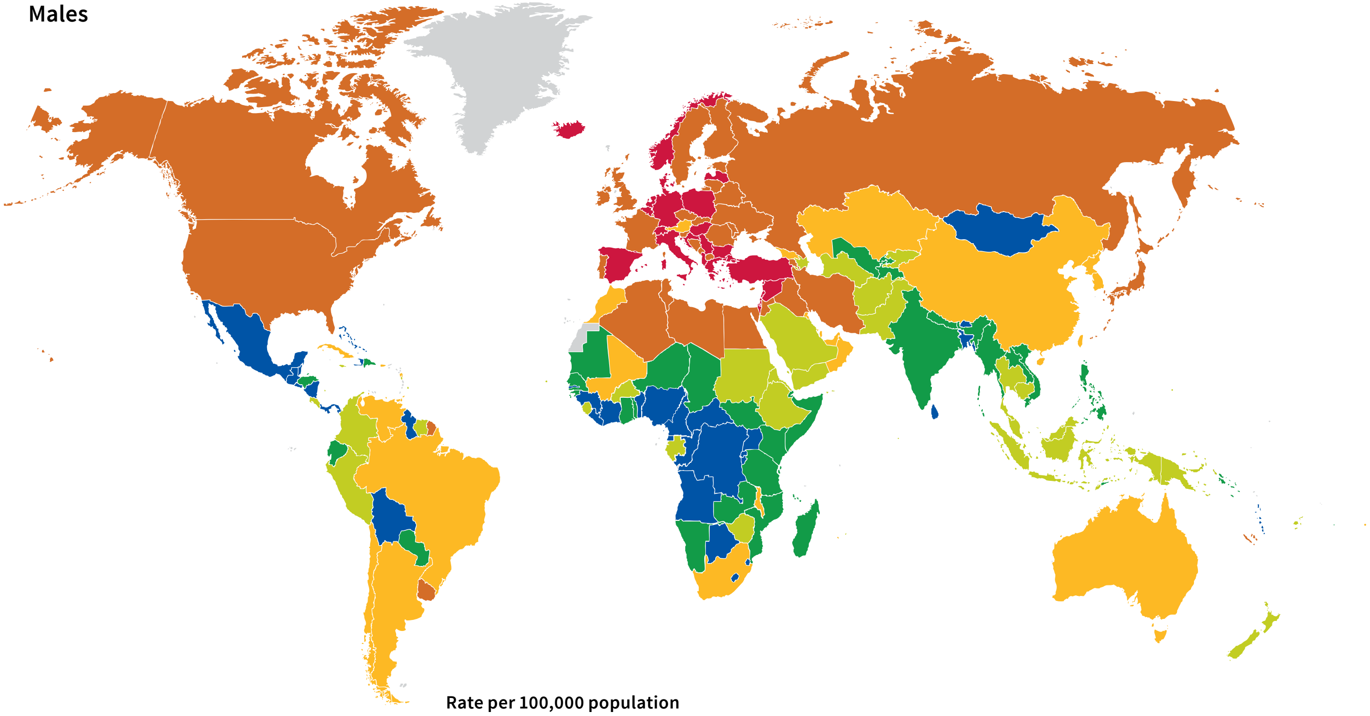
New cases: An estimated 549,400 new cases of bladder cancer will occur in 2018. The majority of bladder cancer occurs in men, and there is about a 15-fold variation in incidence rates internationally. Incidence is highest in Europe, Northern America, Western Asia, and Northern Africa, and lowest in Middle Africa and South-Central Asia (Figure 18). Some of this variation reflects differences in the diagnosis and reporting of malignant noninvasive (in situ) tumors.[180, 181]

Deaths: An estimated 200,000 deaths from bladder cancer will occur in 2018. Mortality rates are generally highest in Southern and Western Europe and Northern America and lowest in Middle and Western Africa and Central America. The highest mortality rate among men, in Lebanon (15.3 per 100,000), is 50% higher than the highest rates in Europe (10.3 in Latvia, 9.3 in Poland) and four times higher than that in the US (3.5).

Risk factors: Smoking is the most well-established risk factor for bladder cancer, with incidence about three to four times higher among smokers than nonsmokers.[182]

Figure 18. International Variation in Urinary Bladder Cancer Incidence Rates*, 2018

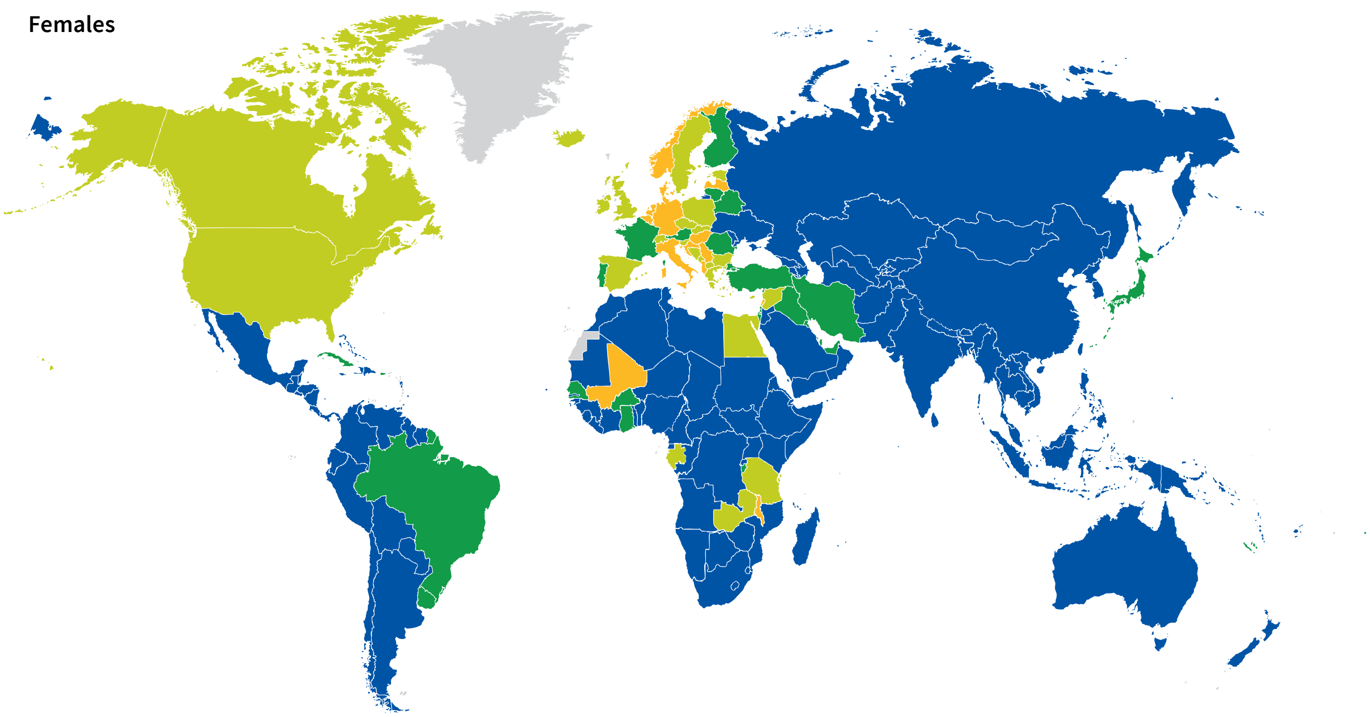
Males



Rate per 100,000 population

≥ 20.4
10.6-20.3
5.9-10.5
3.5-5.8
2.4-3.4
≤ 2.3
No data

Females



*Per 100,000, age standardized to the world standard population.

Source: GLOBOCAN 2018.

Smoking is estimated to cause about 31% of bladder cancer deaths among men and 16% among women worldwide,[113] but as much as 50% of deaths in countries like the US, where the tobacco epidemic began.[183] Risk is also increased among 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. In the developing world, particularly Africa and the Middle East, chronic infection with *Schistosoma haematobium* (a parasitic worm causing urogenital schistosomiasis) is associated with an increased risk of bladder cancer. This parasite, which is transmitted through contaminated water, is responsible for about 40% of bladder cancer cases in endemic areas of Africa and the Middle East and about 2% of cases worldwide.[2] Bladder cancers caused by schistosomiasis have a different histology (squamous cell carcinoma) compared with those associated with other risk factors (transitional cell carcinoma).

Global trends: Bladder cancer trends primarily reflect smoking patterns, in addition to changes in occupational or environmental exposures. However, incidence trends across countries are difficult to interpret because of differences in reporting of in situ tumors, which vary not only between countries, but also between registries within a country.[184] In Europe, incidence rates are declining in men and women in Northern and Western Europe, but increasing in some Southern and Eastern European and Baltic countries.[185] 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.[95] Incidence and mortality rates in Asia have been declining or stable in both sexes.[185] In Latin America and the Caribbean, mortality has been largely stable, although rates have increased in recent decades among men and women in Cuba and Brazil.[185] Improvements in treatment may contribute to decreasing mortality rates in high-income countries.[185]

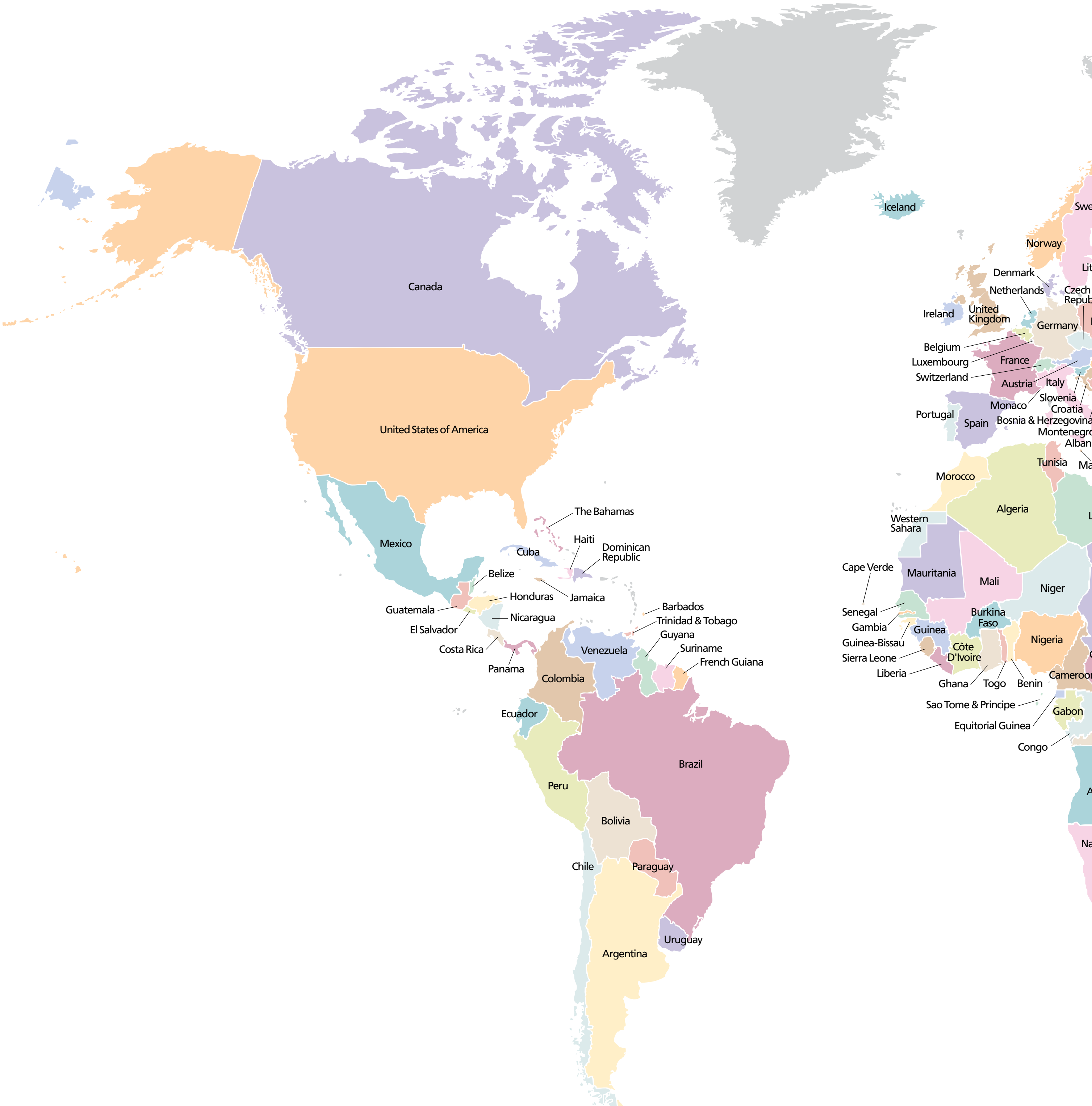
Signs and symptoms: In higher-resource countries, bladder cancer is usually detected early because of blood in the urine or other symptoms, including increased frequency or urgency of urination or pain or irritation during urination.

Prevention and early detection: Not smoking 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.[186] There is currently no screening method recommended for people at average risk. People at increased risk may be screened by examination of the bladder wall with a cystoscope (a slender tube fitted with a camera lens and light that is inserted through the urethra), microscopic examination of cells from urine or bladder tissue, or other tests.

