Global Cancer Statistics, 2012

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Cancer constitutes an enormous burden on society in more and less economically developed countries alike. The occurrence of cancer is increasing because of the growth and aging of the population, as well as an increasing prevalence of established risk factors such as smoking, overweight, physical inactivity, and changing reproductive patterns associated with urbanization and economic development. Based on GLOBOCAN estimates, about 14.1 million new cancer cases and 8.2 million deaths occurred in 2012 worldwide. Over the years, the burden has shifted to less developed countries, which currently account for about 57% of cases and 65% of cancer deaths worldwide. Lung cancer is the leading cause of cancer death among males in both more and less developed countries, and has surpassed breast cancer as the leading cause of cancer death among females in more developed countries; breast cancer remains the leading cause of cancer death among females in less developed countries. Other leading causes of cancer death in more developed countries include colorectal cancer among males and females and prostate cancer among males. In less developed countries, liver and stomach cancer among males and cervical cancer among females are also leading causes of cancer death. Although incidence rates for all cancers combined are nearly twice as high in more developed than in less developed countries in both males and females, mortality rates are only 8% to 15% higher in more developed countries. This disparity reflects regional differences in the mix of cancers, which is affected by risk factors and detection practices, and/or the availability of treatment. Risk factors associated with the leading causes of cancer death include tobacco use (lung, colorectal, stomach, and liver cancer), overweight/obesity and physical inactivity (breast and colorectal cancer), and infection (liver, stomach, and cervical cancer). A substantial portion of cancer cases and deaths could be prevented by broadly applying effective prevention measures, such as tobacco control, vaccination, and the use of early detection tests. **CA Cancer J Clin 2015;65:87-108. © 2015 American Cancer Society.**

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Introduction

Cancer is a leading cause of death in both more and less economically developed countries; the burden is expected to grow worldwide due to the growth and aging of the population, particularly in less developed countries, in which about 82% of the world's population resides. The adoption of lifestyle behaviors that are known to increase cancer risk, such as smoking, poor diet, physical inactivity, and reproductive changes (including lower parity and later age at first birth), have further increased the cancer burden in less economically developed countries. In this article, we provide an overview of the global cancer burden, including the estimated number of new cancer cases and deaths in 2012 and the incidence and mortality rates by region for selected cancer sites. These statistics are based on GLOBOCAN worldwide estimates of cancer incidence and mortality produced by the International Agency for Research on Cancer (IARC) for 2012.[1] We comment on the scale and profiles of cancer worldwide and associated risk factors for a number of common cancers, alongside preventive measures that have the potential to reduce the future cancer burden.

Data Sources and Methods

Data from GLOBOCAN 2012, produced by the IARC, were used.[1] GLOBOCAN provides estimates of cancer incidence, mortality, and prevalence worldwide, and for countries and regions. Incidence data are derived from population-based cancer registries (PBCR) that may capture the population of an entire country but more often cover smaller, subnational areas,

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such as urban environments like major cities. Although the quality of information from less developed countries is often considered limited compared with that from more developed countries, PBCR are a key source of information on the local scale and profile of cancer and are critical in developing and evaluating cancer control programs. The total number of cancer deaths by country are collected annually and are made available by the World Health Organization (WHO).[2] The advantages of this source of data are its national coverage and long-term availability, although not all data sets are of the same quality or completeness.

Incidence and mortality rates were estimated using GLOBOCAN[1] by country, using the most recently available data collected by the IARC or available in routine reports from the registries themselves. The data sources and methods are described in further detail elsewhere.[3] For incidence data, countries are classified based on data quality and availability as follows:

1. High-quality national data (data included in *Cancer Incidence in Five Continents* volume IX and/or X[4,5]) or high-quality regional data (coverage greater than 50% of the population).
2. High-quality regional data (coverage between 10% and 50%).
3. High-quality regional data (coverage less than 10%).
4. National data (PBCR).
5. Regional data (PBCR).
6. Frequency data (hospital-based or pathological-based series).
7. No data.

For mortality data, countries are classified as follows, with quality criteria defined by Mathers et al[6]:

1. High-quality complete vital registration.
2. Medium-quality complete vital registration.
3. Low-quality complete vital registration.
4. Incomplete or sample vital registration.
5. Other sources (cancer registries, verbal autopsy surveys, etc).
6. No data.

GLOBOCAN presents country-specific incidence and mortality rates for 27 types of cancer and for all cancers (except nonmelanoma skin) combined by sex and for 10 age groups (birth-14, 15-39, 40-44, 45-49,. . .70-74, and 75 years and older). The full GLOBOCAN 2012 database, as well as detailed descriptions of sources and methods used for individual countries, is available online (globocan.iarc.fr).[1] Estimates for the 21 world regions (Fig. 1) and for more and less developed regions are calculated as the population-weighted average of the incidence and mortality rates of the component countries. More developed countries, as defined by the United Nations, include all regions of Europe plus Northern America, Australia/New Zealand, and Japan; less developed countries include all regions of Africa, Asia (excluding Japan), Latin America and the Caribbean, Melanesia, Micronesia, and Polynesia.[7] Rates are age-standardized (per 100,000 person-years) using the World Standard Population as proposed by Segi and modified by Doll et al.[8,9] The cumulative risk of developing or dying of cancer before the age of 75 years (in the absence of competing causes of death) is also calculated and is expressed as a percentage. Although wide variations in the cancer burden occur within regions and countries, data are generally presented here at the regional level for the purpose of providing a summary of global data.

Results and Discussion

Estimated Number of New Cancer Cases and Deaths

An estimated 14.1 million new cancer cases and 8.2 million cancer deaths occurred in 2012 worldwide (Fig. 2). Lung and breast cancer are the most frequently diagnosed cancers and the leading causes of cancer death in men and women, respectively, both overall and in less developed countries. In more developed countries, however, prostate cancer is the most frequently diagnosed cancer among men and lung cancer is the leading cause of cancer death among women. Other frequently diagnosed cancers worldwide include those of the liver, stomach, and colorectum among males and those of the stomach, cervix uteri, and colorectum among females. In more developed countries, bladder cancer among males and uterine cancer among females are also frequently diagnosed. In less developed countries, liver and stomach cancer among men are the second and third most frequently diagnosed cancers, respectively, and leading causes of cancer death.

Less developed countries account for only 57% of cases and 65% of cancer deaths worldwide, in spite of their relatively larger share of the population. This is largely because of the younger age structure, immaturity of the tobacco epidemic, and competing causes of death, such as infection, in less developed countries. However, the burden of cancer will continue to shift to less developed countries due to growth and aging of the population and increasing prevalence of known risk factors.[10]

Incidence and Mortality Rates for All Cancers Combined and Leading Cancer Sites

Prostate, colorectal, female breast, and lung cancer incidence rates can be several times higher in more developed countries compared with less developed countries (Table 1). Liver, stomach, and cervical cancers are more common in less developed countries; these cancers are predominantly attributable to infection, which accounts for 77%, 75%, and 100% of cases worldwide, respectively.[11] In general, cancer rates are higher in more developed regions. For example,