Survival: Similar to incidence, comparisons of survival across countries is difficult because of variable representation of in situ tumors. For all stages combined, the 5-year relative survival rate in the United States is 78%.[95] Half of all bladder cancer patients in the United States are diagnosed before the tumor has spread beyond the layer of cells in which it developed (in situ), for which cases the 5-year survival rate is 96%.[95] In Europe, the overall 5-year relative survival rates (including in situ tumors where recorded) average 69% and range from 49% in Scotland to 79% in Malta.[184]

Uterine Cervix

New cases: Cervical cancer will be the second most commonly diagnosed cancer in women in low- and medium-HDI countries in 2018. There will be an estimated 569,800 new cases worldwide. The highest incidence rates will be in sub-Saharan Africa, Melanesia, Micronesia, and South-Eastern Asia, and the lowest will be in Western Asia, Australia and New Zealand, Northern America, and Western Europe (Figure 19). The large geographic variation in cervical cancer rates primarily reflects differences in the availability of screening, which can detect and allow for the removal of precancerous lesions, and to a lesser extent human papillomavirus (HPV) infection prevalence.[187, 188]


Canada
United States of America
Iceland
Norway
Denmark
Netherlands
Czech
Ireland
United Kingdom
Germany
Belgium
Luxembourg
France
Switzerland
Austria
Italy
Slovenia
Croatia
Monaco
Portugal
Spain
Bosnia & Herzegovina
Tunisia
Morocco
Algeria
Western Sahara
Mexico
The Bahamas
Haiti
Dominican Republic
Cuba
Belize
Jamaica
Honduras
Guatemala
Nicaragua
El Salvador
Costa Rica
Panama
Barbados
Trinidad & Tobago
Guyana
Suriname
French Guiana
Venezuela
Colombia
Ecuador
Brazil
Peru
Bolivia
Chile
Paraguay
Uruguay
Argentina
Cape Verde
Mauritania
Mali
Niger
Senegal
Gambia
Guinea-Bissau
Sierra Leone
Liberia
Guinea
Burkina Faso
Côte D'Ivoire
Nigeria
Ghana
Togo
Benin
Sao Tome & Principe
Gabon
Equitorial Guinea
Congo


Russia
Finland
Estonia
Latvia
Belarus
Slovakia
Hungary
Poland
Ukraine
Moldova
Romania
Serbia
Bulgaria
Georgia
Armenia
Azerbaijan
Kazakhstan
Uzbekistan
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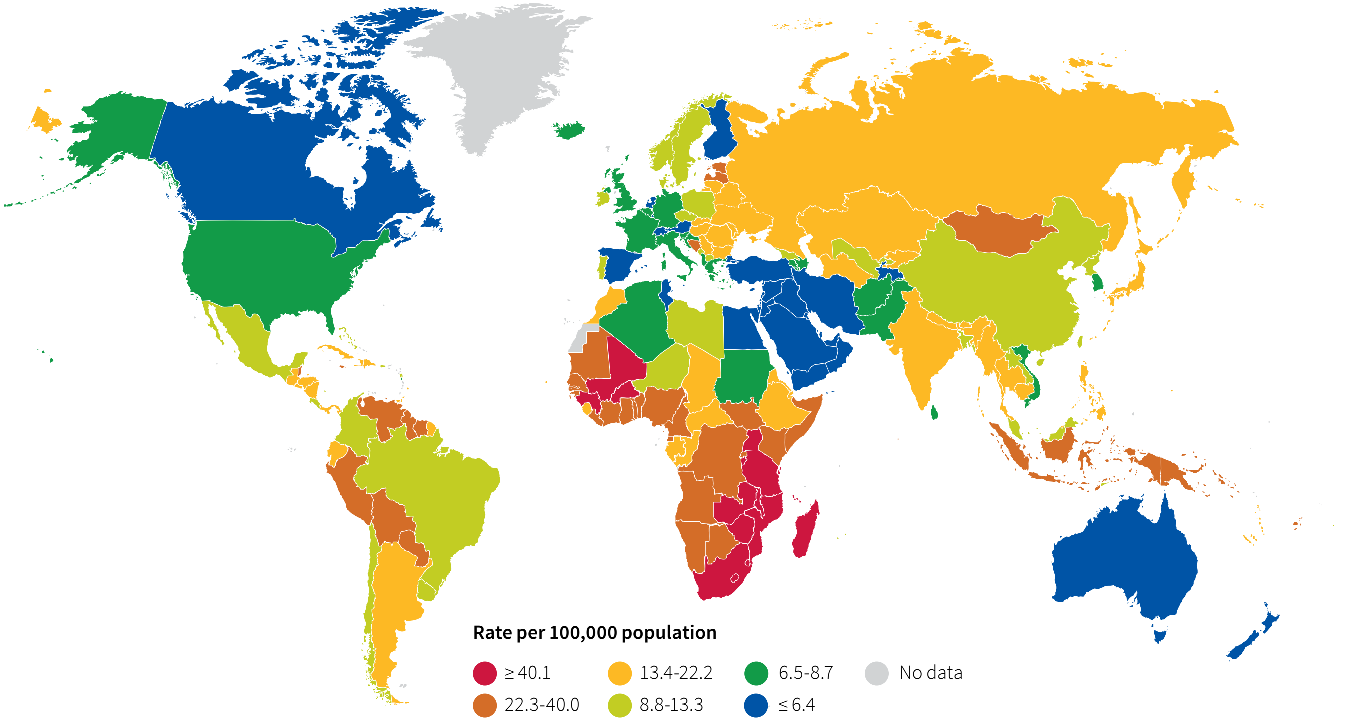
Egypt
Nepal
Bhutan
India
Bangladesh
Myanmar
Laos
Thailand
Vietnam
Cambodia
Taiwan
Philippines
Palau
Sri Lanka
Brunei
Malaysia
Singapore
Indonesia
Papua New
Guinea
Solomon
Islands
Timor-Leste
Samoa
Vanuatu
Fiji
Cook
Isands
New
Caledonia
Australia
New Zealand
Chad
Sudan
Eritrea
Djibouti
Somalia
Ethiopia
South
Sudan
Uganda
Kenya
Congo,
DR
Rwanda
Burundi
Tanzania
Seychelles
Comoros
Malawi
Zambia
Zimbabwe
Botswana
Mozambique
Madagascar
Mauritius
Swaziland
Lesotho
South
Africa

Figure 19. International Variation in Uterine Cervix Cancer Incidence Rates*, 2018



*Per 100,000, age standardized to the world standard population.
Source: GLOBOCAN 2018.

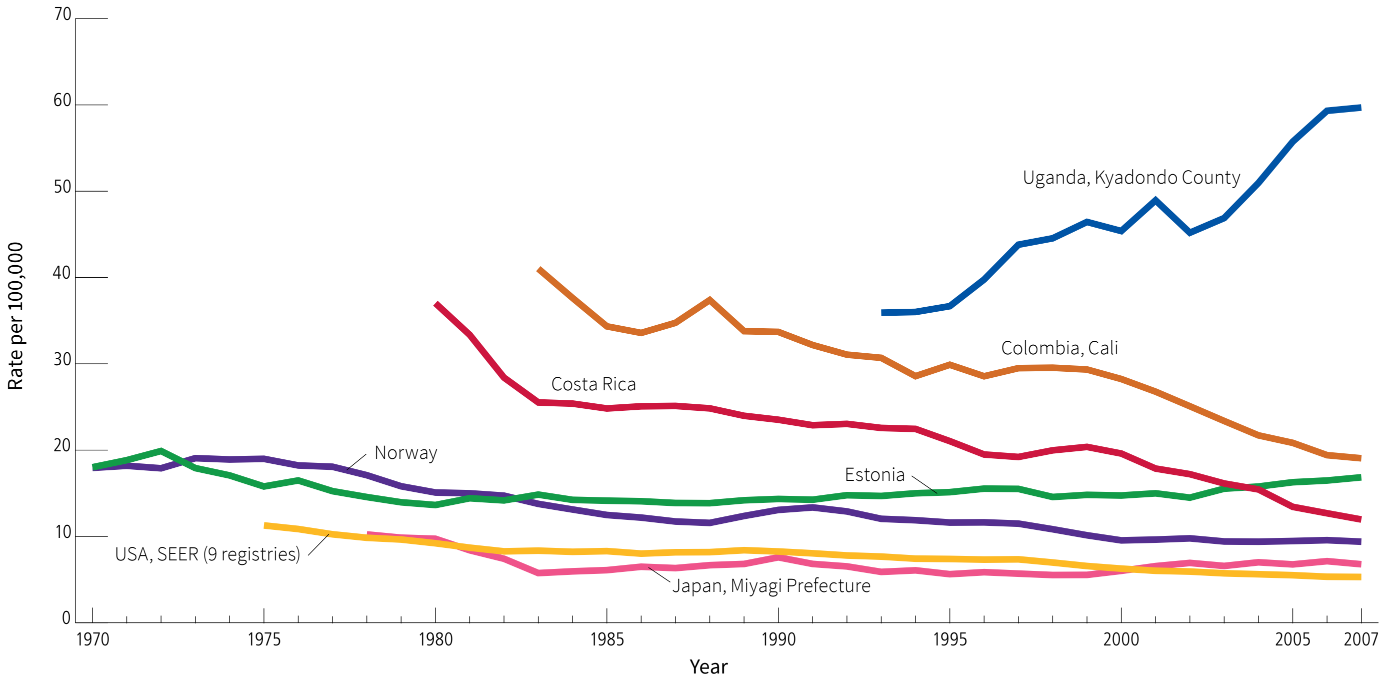
Deaths: Cervical cancer will be the fourth-leading cause of cancer death in women worldwide, with an estimated 311,400 deaths in 2018. However, it is the leading cause of cancer death in women in low-HDI countries (Figure 1). Nearly 70% of cervical cancer deaths will occur in South-Central Asia (75,100 deaths), Eastern Asia (54,500), and sub-Saharan Africa (76,400).[1] India, the second most populous country in the world, accounts for almost 20% (60,100) of cervical cancer deaths.

Risk factors: Almost all cervical cancers are caused by persistent infection with certain types of HPV, although these infections are common in healthy women and only rarely cause cancer. Although women who begin having sex at an early age or who have had many sexual partners are at increased risk for HPV infection and cervical cancer, HPV infection can occur with only one sexual contact. 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.[189] Factors that increase risk of both persistent HPV infection and progression to cancer include a suppressed immune system, a high number of childbirths, and cigarette smoking.[190] Long-term use of oral contraceptives is also associated with increased risk of cervical cancer that gradually declines after discontinuation.

Global trends: In several Western countries where screening programs have long been established, cervical cancer incidence rates have decreased by 50% or more over the past five decades (Figure 20).[191] For example, in Norway, cervical cancer incidence rates decreased from 21.1 per 100,000 in 1974 to 11.3 per 100,000 in 2015.[192] Incidence rates have also decreased in some high-incidence areas of Latin America and Asia with minimal screening activities.[188] This may be due to improved socioeconomic conditions and/or declining fertility.[188]

In contrast to favorable overall trends, cervical cancer rates appear to be rising in Uganda, Zimbabwe, and some countries of Eastern Europe (Estonia, Lithuania, and Bulgaria).[141, 142, 188, 193] Rates are also increasing among

Figure 20. Trends in Cervical Cancer Incidence Rates*, Select Countries, 1970-2007



*Per 100,000, age standardized to the world standard population. Rates have been smoothed using 3-year averages.
Source: WHO Cancer Mortality Database.

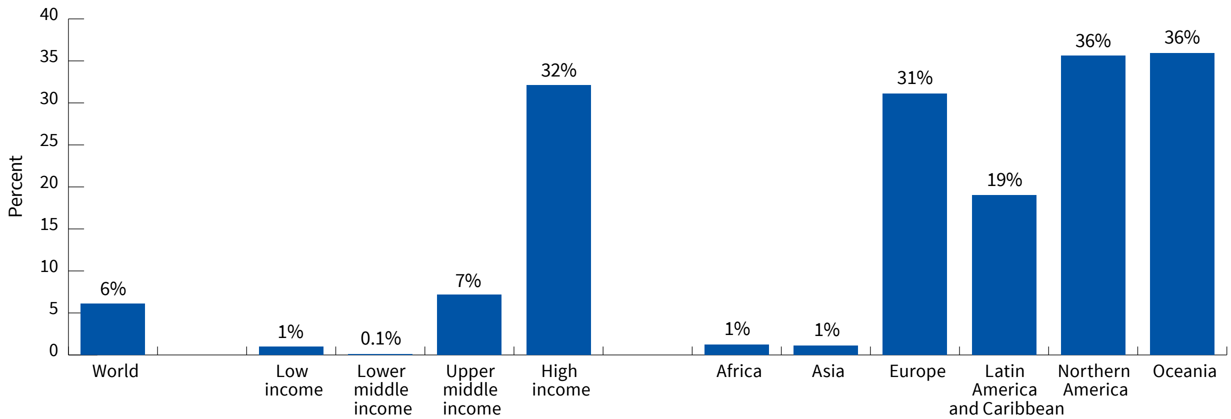
younger women in several countries in Europe, Central Asia, Japan, and China.[189, 194] These cohort-driven trends are thought to reflect increased prevalence of infection with high-risk HPV strains caused by changing sexual behaviors, in combination with inadequate screening; changing patterns of factors that contribute to progression of infection to cancer may have also played a role.[141, 142, 189, 194]

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

Prevention and early detection: Vaccines that protect against the types of HPV that cause 90% of cervical cancers, as well as several other cancers and diseases, are recommended by the WHO to be given to girls ages 9 to 13 as a priority target population.[195] While initial guidelines recommended three doses, the WHO now recommends two doses, which reduces the cost and can improve adherence.[196] Trials are underway to assess the efficacy of one dose.[197] Vaccination coverage is suboptimal in most countries. In 2014, about 6% of females ages 10 to 20 worldwide had received a full vaccine course, with wide variation by income level and world region (Figure 21).[198] There is also variation in vaccine coverage among countries of the same HDI level. 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 has supported HPV vaccination demonstration projects in more than 20 countries.[199] Rwanda has achieved greater than 98% coverage in the HPV vaccine target population due to government commitment, school-based delivery, and a strategy to reach out-of-school girls.[200]

Screening can also prevent cervical cancer through detection and treatment of precancerous lesions, as well as detecting cancer early, when it is more treatable. HPV-vaccinated women should still be screened for

Figure 21. Estimated Full-course Human Papillomavirus Vaccination Coverage (%) among Girls 10-20 Years, 2014



Source: Bruni L, Diaz M, Barrionuevo-Rosas L, et al. Global estimates of human papillomavirus vaccination coverage by region and income level: a pooled analysis. *Lancet Global Health*. 2016;4: e453-463.

cervical cancer because vaccines cannot protect against established infections, nor do they protect against all of the types of HPV that cause cervical cancer. There are several types of tests used for cervical cancer screening. 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, which detects HPV infections associated with cervical cancer, can forecast cervical cancer risk many years into the future. HPV tests can also identify women at risk for a type of cervical cancer (adenocarcinoma) that is often missed by Pap tests. In the United States and many other very high-HDI countries, the HPV test is recommended for use in conjunction with the Pap test, or when Pap test results are uncertain; a minority of very high-HDI countries recommend HPV testing as the primary screening method.[156]

Many low-resource countries do not have the technical and public health infrastructure to support Pap testing. Alternative screening techniques include visual inspection using acetic acid or Lugol's iodine, which are highly cost-effective, in addition to HPV tests. HPV tests are more consistently accurate, although their price and other infrastructure requirements make them inaccessible for many low-resource settings. A clinical trial in rural India found that a single round of HPV testing reduced the number of cervical cancer deaths by about 50%.[201, 202] A few studies have even shown promising results from using self-collection methods in low- and middle-income countries.[203-205] Despite successes with alternative screening methods, receipt of treatment following a positive test remains challenging; therefore, the WHO recommends "screen and treat" strategies, in which a woman with a positive screening test receives treatment in the same clinical encounter whenever possible.[206]

Survival: When detected at an early stage, invasive cervical cancer is one of the most successfully treated cancers. The 5-year net survival rate ranges from 49% in Colombia to 77% in South Korea and 78% in Costa Rica, although it is between 60% and 70% in most countries (Table 5).

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Special Section: The Obesity Epidemic

Introduction

Overweight and obesity, collectively referred to as "excess body weight," are the terms used to describe the accumulation of excess body fat that causes many chronic diseases and reduces life expectancy.[1] The proportion of the population that is overweight or obese has been increasing since the 1970s, and in 2016, approximately 40% of adults and 18% of children (ages 5-19 years) worldwide were overweight or obese, equating to almost 2 billion adults and 340 million children.[2] This trend is taking a toll on health; in 2015, an estimated 4 million deaths were attributable to excess body weight.[3] The economic impact of obesity-related illness is no less daunting, estimated at US $2.0 trillion globally in 2014.[4] Except for a possible plateau in high-income countries in recent years, the prevalence of excess body weight has increased in most countries across all population groups.[2] Some of the the steepest increases are in low- and middle-income countries, likely a result of the introduction of the "western lifestyle", consisting of energy-dense, nutrient-poor foods alongside reduced physical activity levels.[5]

A sizable body of evidence shows that excess body weight is associated with risks of developing many types of cancers: breast (postmenopausal), colorectum, corpus uteri (endometrium), esophagus (adenocarcinoma), gallbladder, kidney, liver, meningioma (cancer in the tissue covering the brain and spinal cord), multiple myeloma (cancer of plasma cells), ovary, pancreas, prostate (advanced stage), stomach (cardia), thyroid, oral cavity, pharynx, and larynx.[6, 7] The global cancer burden associated with overweight and obesity was estimated at 544,300 cases in 2012.[8] This number will undoubtedly rise in the coming decades, given the continuing increase in the size of the overweight and obese population.[8]

This special section presents global and regional patterns in excess body weight, drivers of the epidemic, and the attributable cancer burden. Core policy actions to prevent and control excess body weight are also discussed.

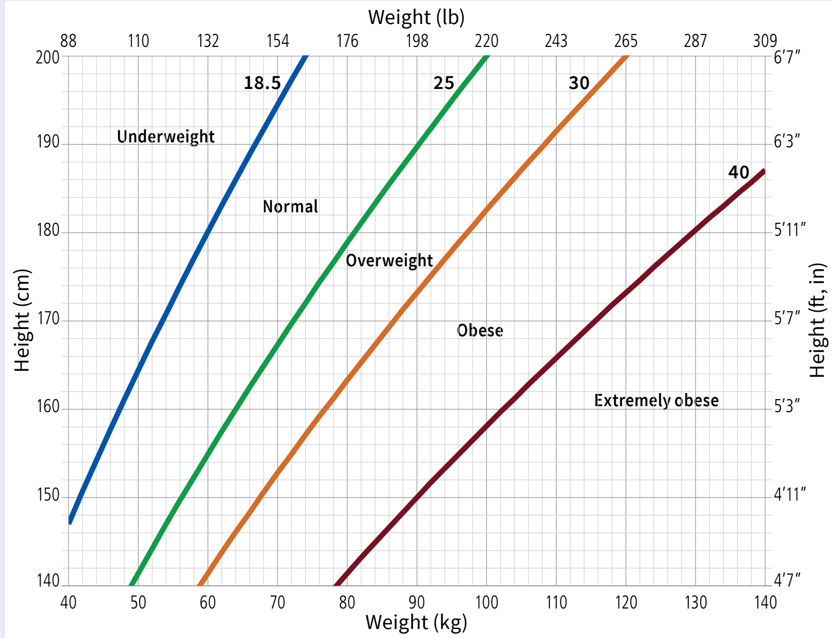
Defining Excess Body Weight

Body mass index (BMI), defined as body mass in kilograms divided by the square of height in meters (kg/m^2), is the most commonly used measure to approximate overall body fatness for the purposes of classifying and reporting overweight and obesity.[9] The World Health Organization (WHO) classifies adults with a BMI below 18.5 as "underweight." and between 18.5 and 24.9 as "normal."[1] Above the normal range, there are conventional gradings for "overweight" ($25 \le BMI < 30$) and "obese" ($BMI \ge 30$). BMI is a useful measure because it is relatively simple to calculate and is strongly associated with direct measures of body fatness (e.g., bone density scanning) and other metabolic indicators, such as triglycerides, total cholesterol, blood pressure, and fasting glucose levels.[10] However, BMI is an indirect measure of body fat and does not differentiate between fat and lean mass or specify the location of fat tissue, which varies among individuals and by age, sex, and ethnicity.[9] For example, WHO expert panel concluded that a substantial proportion of Asian people with "normal" BMI are at increased risk for type 2 diabetes and cardiovascular disease.[11] Other measurements that reflect the distribution of body fat – that is, whether more fat is carried around the hips or the abdomen – are increasingly being used along with BMI as indicators of disease risks. These measurements include waist circumference and the waist-to-hip ratio (the waist circumference divided by the hip circumference), both of which approximate abdominal (also called "central") obesity.

Among children, overweight and obesity are defined not by absolute BMI cut-points, but relative to a historical healthy-weight group.[1, 12] The WHO provides different sets of standards for school-age children (ages 5-19 years) and children under 5 years of age, and its reference populations and definitions of overweight and obesity differ from those used by the International Obesity Task Force (IOTF) and the United States (US) Centers for Disease Control and Prevention (CDC).[13] Studies comparing the different definitions have found that the WHO classification produces slightly higher estimates of overweight and obesity prevalence than those of the IOTF

Height, Weight, and Body Mass Index (BMI) Chart for Adults

Body mass index is a simple measure used to classify underweight, normal, overweight, and obesity. It is calculated by dividing a person's weight (in kilograms) by their height (in meters) squared (commonly expressed as kg/m^2). BMI provides a more accurate measure of obesity than weight alone, and for most people it is a good (although indirect) indicator of body fatness. However, it is not possible to specify a single BMI goal that applies to all persons because of individual differences in both the proportion of lean-to-fat mass and the distribution of fat. It is recommended that people aim to keep their BMI as low as possible within in the normal range of BMI (18.5≤BMI<25).



and the CDC, indicating a need to harmonize these standards.[14-16] In this section, data are presented from the Non-communicable Disease Risk Factor Collaboration, which uses the WHO standard.[2]

Prevalence and Trends in Excess Body Weight

Between 1975 and 2016, the global age-standardized mean BMI of adults increased from 21.7 kg/m^2 to 24.5 kg/m^2 for men and from 22.1kg/m^2 to 24.8 kg/m^2 for women.[2] During the same period, the global age-standardized prevalence of excess body weight (BMI≥25) nearly doubled among adults 20 years of age and older, from 21% in men and 24% in women in 1975 to approximately 40% in 2016 in both sexes (Figure S1). Notably, the prevalence of obesity (BMI≥30) quadrupled in men, from about 3% to 12%, and more than doubled in women, from 7% to 16%. These changes, along with population growth, resulted in a more than 6-fold increase in the number of obese adults worldwide, from 100 million in 1975 to 671 million in 2016. During the same period, the age-standardized mean BMI among children ages 5-19 years increased from 16.8 kg/m^2 to 18.5 kg/m^2 for boys and from 17.2 kg/m^2 to 18.6 kg/m^2 for girls. The prevalence of excess body weight increased from 5% to 27% in boys and from 6% to 24% in girls, with a greater relative increase in obesity prevalence, from 0.9% to 8% in boys and from 0.7% to 6% in girls.

International variation and regional trends

The increasing prevalence of obesity (BMI≥30) is apparent across all 9 world regions to varying degrees, beginning in the 1970s and 1980s in most high-income Western countries and somewhat later in low- and middle-income countries (Figure S2).[2] Between 1995 and 2016, the largest absolute increase occurred among men in high-income Western countries (from 9% to 30%) and among women in Central Asia, the Middle East, and North Africa (from 12% to 35%). The smallest absolute increase was among men in South Asia (from 0.2% to 3%) and among women in high-income Asian Pacific countries (from 1% to 4%). The largest relative increases were in historically low-risk regions. For example, there was more than a 20-fold increase in East and South-Eastern Asia, from 0.3% to 6% in men; about a 10-fold increase among men in sub-Saharan Africa, from 0.5% to 5%; and a 5-fold increase among women in sub-Saharan Africa, from 3% to 15%.

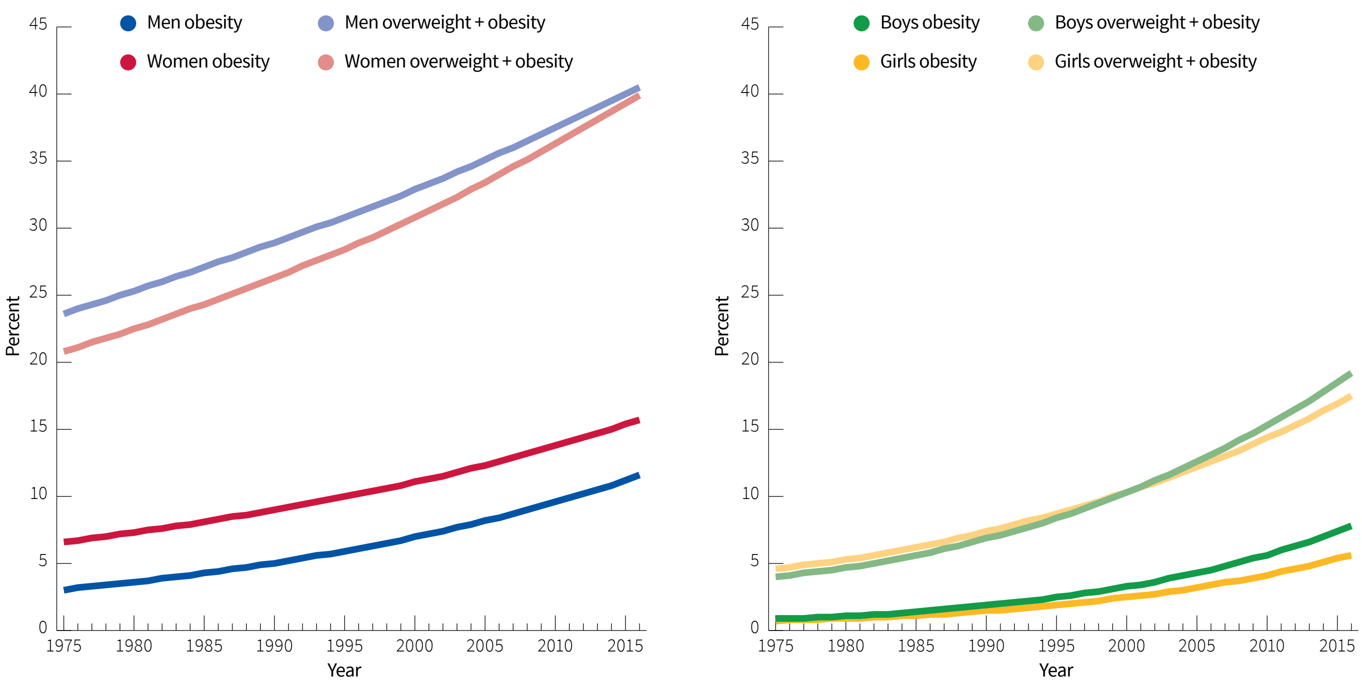
Similar regional patterns occurred among children ages 5-19 years, with the largest absolute increase in obesity among boys in high-income Western countries, from 4%

in 1975 to 17% in 2016, and among girls in Central Asia, the Middle East, and North Africa, from 0.9% to 11% (Figure S2). Additional regions with absolute increases greater than 10% were East and South-Eastern Asia (boys), Latin America and the Caribbean (boys), and Central Asia, the Middle East, and North Africa (boys and girls). The largest relative increases, however, occurred in South Asia from 0.05% to 3% among boys and from 0.01% to 2% among girls; East and South-Eastern Asia from 0.2% to 12% among boys and from 0.07% to 6% among girls; and sub-Saharan Africa from 0.04% to 2% among boys and 0.07% to 3% among girls.

Between 1975 and 2016, there was more than a 9-fold increase in the number of obese men (from 30.7 million to 281 million), and more than a 5-fold increase in obese women (from 69.3 million to 390 million) (Figure S3). The global burden of obesity (number of obese people) also shifted from predominantly high-income Western countries and Central and Eastern Europe in 1975 to more diverse regions in 2016. Most notably, East and South-Eastern Asia accounted for 3% of the world's obese men and women in 1975 but 15%-17% in 2016, reflecting population growth and extended longevity, as well as increased obesity prevalence. Increases were also substantial in South Asia (from 1% to 6% in men and 2% to 8% in women); sub-Saharan Africa (from 1% to 4% in men and 3% to 8% in women); and Central Asia, the Middle East, and North Africa in men (from 7% to 14%). Nevertheless, high-income Western countries remained the largest contributor to the global obesity burden in 2016 both among men (33%) and women (26%).

Among men, obesity prevalence in 2016 was highest in Polynesian countries (41%-60%) and the US, Canada, Kuwait, Qatar, Saudi Arabia, Australia, and New Zealand (31%-37%), and lowest in most of sub-Saharan Africa (e.g., Uganda, 2%) and South-Eastern Asia (e.g., Vietnam, 2%) (Figure S4). Among women, prevalence was highest in Polynesian countries (52%-65%), South Africa, Puerto Rico, Bermuda, and several Middle Eastern countries (all countries, 40%-50%), and lowest in parts of sub-Saharan Africa (e.g., Ethiopia, 7%), most countries in South-Eastern Asia (e.g., Vietnam, 3%), and Japan (4%). The

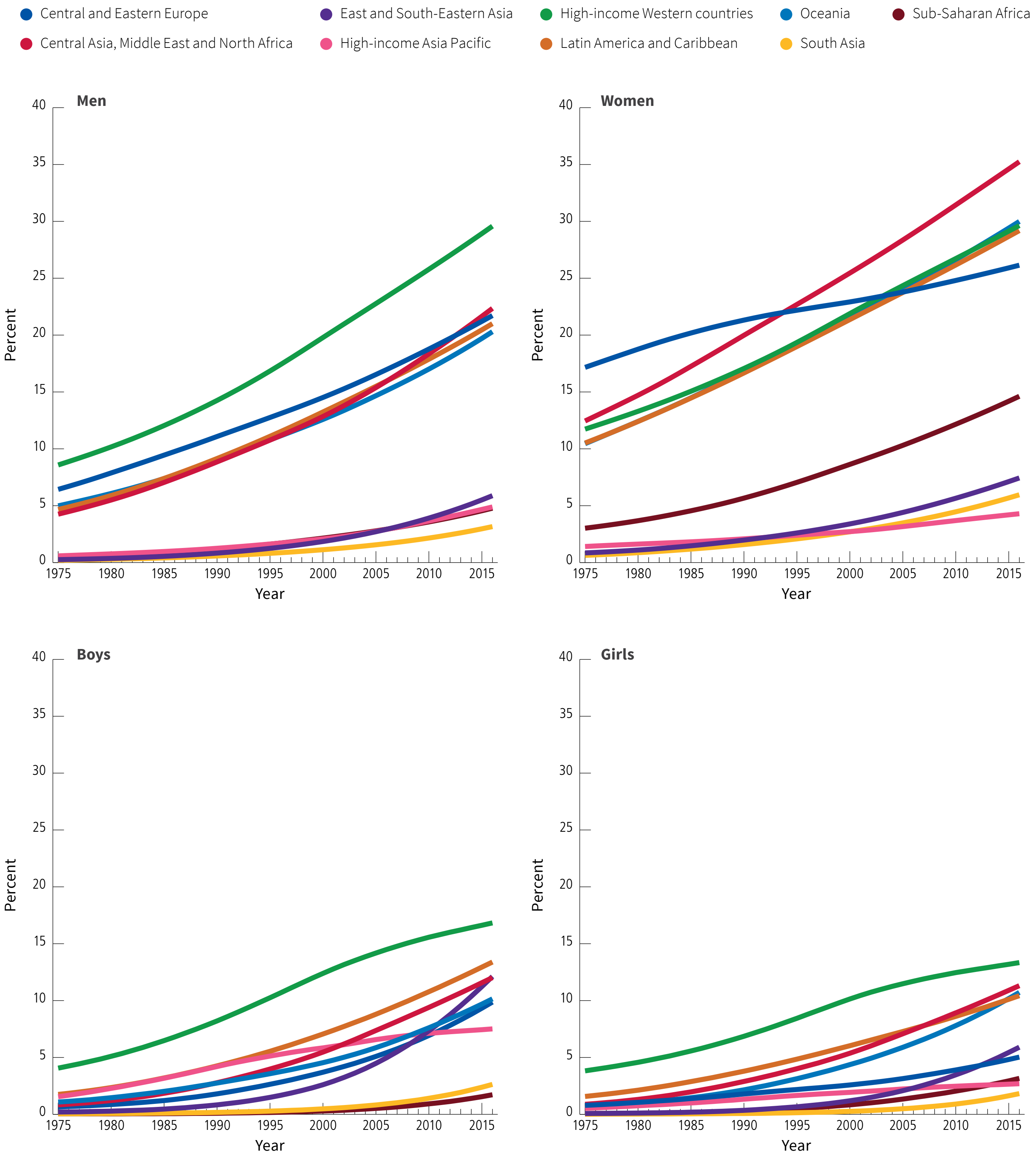
Figure S1. Trends in the Prevalence (%) of Excess Body Weight among Adults and Children by Sex, 1975-2016



Among adults (age ≥20 years), overweight was defined as BMI≥25; obesity was defined as BMI≥30. Among youth (age 5-19 years), overweight was defined as more than 1 standard deviation (SD) above the median of the WHO growth reference; obesity was defined as more than 2 SD above the median.

Source: http://ncdrisc.org/obesity-prevalence-map.html.

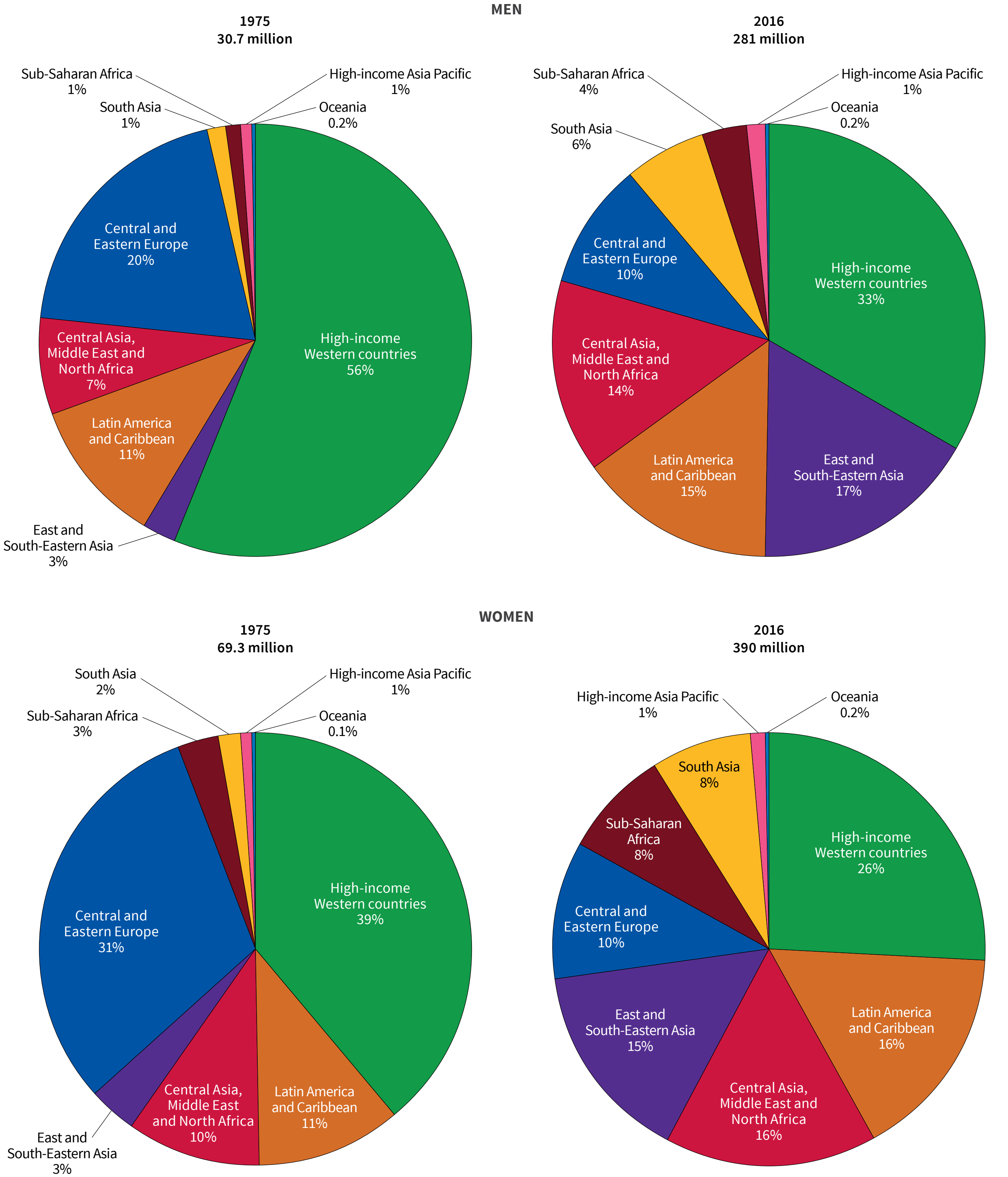
Figure S2. Regional Trends in the Prevalence of Obesity* among Adults and Children by Sex, 1975-2016



*Among adults (age ≥20 years), obesity was defined as BMI≥30. Among children (age 5-19 years), obesity was defined as more than 2 standard deviations (SD) above the median of the WHO growth reference.

Source: http://ncdrisc.org/obesity-prevalence-map.html.

Figure S3. Regional Contribution to the Global Obesity* Burden among Adults by Sex in 1975 and 2016



*Obesity was defined as BMI≥30.

Source: http://ncdrisc.org/obesity-prevalence-map.html.

lowest obesity prevalence among high-income Western countries was in Switzerland for women (18%), boys (7%), and girls (5%), and in Italy for men (21%). In sub-Saharan Africa, the highest prevalence was in South Africa for women (41%), men (16%), and girls (13%), and in Seychelles for boys (11%).

Key Drivers of the Global Increase in Excess Body Weight

The pace of the rise in excess body weight differs across and within populations because of complex interrelated factors that influence body weight. Changes in the availability and quality of foods during the past 3-4 decades are generally accepted as key environmental drivers of the obesity epidemic.[17, 18] Between 1980 and 2013, global energy availability (i.e., food calories based on national food supply data adjusted for waste and assumed to be proportional to energy consumption) increased from 2,390 to 2,710 kcal per person per day.[19] Changes in the food environment that have promoted overconsumption of calories include rapid increases in both food portion size and the supply of affordable, palatable, energy-dense, ready-to-eat food; widespread use of sweetening agents, such as high-fructose corn syrup,[20] and the consumption of sugar-sweetened beverages;[21] improved distribution systems to make unhealthy food much more accessible and convenient; and more pervasive food marketing strategies consisting of abundant cues to overconsume palatable foods.[20-22]

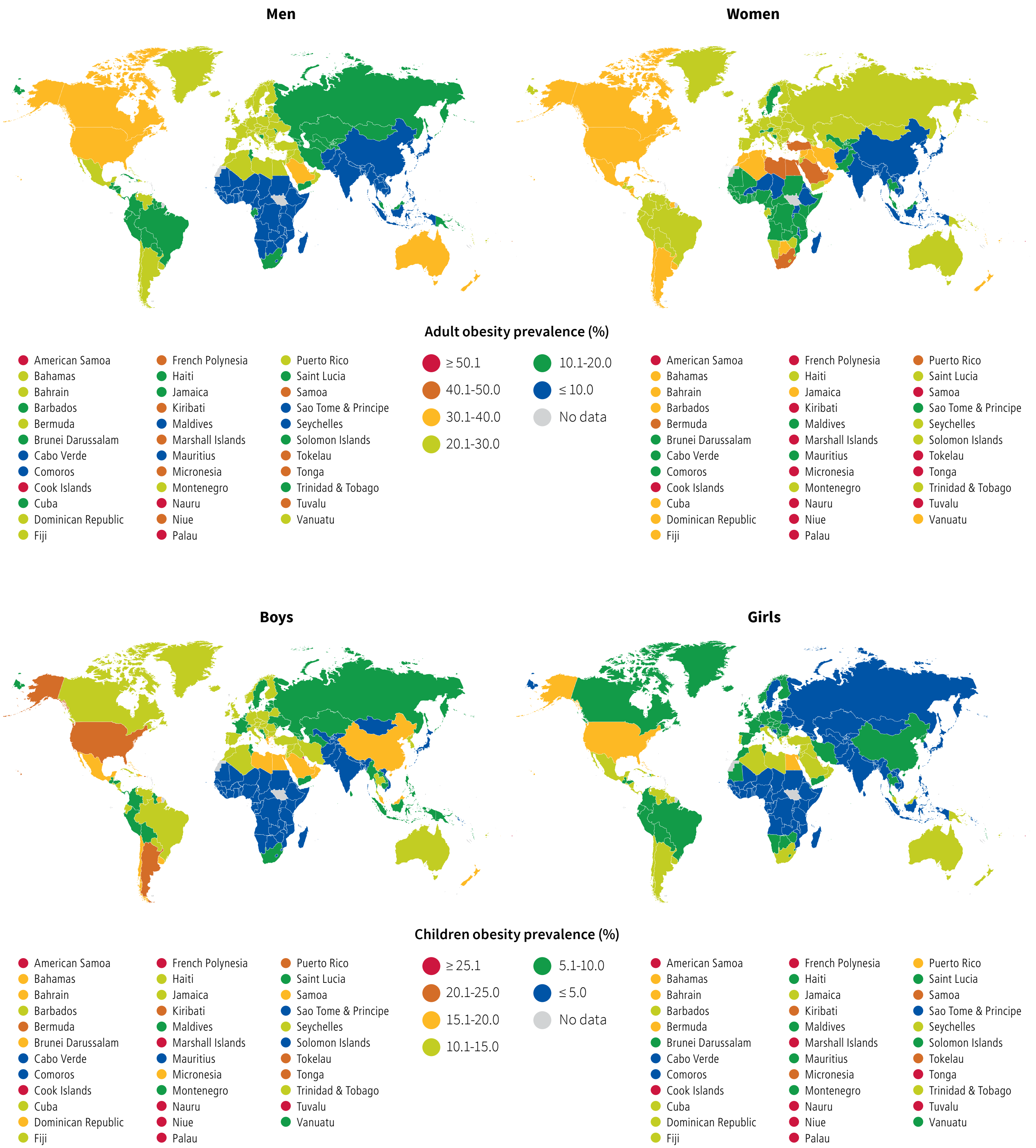
The increasingly sedentary nature of many forms of work and leisure-time activities (e.g., increased screen time), the change from active modes of transportation (e.g., walking, cycling) to motorized vehicles, and urbanization generally have contributed to a pervasive global phenomenon of physical inactivity.[23] Reduced physical activity at a population level contributes to reduced energy expenditure and caloric imbalance. For example, in China, alongside a change in dietary intake, the overall shift in physical activity was shown to be a contributor of long-term increases in weight gain and obesity.[24]

Environmental factors that moderate the effects of this general change in energy input and output include socioeconomic status, sociocultural environment, and transportation systems.[17] Excess body weight is most prevalent in individuals from wealthy, urban environments in low-income countries and among disadvantaged groups (i.e., those with lower income and less education) in high-income countries.[25-27] Socioeconomic disparities in excess body weight are more striking among women than among men in many countries.[28, 29] Increased body weight among women during pregnancy contributes to the health risks in their children and amplifies health inequities across generations.[30] Among women living in some Middle Eastern countries, limited access to sports and exercise activities due to cultural and traditional restrictions may contribute to their high prevalence of excess body weight.[31]

Cultural body-size preferences are thought to be related to obesity in some countries. Increased food access and reduced physical activity may have a stronger influence in countries where large body size is associated with positive attributes,[32-34] compared with countries where small body size is valued.[17] However, the obesity epidemic may be shifting societal norms. In the US, the percentage of overweight (but not obese) individuals who described their weight as "about right" increased significantly between the early 1990s and the early 2010s, suggesting changes in perceptions about healthy body size.[35] Considerably lower obesity rates in high-income Asian Pacific countries may be related in part to strong weight bias and stereotype of a thin ideal for beauty.[36-38]

Neighborhood built environments and transportation systems influence opportunities for physical activity,[39] and thus consequently body weight. Road connectivity, proximity to local destinations, and the presence of paths for walking and bicycling are important for active transportation alongside policies and social norms conducive to an active lifestyle. An international study showed that adults in the most activity-supportive environments were twice as likely to meet physical activity guidelines as those in the least-supportive neighborhoods.[40] In countries where the default option (i.e., "path of least resistance") and the social norm are active transport, the levels of transportation-related physical activity are very high.[41-43] The high prevalence of active transport (cycling) in the Netherlands likely contributes to the country's relatively low obesity.[17]

Figure S4. International Variation in the Prevalence of Obesity* among Adults and Children by Sex, 2016



*Among adults (age ≥20 years), obesity was defined as BMI ≥30. Among children (age 5-19 years), obesity was defined as more than 2 SD above the median of the WHO growth reference.

Source: Worldwide trends in body mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2,416 population-based measurement studies in 128.9 million children, adolescents, and adults. *Lancet* 2017, published online October 2017.

Denmark and Germany also have specific policies put in place to make cycling safe and convenient.[44]

Genetic makeup also influences body weight, and some populations may have increased genetic susceptibility to obesity.[45] For example, a population-specific genetic variant that may predispose to increased body weight was found among Samoans (65% of women and 59% of men are obese).[46, 47] Nevertheless, the population gene pools are relatively constant for many generations and unlikely to play a large role in the dramatic change in body weight that has occurred over the past 30-40 years.

Cancers Attributable to Excess Body Weight

Substantial evidence supports causal links between excess body weight and many types of cancer. The International Agency for Research on Cancer Report in 2016 concluded that there is sufficient evidence for a causal association between excess body weight and the risk of cancers of the breast (postmenopausal), colorectum, corpus uteri (endometrium), esophagus (adenocarcinoma), gallbladder, kidney, liver, meningioma, multiple myeloma, ovary, pancreas, stomach (cardia), and thyroid.[7] Additionally, the most recent World Cancer Research Fund and American Institute for Cancer Research Expert Report included advanced prostate cancer and cancers of the oral cavity, pharynx, and larynx as cancers with probable evidence.[6] The association between cancer and body weight is often expressed in terms of relative risk per 5kg/m^2 excess BMI. This corresponds to weight gains of about 15kg (or 33 pounds) in a person with 173cm (about 68 inches) height and 13kg (or 28.6 pounds) in a person with 161cm (about 63 inches) height. Although the strength (relative risk) of the association is modest for most cancers (Table S1), the high prevalence of excess body weight leads to a substantial burden of cancers.

The following section describes the results from a study that quantified the numbers and percentages of cancer cases in 2012 attributable to excess body weight (BMI≥25) in 2002, assuming 10-year lag time between exposure and cancer development.[8] The estimates incorporate the prevalence of excess body weight and the relative risk of the association between BMI and cancer risk.

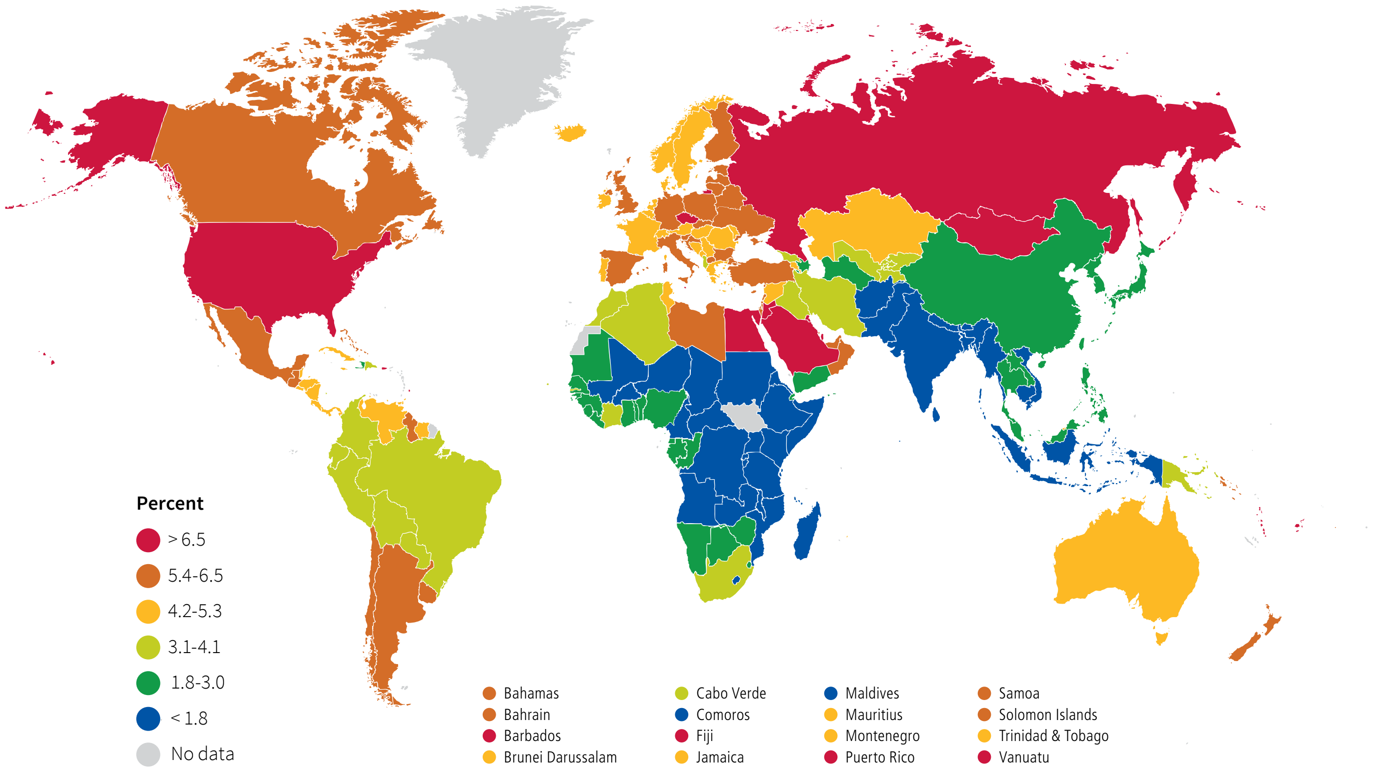
Table S1. Relative Risk of Each Cancer Associated with 5-unit Increase in Body Mass Index

	Relative risk* (95% CI)
Breast (postmenopausal)[6,7]	1.12 (1.09-1.15)
Colon and rectum[6,7]	1.05 (1.03-1.07)
Corpus uteri (endometrium)[6,7]	1.50 (1.42-1.59)
Esophageal adenocarcinoma[6,7]	1.48 (1.35-1.62)
Gallbladder[6,7]	1.25 (1.15-1.37)
Kidney[6,7]	1.30 (1.25-1.35)
Liver[6,7]	1.30 (1.16-1.46)
Meningioma[7†]	1.54 (1.32-1.79)‡
Oral cavity, pharynx, and larynx[6†]	1.15 (1.06-1.24)§
Multiple Myeloma[7†]	1.12 (1.07-1.18)
Ovary[6,7]	1.06 (1.02-1.11)
Pancreas[6,7]	1.10 (1.07-1.14)
Prostate (advanced)[6†]	1.08 (1.04-1.21)
Stomach Cardia[6,7]	1.23 (1.07-1.40)
Thyroid[7†]	1.06 (1.02-1.10)

BMI, body mass index; CI, confidence interval. *Relative risk for BMI is shown as an incremental cancer risk associated with every 5-unit increase in BMI; that is, risk among individuals with 5-unit higher BMI relative to risk among individuals with any given BMI. †Cancers determined to be causally related to body fatness by either IARC or WCRF/AICR, but not by both organizations. ‡Risk for persons with obesity (BMI≥30) relative to persons with normal weight (18.5≤BMI<25).[68] §Among non-smokers.

Overall 544,300 cancer cases worldwide in 2012 were estimated to be attributable to excess body weight, which represented approximately 4% of all cancer cases and ranged from 0.4% to 8% across countries (Figure S5).[8] The countries with more than 7% of the cancer burden due to excess body weight are Egypt, Mongolia, Puerto Rico, Saudi Arabia, Russia, Fiji, and the Czech Republic. Countries with less than 1% include Ethiopia, India, Uganda, Bangladesh, Malawi, and 10 more countries, all in sub-Saharan Africa, South Asia, South-Eastern Asia. It is important to note that these fractions likely underestimate the actual cancer burden associated with excess body weight for several reasons, including the inability to account for the cumulative effect of body fatness over a lifetime or the influence of related factors, such as smoking, and the use of BMI instead of direct measurement of fat mass.[48, 49]

Figure S5. International Variation in the Proportion (%) of Cancer Cases Attributable to Excess Body Weight, 2012



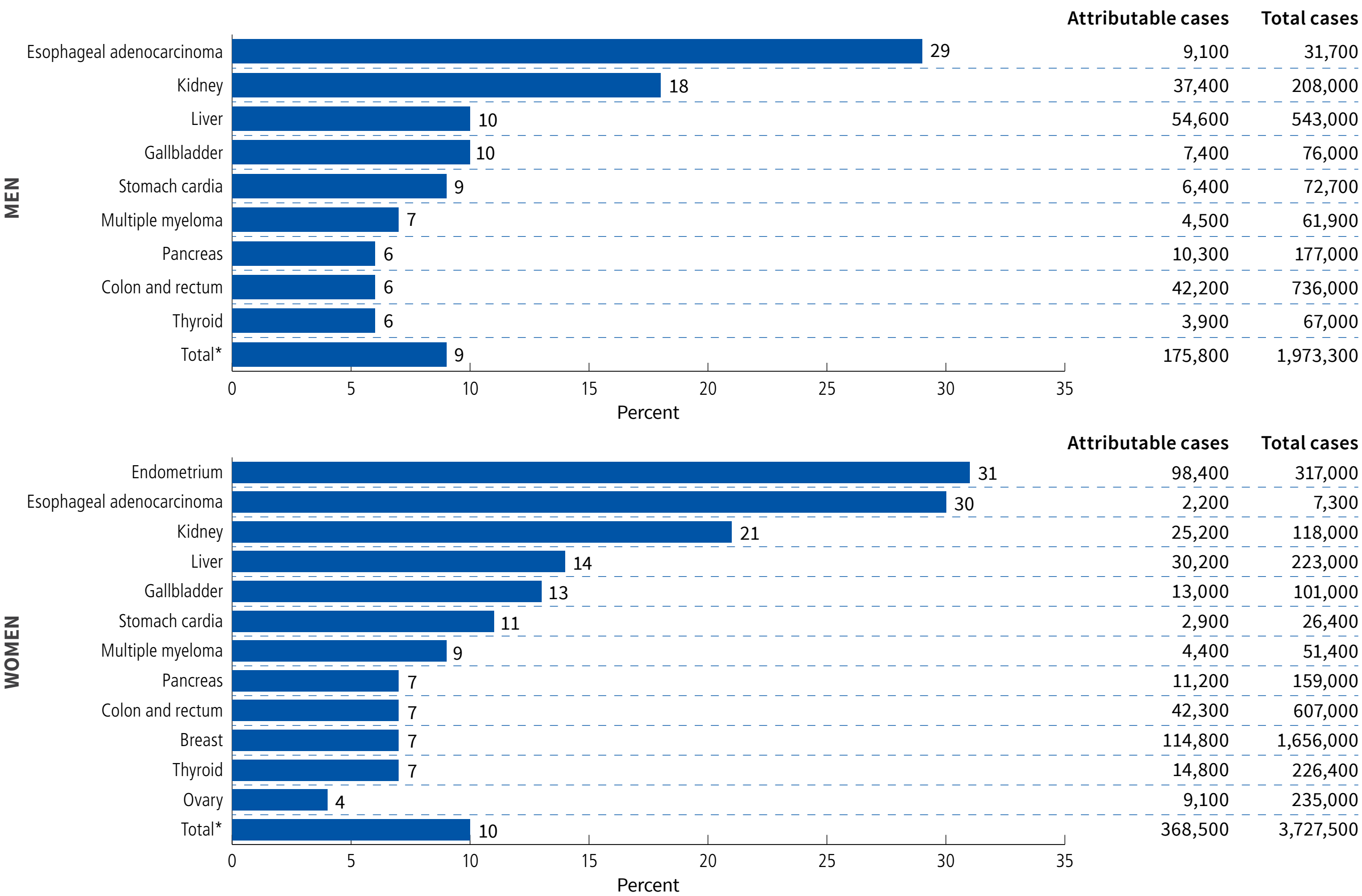
Source: Unpubished data from Pearson-Stuttard J, Zhou B, Kontis V, Bentham J, Gunter MJ, Ezzati M. Worldwide burden of cancer attributable to diabetes and high body mass index: a comparative risk assessment. *Lancet Diabetes Endocrinol.* 2018;6(6):e6-e15.

The percentage of cases attributable to excess body weight differs substantially by cancer type based on the strength of the relationship. For example, among women, excess body weight accounted for about one-third of endometrial cancers (98,400 out of 317,000 cases) and esophageal adenocarcinomas (2,200 cases out of 7,300 cases), compared with only 4% of ovarian cancers (9,100 cases out of 235,000 cases; Figure S6). Among men, about 29% of esophageal adenocarcinoma cases were attributable to excess body weight compared with about 6% of cancers of the pancreas, colorectum, or thyroid.

The total number of cancer cases attributable to excess body weight was more than twice as high in women (368,500 cases) as in men (175,800 cases) (Figure S7). Breast cancer is the largest contributor (114,800 cases; 31%) among women followed by endometrial cancer (98,400 cases; 27%) and colorectal cancer (42,300 cases; 12%). In contrast, the largest contributor among men was liver cancer (54,600 cases; 31%), followed by colorectal cancer (42,200 cases; 24%), and kidney cancer (37,400 cases; 21%).

Figure S8 shows regional contributions to the worldwide cancer burden due to excess body weight. Almost half of cancer cases attributable to excess body weight occurred in high-income Western countries (252,500 cases; 46%), reflecting both a higher prevalence of excess body weight and higher incidence rates for many obesity-related cancers. Despite a relatively low prevalence of excess body weight, the East and South-Eastern Asia region had the second-largest share (87,600 cases or 16%) due to its large population and disproportionately higher burden of liver cancer. Central and Eastern Europe had the third-largest share (77,700 cases or 14%), followed by Latin America and the Caribbean (9%), and Central Asia, the Middle East, and North Africa (6%).

Figure S6. Cancer Burden Attributable to Excess Body Weight by Sex and Cancer Type, 2012



*Total percentage is calculated among the excess body weight-related cancers in the figure, not among all cancers.

Source: Pearson-Stuttard J, Zhou B, Kontis V, Bentham J, Gunter MJ, Ezzati M. Worldwide burden of cancer attributable to diabetes and high body-mass index: a comparative risk assessment. *Lancet Diabetes Endocrinol*. 2018;6(6):e6-e15.

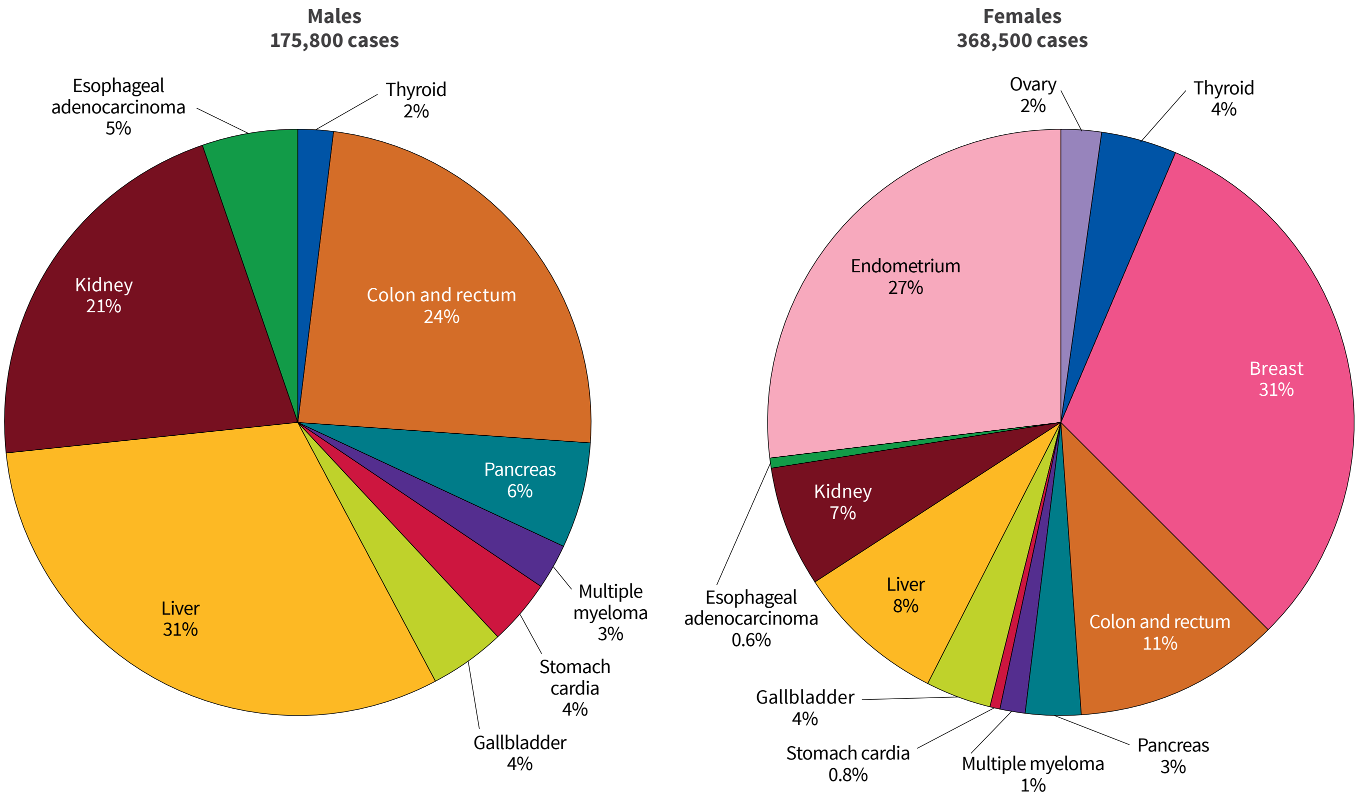
Each region has a considerably different composition of cancer types contributing to the burden associated with excess body weight (Figure S8). Female breast cancer is the top contributor in 5 out of 9 regions including South Asia (30%); sub-Saharan Africa (30%); Latin America and the Caribbean (26%); high-income Western countries (25%); and Central Asia, the Middle East, and North Africa (23%), whereas liver cancer contributed most in East and South-Eastern Asia (42%), Oceania (30%), and high-income Asia Pacific (22%). The contribution of female-specific cancers (e.g., breast, endometrium, and ovary) was particularly high in Oceania (50%), sub-Saharan Africa (53%), and South Asia (51%) and was lowest in high-income Asia Pacific (22%) and East and South-Eastern Asia (26%).

Cancers for Which Evidence Is Sufficient

Breast (Postmenopausal)

About 7% of all postmenopausal (≥50 years) breast cancers (114,800 cases) in 2012 were attributable to excess body weight (Figure S6). Each 5-unit increase in BMI is associated with a 12% increased risk of postmenopausal breast cancer overall that is stronger for Asians (37%) compared to North Americans and Europeans (10%).[6] The increased risk has been consistently shown among women who had never or previously used menopausal hormone therapy (MHT), but not among women who are current users.[6] The associations were significant for hormone receptor positive tumors but inconclusive

Figure S7. Contribution of Each Cancer to the Total Cancer Burden Attributable to Excess Body Weight by Sex, 2012



Source: Pearson-Stuttard J, Zhou B, Kontis V, Bentham J, Gunter MJ, Ezzati M. Worldwide burden of cancer attributable to diabetes and high body-mass index: a comparative risk assessment. *Lancet Diabetes Endocrinol.* 2018;6(6):e6-e15

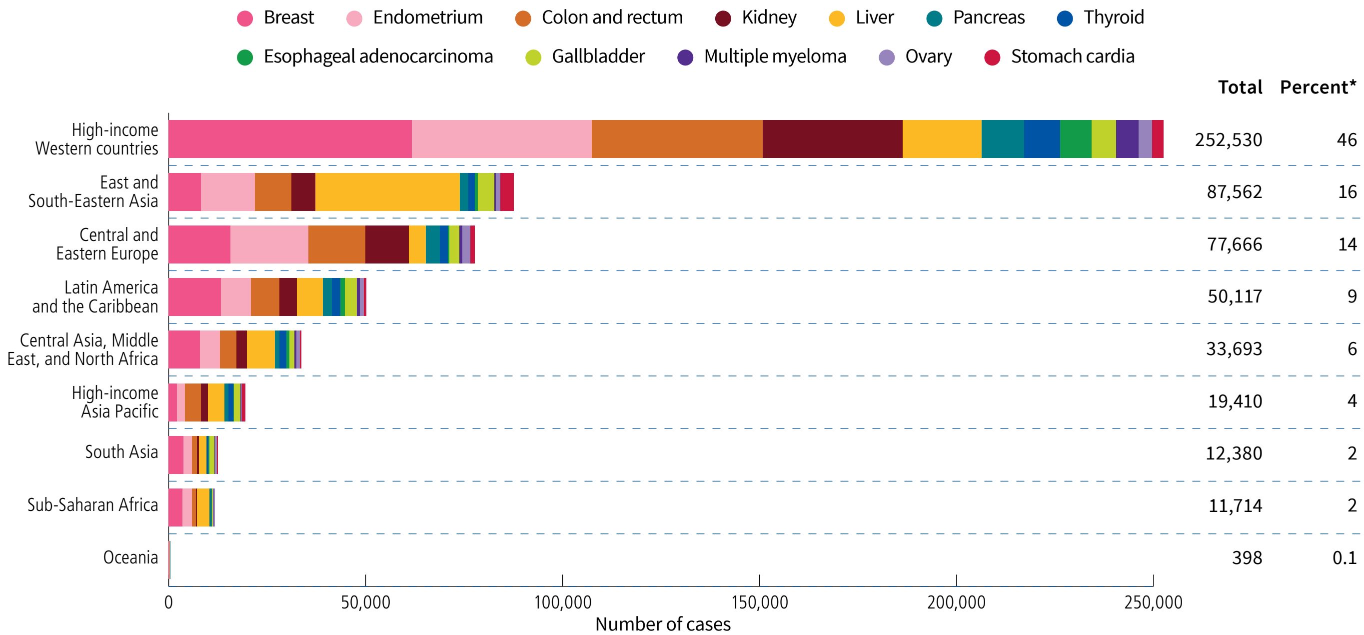
among hormone receptor negative tumors.[50] Central obesity measured by waist circumference is associated with a 6% increased risk of postmenopausal breast cancer (per excess 10 cm).[6] Adult weight gain is also associated with increased risk. In a study following women for up to 40 years, long-term weight gain of 20 kg (about 44 pounds) or more from age 18 is associated with a 37% increased risk of postmenopausal breast cancer compared to stable weight.[51]

In contrast, BMI is inversely associated with risk of breast cancer among premenopausal women.[52,53] A recent analysis including 19 prospective studies showed a 23% and 12% per 5-unit increase in BMI decreased risk of breast cancer at ages 18-24 years and 45-54 years, respectively.[57] This association may differ by race; studies conducted among Asian populations have reported that higher BMI is associated with increased risk of both pre- and postmenopausal breast cancer.[54,55]

Colon and Rectum

Seven percent of colorectal cancers in women (42,300 cases) and 6% in men (42,200 cases) worldwide in 2012 were attributable to excess body weight (Figure S6). Each 5-unit increase in BMI is associated with a 5% increased risk of colorectal cancer.[6] The association appears stronger for men (8% per 5-unit increase in BMI) than for women (5% per 5-unit increase in BMI), and for colon (5-8% per 5-unit increase in BMI) than for rectum (2% per 5-unit increase in BMI). Each 0.1 unit increase in waist-to-hip ratio is associated with a 20% increased risk of colon cancer.[6] A study comparing various indices of body fatness suggested that visceral adipose tissue (fat that is stored within the abdominal cavity and lines a number of important internal organs) may mediate the link between excess body weight and cancer risk.[56] A few prospective studies suggested that weight gain during adulthood is associated with increased risk of colorectal cancer among men,[57,58] whereas excess body weight during

Figure S8. Cancer Burden Attributable to Excess Body Weight by Region and Cancer Site, 2012



	Oceania	Sub-Saharan Africa	South Asia	High-income Asia Pacific	Central Asia, Middle East and North Africa	Latin America and the Caribbean	Central and Eastern Europe	East and South-Eastern Asia	High-income Western countries
Breast (Postmenopausal)	77	3,493	3,753	2,132	7,878	13,232	15,630	8,152	61,787
Endometrium	110	2,315	2,057	1,923	5,088	7,638	19,838	13,690	45,644
Colon and rectum	31	1,036	1,299	4,092	4,214	7,165	14,456	9,257	43,370
Kidney	6	336	595	1,787	2,620	4,561	10,976	6,134	35,525
Liver	117	3,122	1,816	4,198	7,131	6,487	4,335	36,579	20,009
Pancreas	5	342	245	1,020	1,126	2,289	3,554	2,212	10,878
Thyroid	27	242	323	1,274	1,776	2,198	2,018	1,736	9,071
Esophageal adenocarcinoma	0	90	195	131	777	1,088	442	694	7,907
Gallbladder	9	192	1,296	1,653	1,220	3,052	2,422	4,140	6,242
Multiple myeloma	4	190	175	194	614	882	868	503	5,729
Ovary	13	352	488	199	776	1,001	1,963	1,074	3,510
Stomach cardia	0	4	139	806	473	524	1,165	3,392	2,859

*Total percentage is calculated among the excess body weight-related cancers in the figure, not among all cancers.

Source: Unpublished data from: Pearson-Stuttard J, Zhou B, Kontis V, Bentham J, Gunter MJ, Ezzati M. Worldwide burden of cancer attributable to diabetes and high body-mass index: a comparative risk assessment. Lancet Diabetes Endocrinol. 2018;6(6):e6-e15.

young adulthood (ages 18-20 years) is associated with increased risk among women.[59, 60]

Corpus Uteri (Endometrium)

Worldwide, excess body weight accounted for an estimated 31% of endometrial cancers (98,400 cases) in 2012 (Figure S6). The majority of uterine corpus cancers (more than 80%) occur in the endometrium, or inner lining of the uterine corpus.[61] Compared with normal-weight women, risk is increased linearly, by 1.5-fold among those who are overweight ($25 \leq BMI < 30$), 2.5-fold among those with class 1 obesity ($30 \leq BMI < 35$), 4.5-fold among those with class 2 obesity ($35 \leq BMI < 40$), and 7.1-fold among those with class 3 obesity ($BMI \geq 40$).[62] Each 5-unit increase in BMI is associated with an approximately 50% increased risk of endometrial cancer,[63] and there is some evidence that risk is increased even among women in the high end of the normal BMI range.[63] The endometrial cancer risk associated with excess body weight is higher for women who have never used MHT (90% increased risk per 5-unit increase in BMI) than in those who have ever used MHT (18% per 5-unit increase in BMI),[64] and is higher for type I (mostly endometrioid adenocarcinoma; 16-23% per 2-unit increase in BMI) than for type II (serous and mixed cell; 12% per 2-unit increase in BMI) tumors.[63] Central obesity is also associated with increased risk of endometrial cancer, by 30% per 10 cm increase in waist circumference, and by 21% per 0.1 unit increase in waist-to-hip ratio.[6, 62] An analysis combining seven prospective studies showed that highger BMI during early adulthood (ages 18-25 years) is associated with increased risk of endometrial cancer (42% per 5-unit increase in BMI).[6]

Esophageal Adenocarcinoma

Nearly 30% (11,300 cases) of esophageal adenocarcinomas worldwide in 2012 were attributable to excess body weight (Figure S6). Each 5-unit increase in BMI is associated with a 48% increased risk of esophageal adenocarcinoma after adjustment for smoking status.[65] Among nonsmokers, the association is stronger, with a 62% increased risk per 5-unit increase in BMI.[6] Central obesity is associated with a 34% increased risk of esophageal adenocarcinoma per 10 cm excess waist circumference and by a 38% increased risk per 0.1 unit excess waist-to-hip ratio.[6]

Gallbladder

About 13% of gallbladder cancers in women (13,000 cases) and 10% in men (7,400 cases) worldwide in 2012 were attributable to excess body weight (Figure S6). Each 5-unit increase in BMI is associated with a 25% increased risk of gallbladder cancer.[6]

Kidney

About 20% of kidney cancers (25,200 women and 37,400 men) worldwide in 2012 were attributable to excess body weight (Figure S6). Each 5-unit increase in BMI is associated with a 30% increased risk of kidney cancer.[6] Central obesity is associated with an 11% increased risk per 10 cm excess waist circumference and a 26% per 0.1 unit excess waist-to-hip ratio.[6]

Liver

About 10% of liver cancers in men (54,600 cases) and 14% in women (30,200 cases) worldwide in 2012 were attributable to excess body weight (Figure S6). Each 5-unit increase in BMI is associated with a 30% increased risk of liver cancer.[6] The relative risk appears to be larger among Europeans (59% excess risk) than among Asians (18% excess risk).[6]

Meningioma

Meningioma is one of the most common primary central nervous system tumors, representing approximately 36% of cases worldwide.[66] Compared to normal-weight individuals, risk of meningioma is increased by 21% among overweight and 54% among obese individuals.[67, 68]

Multiple Myeloma

Worldwide, excess body weight accounted for 7% (4,500 cases) of multiple myeloma cases in women and 9% (4,400 cases) of the cases in men (Figure S6). Each 5-unit increase in BMI is associated with a 12% increased risk of multiple myeloma.[69] A pooled analysis of three large prospective cohort studies found that increased BMI early in adulthood (ages 18-30 years) is associated with increased risk of multiple myeloma (by 28% per 5-unit increase in BMI).[70]

Ovary

About 4% (9,100 cases) of ovarian cancers worldwide in 2012 were attributable to excess body weight (Figure S6). Each 5-unit increase in BMI is associated with a 6% increased risk of ovarian cancer.[6] Similar to breast cancer and endometrial cancer, the association appears to be confined to women who have never used MHT.[71] A few studies have suggested that higher BMI increases risk only for less common subtypes (e.g., endometroid carcinoma and mucinous carcinoma);[71, 72] however, further studies are needed to confirm these subtype associations.

Pancreas

Worldwide, excess body weight accounted for about 6% (10,300 cases) of pancreatic cancer cases in men and 7% (11,200 cases) in women in 2012 (Figure S6). Each 5-unit increase in BMI is associated with a 10% increased risk of pancreatic cancer.[6] Central obesity, measured as waist circumference (11% per 10 cm) or waist-to-hip ratio (19% per 0.1 unit), is also associated with increased risk.[6] Excess body weight during early adulthood (ages 18-21 years) appears to be associated with increased risk of pancreatic cancer later in life.[73]

Stomach Cardia

An estimated 9% (6,400 cases) of stomach cardia cancers among men and 11% (2,900 cases) among women worldwide in 2012 were attributable to excess body weight (Figure S6). Stomach cancer that develops in the cardia region of the stomach (the upper part closest to the esophagus) comprises about 27% of all stomach cancers worldwide.[74] Each 5-unit increase in BMI is associated with a 23% increased risk of stomach cardia cancer.[6] Excess body weight has not been found to be associated with non-cardia stomach cancer.[75, 76]

Thyroid

Excess body weight accounted for 7% (14,800 cases) and 6% (3,900 cases) of thyroid cancer among men and women, respectively, in 2012 (Figure S6). Each 5-unit increase in BMI is associated with a 6% increased risk of thyroid cancer.[77] Excess body weight in early adulthood (ages 18-21 years) appears to be associated with increased risk of thyroid cancer in later life (by 13% per 5-unit increase in BMI).[77]

Cancers for Which Evidence Is Probable

Oral Cavity, Pharynx, and Larynx

There is accumulating evidence that body fatness may increase the risk of cancers of the oral cavity, pharynx, and larynx[6]. A pooled analysis including 20 prospective studies showed that each 5-unit increase in BMI was associated with a 15% increased risk of these cancers among nonsmokers.[78] However, central obesity measured by waist circumference (4% increased risk per 5 cm) and waist-to-hip ratio (7% increased risk per 0.1 unit) was associated with increased risk among both smokers and nonsmokers.

Prostate (Advanced)

Accumulating evidence suggests that excess body weight may increase the risk of advanced, high-grade, and fatal prostate cancer.[6] Each 5-unit increase in BMI is associated with an 8% increased risk of advanced-stage prostate cancer. Both waist circumference (12% per 10 cm) and waist-to-hip ratio (15% per 0.1 unit) are associated with increased risk.[6]

Cancer Survival

The literature on the influence of excess body weight on cancer survival is limited, but suggests less favorable outcomes for several cancers.[79] The relationship has been most extensively studied with respect to breast cancer survivors.[80-82] A study combining 82 studies concluded that increased body weight is associated with poorer overall and breast cancer-specific survival for both pre- and postmenopausal women regardless of when BMI was ascertained. Each 5-unit increase in BMI before, <12 months after, and ≥12 months after diagnosis increased risk by 17%, 11%, and 8%, respectively, for total mortality and 18%, 14%, and 29%, respectively, for breast cancer mortality.[81] Similarly adverse effects of excess body weight before or at the time of diagnosis have been reported for cancers, including prostate,[83, 84] colorectum,[85-87] pancreas,[88] and ovary.[89, 90] Weight gain after cancer diagnosis has been associated with worse survival in some[91-93] but not all studies.[94]

How Excess Body Weight Increases Cancer Risk

Various theories have been proposed to explain how excess body weight increases cancer risk, although specific mechanisms are not yet fully understood. Alterations in hormonal systems and chronic inflammation are the most well-studied hypotheses.[95, 96] People with excess weight often have high levels of insulin, a metabolic hormone associated with increased risk of multiple types of cancer (e.g., colorectal, kidney, and endometrial).[96, 97, 98] Similarly, excess amounts of the sex hormone estrogen, which are produced by fat tissue in the body, are associated with increased risk of breast and ovarian cancers.[99, 100] In addition, excess body weight contributes to chronic inflammation, which can cause DNA damage and uncontrolled cell growth.[95] Examples of specific inflammatory conditions linked to both obesity and cancer include chronic acid reflux/Barrett's esophagus and esophageal cancer[101, 102] and gallbladder inflammation resulting from a history of gallstones and gallbladder cancer.[103, 104] Alterations in the immune system that are caused by the presence of excess body fat may also contribute to increased cancer risk. Research also shows that the gut microbiome might play an important role in many obesity-related biologic pathways that affect cancer risk.[105]

Weight Loss and Cancer Risk

Evidence for an association between weight loss and cancer risk is limited.[106, 107] Observational studies are often limited due to the small number of individuals who successfully maintain weight loss and lack of information on whether the weight loss was intentional or from illness.[107, 108] In a recent systematic review considering 34 studies, 16 studies found a significant reduction in the risk of incident cancer in people who lost weight.[107] When considering all types of weight loss (intentional and non-intentional), the benefit of weight loss was strongest in women, predominantly noted for postmenopausal breast cancer and endometrial cancer; only a few significant positive associations were found in men.[107] Intentional weight loss (including surgical weight loss) resulted in a 24%-78% reduction in the overall incidence of cancer, mainly driven by women and obesity-related cancers in most[109-113] but not all studies.[107, 114] Despite inconclusive data, achieving a healthy bodyweight might extend life expectancy and is sensible, given the health harms associated with excess body weight.[3]

The Global Fight against Excess Body Weight

The WHO provides global leadership and policy to strengthen national efforts to prevent and control obesity. In 1997, the WHO held the first Expert Consultation on Obesity, recognizing the global obesity epidemic and its overwhelming public health consequences.[124] Since then, the WHO has spearheaded several technical meetings and consultations to address various issues related to the prevention and control of obesity. In 2004, the World Health Assembly adopted the WHO Global Strategy on Diet, Physical Activity, and Health in recognition of the opportunity for reducing deaths and diseases worldwide by improving diet and promoting physical activity. In 2013, the World Health Assembly endorsed the Global Action Plan for the Prevention and Control of Noncommunicable Diseases 2013-2020 and agreed on a set of nine voluntary global targets for 2025, one of which is halting the rise in diabetes and obesity.[115] Shortly thereafter, the WHO director-general established a high-level Commission on Ending Childhood Obesity that developed recommendations for policy makers to halt the rise in childhood obesity.

Isolated attempts in some countries provide important evidence that progress against obesity is feasible.[117] Evidence-based and cost-effective strategies to prevent and control obesity focus on promoting a healthy diet and physical activity through policy and system approaches.[115, 117-121] In particular, concerted action by governments and stakeholders (e.g., nongovernmental organizations, private sector) has been suggested to address the strong commercial forces seeking profit from the overconsumption of palatable foods. [117, 119, 120, 122] The WHO recommended strategies include population-wide policy-led interventions to rectify the production, distribution, and marketing of unhealthy foods and changes in the built environment to promote adequate levels of physical activity (Table S2). Interventions aimed at motivating behavioral changes include setting-based (preschools, schools, workplaces, religious settings, and hospitals) health promotion and education programs; mass media campaigns; social marketing to improve the knowledge and skills of the community and individuals; and routine primary health care and counseling to facilitate obesity prevention and management. The Global Action Plan proposes that countries consider the use of economic tools that are justified by evidence, which may include taxes and subsidies as appropriate to national context. Several factors should be considered in implementing the intervention strategies according to national circumstances and local settings, such as feasibility and its impact on health equity of interventions.[118, 123]

Finally, while population-level efforts to prevent excess body weight should be an area of focus, they should be matched with enhancing access to health care interventions for weight management, including screening for and management of excess body weight as a means of secondary intervention. These interventions should focus on education and opportunity for sustainable lifestyle change (i.e., healthful eating and physical activity).

Table S2. Recommended Intervention Strategies to Prevent and Control Excess Body Weight

Interventions to improve food system/environment and the built environment	
Reduce unhealthy diet	Eliminate industrial trans-fats through the development of legislation to ban their use in the food chain.
	Reduce sugar consumption through effective taxation on sugar-sweetened beverages.
	Implement subsidies to increase the intake of fruits and vegetables.
	Replace trans-fats and saturated fats with unsaturated fats through reformulation, labeling, fiscal policies, or agricultural policies.
	Limit portion and package size to reduce energy intake and the risk of excess body weight.
	Implement nutrition labeling to reduce total energy intake (kcal), sugars, sodium, and fats.
Reduce physical inactivity	Ensure that macrolevel urban design incorporates the core elements of residential density, connected street networks that include sidewalks, easy access to a diversity of destinations, and access to public transport.
	Provide convenient and safe access to quality public open space and adequate infrastructure to support walking and cycling.
Behavioral change communication	
Reduce unhealthy diet	Promote and support exclusive breastfeeding for the first 6 months of life.
	Implement nutrition education and counseling in different settings (for example, in preschools, schools, workplaces, and hospitals) to increase the intake of fruits and vegetables.
	Implement mass media campaigns on healthy diets, including social marketing to reduce the intake of total fat, saturated fats, sugars, and salt, and to promote the intake of fruits and vegetables.
Reduce physical inactivity	Implement a community-wide public education and awareness campaign for physical activity that includes a mass media campaign combined with other community-based education and motivational and environmental programs aimed at supporting behavioral change of physical activity levels.
	Provide physical activity counseling and referral as part of routine primary health care services using a brief intervention.
	Implement whole-of-school programs that include quality physical education and availability of adequate facilities and programs to support physical activity for all children.
	Implement multicomponent workplace physical activity programs.
	Promote physical activity through organized sport groups and clubs, programs, and events.

Source: Adapted from World Health Organization. (2017). Tackling NCDs: 'best buys' and other recommended interventions for the prevention and control of noncommunicable diseases. World Health Organization. http://www.who.int/iris/handle/10665/259232. License: CC BY-NC-SA 3.0 IGO.
An up-to-date list of WHO tools and resources for each objective can be found at http://www.who.int/nmh/ncd-tools/en.

What Is the American Cancer Society Doing to Help Reduce Excess Body Weight and the Associated Cancer Burden?

The American Cancer Society has been focused on the health harms of excess body weight for many decades and is tackling this issue on every front, from research to community action. For nearly 40 years, our scientists have conducted research on the association between excess body weight and cancer risk, mortality, and survival. In 1979, data from American Cancer Society Cancer Prevention Study-I provided the first prospective epidemiologic evidence that excess body weight contributes to a higher risk of death from cancer, overall, as well as cancers of the uterus, gallbladder, kidney, stomach, colon, and breast.[125] Since that time, American Cancer Society researchers and data from our studies have contributed extensively to the scientific evidence, including participation on expert panels evaluating the cancer-causing effects of excess body weight, such as those convened by the International Agency for Research on Cancer.[7] Currently, American Cancer Society researchers are studying relationship between excess body weight throughout life and cancer incidence and survival, as well as the biologic pathways that might influence risk. In addition, our Surveillance Research group reports annually on the current patterns and trends in the prevalence of excess body weight.

In addition to the research conducted by scientists within the American Cancer Society, our Extramural Research department supports researchers at other institutions. As of August 2018, the American Cancer

Society has more than $21 million committed to grants supporting high-quality scientific research focused on energy balance, obesity, and/or healthy eating and active living. Current research topics include studies examining the relationship between excess body weight and the risk of prostate cancer, particularly among African American men, and the association of excess body weight and dietary components with the risk of colorectal cancer.

For over three decades, the American Cancer Society has published Nutrition and Physical Activities Guidelines for Cancer Prevention (and Survivorship). Published approximately every 5 years, the guidelines reflect the most current scientific evidence related to dietary and activity patterns and cancer risk, and aim to affect dietary and physical activity patterns and eventually to prevent and control excess body weight and the cancers associated with it. Indeed, studies have shown that adherence to the guidelines is consistently associated with reductions of overall cancer incidence and mortality in the US.[126-129] The condensed version is available on the American Cancer Society website[130] and the full article, which is written for health care professionals, is in the January/February 2012 issue of *CA: A Cancer Journal for Clinicians*, and is available free online.[131] An update to these guidelines is expected to publish in mid-2019.

While the guidelines focus on recommendations for individual choices regarding diet and physical activity patterns, they also recognize that our environments – where we live, learn, work, shop, and play – have an impact on our ability to engage in healthy behaviors. The American Cancer Society is working in communities, health systems (including primary care and hospital systems), schools, and workplaces to impact policies and practices that create environments that are supportive of healthy eating and physical activity.

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The Global Fight against Cancer

The ultimate mission of the American Cancer Society is to lead the fight for a world without cancer. Today, cancer accounts for about 1 in every 6 deaths worldwide – more than HIV/AIDS, tuberculosis, and malaria combined. By 2040, the global burden is expected to reach 27.5 million new cancer cases and 16.3 million cancer deaths solely due to the growth and aging of the population. However, these projections may be underestimates given the adoption of unhealthy behaviors and lifestyles (e.g., smoking, unhealthy diet, and physical inactivity) and changes in reproductive patterns (e.g., fewer children, later age at first childbirth) associated with rapid income growth in economically transitioning countries.

In response to the rising incidence of cancer, global public health organizations are taking action. In 2006, the global cancer community launched the first World Cancer Declaration, which outlined steps to reverse the global cancer crisis by 2020.[1] In 2011, a landmark high-level meeting of the UN General Assembly resulted in a commitment to address chronic noncommunicable diseases (NCDs), including cancer, as a major development challenge. 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. In 2015, a goal to reduce premature mortality from NCDs including cancer by one-third by 2030 was added to the United Nations Development Programme's Sustainable Development Goals.

Worldwide Tobacco Use

Tobacco is a major contributor to the global burden of disease, responsible for more than 20% of cancer deaths worldwide and more than two-thirds of all deaths among long-term tobacco users.

- Tobacco was responsible for more than 7 million deaths in 2016, including 884,000 deaths from secondhand smoke exposure among nonsmokers. More than 75% of tobacco-attributable deaths are in low- and middle-income countries (LMICs).
- Between 1990 and 2016, annual tobacco-attributable deaths remained at 1.6 million in high-income countries, but increased from 4.3 million to 5.5 million in LMICs.
- The tobacco industry has been aggressively pursuing legal challenges to tobacco control interventions around the globe and promoting falsehoods about illicit trade and the livelihoods of smallholder tobacco farmers in order to further promote tobacco use.

The first global public health treaty under the auspices of the World Health Organization (WHO), the Framework Convention on Tobacco Control (FCTC) became a legally binding accord for all ratifying states in 2005. The purpose of the treaty is to fight the devastating health, environmental, and economic effects of tobacco on a global scale by requiring parties to adopt a comprehensive range of tobacco control measures. The FCTC provisions establish international standards for tobacco taxation; restrictions on tobacco marketing; tobacco product standards; ingredient 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 to tobacco farming; liability issues; and scientific and technical cooperation and exchange of information.[2] As of April 2018, 180 countries and the European Union had ratified the treaty, representing more than 90% of the world population. A number of major tobacco-producing nations, including Argentina, Indonesia, Malawi, and the United States, have not yet ratified the treaty.

- About 63% of the world's population was covered by at least one comprehensive tobacco control measure in 2016, up from about 15% in 2008.
- The WHO estimates that 20% of the world's population lives in smoke-free environments and only 10% is covered by tobacco tax policy that is effective for tobacco control purposes.

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 save lives from cancer and tobacco-related diseases globally by assisting and empowering the world's cancer societies and antitobacco advocates. The American Cancer Society Global Cancer Control and Intramural Research departments are raising awareness about the growing global cancer burden and promoting evidence-based cancer and tobacco control programs with a focus on LMICs.

Make cancer control a political and public health priority. Noncommunicable diseases (NCDs) such as cancer, heart disease, and diabetes account for about 70% of the world's deaths. Although 76% of these deaths occur in LMICs, less than 3% of private and public health funding is allocated to prevent and control NCDs in these areas. The American Cancer Society helps make cancer and other NCDs a global public health priority by collaborating with key partners, including the NCD Alliance, the Union for International Cancer Control, the World Health Organization, the International Agency for Research on Cancer, the United Nations Development Programme, the International Union Against Tuberculosis and Lung Disease, the NCD Roundtable, and the Taskforce on Women and Non-Communicable Diseases. An example of recent progress in this effort occurred in 2017 when the World Health Assembly passed a resolution reaffirming cancer control as a critical health and development priority. In 2018, the WHO director general made a global call for action toward the elimination of cervical cancer.

Develop civil society capacity in cancer control globally. Many governments in LMICs are ill-prepared to address adequately the increasing burden of cancer. In many cases, civil society actors (nongovernmental organizations, institutions, and individuals) are also not yet fully engaged or coordinated in their cancer control efforts. The American Cancer Society Strengthening Organizations for a United Response to the Cancer Epidemic (SOURCE) Program is designed to strengthen the civil society response to cancer across the continuum from prevention through end-of-life care in focus countries around the world. This program provides intensive culturally appropriate training, technical assistance, mentoring, and practicum opportunities to cancer-focused organizations in LMICs focused on building and sustaining their capacity across seven key domains of organizational development: governance, financial management, financial sustainability, operations and administration, human resources management, program management, and external relations and partnerships. The program also facilitates the establishment of national cancer umbrella organizations to coordinate the civil society response and elevate the voice of all organizations, big and small, in the cancer fight. As part of the International Cancer Control Partnership, the American Cancer Society also supports country cancer control planning efforts.

Help improve tobacco control worldwide. The American Cancer Society Global Cancer Control department and the Economic and Health Policy Research (EHPR) program in the Intramural Research department are working to end the worldwide tobacco epidemic through research and programs. In 2016, the two teams launched a global tobacco taxation initiative that promotes the Sustainable Development Goal of a 30% reduction in smoking prevalence by 2025. This program actively seeks to engage specific cancer organizations, most of which have not been previously involved in this area, particularly in LMICs, and also provides capacity building and technical assistance to interested organizations and governments. Further, because issues around illicit trade in tobacco products have been closely tied to tobacco taxation, the initiative takes advantage of the EHPR's knowledge and experience to help governments navigate the challenges around implementing tobacco taxation successfully amid tobacco industry opposition. The EHPR team is also leading a multiyear program – with support from the US National Institutes of Health, the Bloomberg Philanthropies, and the World Bank – to examine the livelihoods of tobacco farmers in Indonesia, Kenya, Malawi, the Philippines, and Zambia to dispel the tobacco industry's myth that tobacco control harms smallholder tobacco farmers.

Make effective pain treatment available to all in need. Moderate to severe pain, which is experienced by about 80% of people with advanced cancer, is commonly untreated in resource-limited settings. Improved access to essential pain medicines is arguably the easiest and least expensive need to meet in LMICs. The American Cancer Society leads projects in Nigeria, Ethiopia, Kenya, Uganda, and Swaziland to improve access to essential pain medicines and also supports national morphine production programs that have dramatically reduced the cost of and increased access to pain relief. The American Cancer Society is also training health workers in more than 30 teaching and referral hospitals across the 5 countries through the Pain-Free Hospital Initiative, a 1-year hospital-wide quality improvement initiative designed to change clinical practice by integrating effective, high-quality pain treatment into hospital-based services. In 2018, the Ethiopian Health Ministry committed its own resources to extend the Pain-Free Hospital Initiative to 360 hospitals across the country.

Increase awareness about the global cancer burden. The American Cancer Society works with global collaborators to increase awareness about the growing cancer and tobacco burdens and their disproportionate impact on LMICs. For example, the American Cancer Society collaborates with the International Agency for Research on Cancer (IARC) to produce *Global Cancer Facts & Figures* using IARC's GLOBOCAN estimates. The American Cancer Society also partnered with IARC and the Union for International Cancer Control to produce *The Cancer Atlas, Second Edition* and its interactive website (canceratlas.cancer.org). The *Atlas*, which is available in 10 languages, highlights the complex nature of the global cancer landscape while pointing to strategies governments can use to reduce their cancer burden. Similarly, *The Tobacco Atlas, Sixth Edition* (tobaccoatlas.org), a collaboration with Vital Strategies, is the most comprehensive resource on the evolving worldwide tobacco epidemic. It is available in six languages and not only elucidates the complexities of the harms caused by tobacco use, but also systematically lays out the steps that governments and societies can take to address this epidemic. Tobaccoatlas.org, an accompanying interactive website, receives more than 30,000 visitors each month, about two-thirds of whom are outside the US. The American Cancer Society Intramural Research department also publishes *Global Cancer Facts & Figures* (cancer.org/statistics), which along with an accompanying statistics article in *CA: A Cancer Journal for Clinicians*, provides up-to-date data on cancer incidence, mortality, and survival worldwide. In addition to our print publications, the American Cancer Society's website, cancer.org, provides cancer information to millions of individuals throughout the world. In 2017, approximately 49% of visitors to the website were outside the US. Information is currently available in English, Spanish, Chinese, Bengali, Hindi, Korean, Urdu, and Vietnamese.

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Sources of Statistics

Incidence and mortality counts and rates for 2018 were obtained from GLOBOCAN 2018 (gco.iarc.fr/), published by the International Agency for Research on Cancer (IARC). These are estimates of cancer incidence and mortality burden in 185 countries of the world, using a hierarchical set of methods depending on the accuracy and availability of data.[1] Data sources and methods change with each version of GLOBOCAN, and estimates from different years should not be compared. Population coverage of high-quality population-based cancer registration is 1% in Africa, 6.5% in Asia, 7.5% in Central and South America, 46% in Europe, 77% in Oceania, and 98% in Northern America.[2] Mortality data are available for about 40% of the world's deaths, and are generally of higher quality in high-income countries.[3] IARC also makes available historic incidence and mortality data in its Cancer Incidence in Five Continents database (ci5.iarc.fr/) and World Health Organization Cancer Mortality Database (www-dep.iarc.fr/WHOdb/WHOdb.htm).

Incidence and Mortality Rates

To compare incidence and mortality between populations or over time, we need to estimate cancer rates, taking into account the size of the population by age and sex. The cancer incidence rate is defined as the number of people who are diagnosed with cancer divided by the number of people who are at risk for the disease in the population during a given time period. The cancer mortality rate, or death rate, is defined as the number of people who die from cancer divided by the number of people at risk for death in the population during a given time period. Incidence and mortality rates in this publication are presented per 100,000 people and are age adjusted to the 1960 world standard population to allow comparisons across populations with different age distributions. Age-adjusted rates should only be compared to rates that are adjusted to the same population standard.

Survival

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. 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 the availability of effective and timely treatment. Methodological problems relating to incompleteness of registration and follow-up also contribute to apparent differences. Survival data are lacking for many lower-HDI countries without cancer registries.

There are different methods for calculating cancer survival. For most sites, we present net survival from the CONCORD-3 program, which analyzed data from 322 population-based registries in 71 countries.[6] Net survival is useful for international comparisons because it is not influenced by mortality from other diseases, which may vary between countries.[7] However, for some cancers (non-Hodgkin lymphoma and urinary bladder), CONCORD-3 net survival estimates were not available, so survival from other sources is presented. These survival estimates may be calculated differently from those of the CONCORD-3 program and should not be directly compared.

Development Classifications

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 (HDI) ranking.

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the American Cancer Society concerning the legal status of any country, territory, city, or area of its authorities, or concerning the delimitation of its frontiers or boundaries.

The United Nations

More-developed regions include Europe, Northern America, Australia/New Zealand, and Japan. Less-developed region include Africa, Asia (excluding Japan), Latin America and the Caribbean, Melanesia, Micronesia, and Polynesia.

World Bank Income Group

Economies are divided according to 2016 gross national income per capita in US Dollars, calculated using the World Bank Atlas method. The groups are: low income, $1,005 or less; lower middle income, $1,006 to $3,955; upper middle income, $3,956 to $12,235; and high income, $12,236 or more.

Low-income economies: Afghanistan; Benin; Burkina Faso; Burundi; Central African Republic; Chad; Congo, Dem. Rep.; Comoros; Eritrea; Ethiopia; Gambia, The; Guinea; Guinea-Bissau; Haiti; Korea, Dem. People's Rep. (North Korea); Liberia; Madagascar; Malawi; Mali; Mozambique; Nepal; Niger; Rwanda; Senegal; Sierra Leone; Somalia; South Sudan; Tanzania; Togo; Uganda; Zimbabwe

Lower middle-income economies: Angola; Armenia; Bangladesh; Bhutan; Bolivia; Cabo Verde; Cambodia; Cameroon; Congo, Rep.; Côte d'Ivoire; Djibouti; Egypt, Arab Rep.; El Salvador; Georgia; Ghana; Guatemala; Honduras; India; Indonesia; Jordan; Kenya; Kiribati; Kosovo; Kyrgyz Republic; Lao PDR; Lesotho; Mauritania; Micronesia, Fed. Sts.*; Moldova (Republic of); Mongolia; Morocco; Myanmar; Nicaragua; Nigeria; Pakistan; Papua New Guinea; Philippines; Sao Tome and Principe; Solomon Islands; Sri Lanka; Sudan; Swaziland; Syrian Arab Republic; Tajikistan; Timor-Leste; Tunisia; Ukraine; Uzbekistan; Vanuatu; Vietnam; West Bank and Gaza; Yemen, Rep.; Zambia

Upper middle-income economies: Albania; Algeria; American Samoa; Argentina; Azerbaijan; Belarus; Belize; Bosnia and Herzegovina; Botswana; Brazil; Bulgaria; China; Colombia; Costa Rica; Croatia; Cuba; Dominica*; Dominican Republic; Ecuador; Equatorial Guinea; Fiji; Gabon; Grenada; Guyana; Iran, Islamic Rep.; Iraq; Jamaica; Kazakhstan; Lebanon; Libya; Macedonia, FYR; Malaysia; Maldives ; Marshall Islands*; Mauritius; Mexico; Montenegro; Namibia; Nauru*; Panama; Paraguay; Peru; Romania; Russian Federation; Saint Lucia; Saint Vincent and the Grenadines*; Samoa; Serbia; South Africa; Suriname; Thailand; Tonga; Turkey; Turkmenistan; Tuvalu*; Venezuela, RB

High-income economies: Andorra*; Antigua and Barbuda*; Aruba*; Australia; Austria; Bahamas; Bahrain; Barbados; Belgium; Bermuda ; British Virgin Islands*; Brunei Darussalam; Canada; Cayman Islands*; Channel Islands*; Chile; Curacao*; Cyprus; Czech Republic; Denmark; Estonia; Faroe Islands*; Finland; France; French Polynesia; Germany; Gibraltar*; Greece; Greenland*; Guam; Hong Kong SAR, China*; Hungary; Iceland; Ireland; Isle of Man*; Israel; Italy; Japan; Korea, Rep. (South Korea); Kuwait; Latvia; Liechtenstein*; Lithuania; Luxembourg; Macao SAR, China*; Malta; Monaco*; the Netherlands; New Caledonia; New Zealand; Northern Mariana Islands*; Norway; Oman; Palau*; Poland; Portugal; Puerto Rico; Qatar; Saint Kitts and Nevis*; Saint Martin (French part)*; San Marino; Saudi Arabia; Seychelles*; Singapore; Sint Maarten (Dutch part)*; Slovak Republic; Slovenia; Spain; Sweden; Switzerland; Taiwan, China*; Trinidad and Tobago; Turks and Caicos Islands*; United Arab Emirates; United Kingdom; United States; Uruguay; Virgin Islands (US)*

**GLOBOCAN does not provide estimates*

Human Development Index

The United Nations Development Programme's Human Development 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 2016 groups are:

Low Human Development: Afghanistan; Angola; Benin; Burkina Faso; Burundi; Cameroon; Central African Republic; Chad; Comoros; Congo (Democratic Republic of the); Côte d'Ivoire; Djibouti; Eritrea; Ethiopia; Gambia, The; Guinea; Guinea-Bissau; Haiti; Lesotho; Liberia; Madagascar; Malawi; Mali; Mauritania; Mozambique; Niger; Nigeria; Papua New Guinea; Rwanda; Senegal; Sierra Leone; Solomon Islands; South Sudan; Sudan; Swaziland; Syrian Arab Republic; Tanzania (United Republic of); Togo; Uganda; Yemen; Zimbabwe

Medium Human Development: Bangladesh; Bolivia (Plurinational State of); Bhutan; Botswana; Cabo Verde; Cambodia; Congo; Egypt; El Salvador; Equatorial Guinea;

Gabon; Ghana; Guatemala; Guyana; Honduras; India; Indonesia; Iraq; Kenya; Kiribati*; Kyrgyzstan; Lao People's Democratic Republic; Micronesia (Federated States of); Moldova (Republic of); Morocco; Myanmar; Namibia; Nepal; Nicaragua; Pakistan; Palestine, State of; Paraguay; Philippines; Sao Tome and Principe; South Africa; Tajikistan; Timor-Leste; Turkmenistan; Vanuatu; Vietnam; Zambia

High Human Development: Albania; Algeria; Antigua and Barbuda*; Armenia; Austria; Azerbaijan; Bahamas; Barbados; Belarus; Belgium; Belize; Bosnia and Herzegovina; Brazil; Bulgaria; Canada; China; Colombia; Costa Rica; Cuba; Dominica*; Dominican Republic; Ecuador; Fiji; Georgia; Grenada; Iran (Islamic Republic of); Jamaica; Jordan; Kazakhstan; Lebanon; Libya; Malaysia; Maldives; Mauritius; Mexico; Mongolia; Oman; Palau*; Panama; Peru; Saint Kitts and Nevis*; Saint Lucia; Saint Vincent and the Grenadines*; Samoa; Seychelles*; Serbia; Sri Lanka; Suriname; Thailand; The former Yugoslav Republic of Macedonia; Tonga; Trinidad and Tobago; Tunisia; Turkey; Ukraine; Uruguay; Uzbekistan; Venezuela (Bolivarian Republic of)

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

**GLOBOCAN does not provide estimates*

Other Groupings

Additional regional groupings incorporating both geography and income[4] are used in the Special Section. The groupings are as follows:

Sub-Saharan Africa: Angola; Benin; Botswana; Burkina Faso; Burundi; Cabo Verde; Cameroon; Central African Republic; Chad; Comoros; Congo; Congo (Democratic Republic of the); Côte d'Ivoire; Djibouti; Equatorial Guinea; Eritrea; Ethiopia; Gabon; Gambia, The; 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; Somalia; South Africa; Sudan; Swaziland; Tanzania; Togo; Uganda; Zambia; Zimbabwe

Central Asia; Middle East and North Africa: Algeria; Armenia; Azerbaijan; Bahrain; Egypt; Georgia; Iran; Iraq; Jordan; Kazakhstan; Kuwait; Kyrgyzstan; Lebanon; Libya; Mongolia; Morocco; Occupied Palestinian Territory; Oman; Qatar; Saudi Arabia; Syrian Arab Republic; Tajikistan; Tunisia; Turkey; Turkmenistan; United Arab Emirates; Uzbekistan; Yemen

South Asia: Afghanistan; Bangladesh; Bhutan; India; Nepal; Pakistan

East and South-Eastern Asia: Brunei Darussalam; Cambodia; China; Hong Kong SAR, China; Indonesia; Korea, Dem. People's Rep. (North Korea); Lao PDR; Malaysia; Maldives; Myanmar; Philippines; Sri Lanka; Taiwan; Thailand; Timor-Leste; Vietnam

Oceania: American Samoa; Cook Islands; Fiji; French Polynesia; Kiribati; Marshall Islands; Micronesia, Fed. Sts.; Nauru; Niue; Palau; Papua New Guinea; Samoa; Solomon Islands; Tokelau; Tonga; Tuvalu; Vanuatu

High-income Asia Pacific: Japan; Korea, Rep. (South Korea); Singapore

Latin America and Caribbean: Antigua and Barbuda; Argentina; Bahamas; Barbados; Belize; Bermuda; Bolivia; Brazil; Chile; Colombia; Costa Rica; Cuba; Dominica; Dominican Republic; Ecuador; El Salvador; Grenada; Guatemala; Guyana; Haiti; Honduras; Jamaica; Mexico; Nicaragua; Panama; Paraguay; Peru; Puerto Rico; Saint Kitts and Nevis; Saint Lucia; Saint Vincent and the Grenadines; Suriname; Trinidad and Tobago; Uruguay; Venezuela

High-income Western countries: Andorra; Australia; Austria; Belgium; Canada; Cyprus; Denmark; Finland; France; Germany; Greece; Greenland; Iceland; Ireland; Israel; Italy; Luxembourg; Malta; the Netherlands; New Zealand; Norway; Portugal; Spain; Sweden; Switzerland; United Kingdom; United States

Central and Eastern Europe: Albania; Belarus; Bosnia and Herzegovina; Bulgaria; Croatia; Czech Republic; Estonia; Hungary; Latvia; Lithuania; Former Yugoslav Republic of Macedonia; Moldova; Montenegro; Poland; Romania; Russian Federation; Serbia; Slovakia; Slovenia; Ukraine

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, Cabo Verde, Côte d'Ivoire, The Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Mali, Mauritania, Niger, Nigeria, Sao Tome and Principe, 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 Guiana, Guyana, Paraguay, Peru, Suriname, Uruguay, and Venezuela. **Northern America:** Canada, United States of America. **Eastern Asia:** China, Japan, Democratic People's Republic of Korea (North Korea), Republic of Korea (South Korea), Mongolia. **South-Eastern Asia:** Brunei Darussalam, Cambodia, Indonesia, Lao People's 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, and Spain. **Western Europe:** Austria, Belgium, France, Germany, Luxembourg, the Netherlands, and 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.

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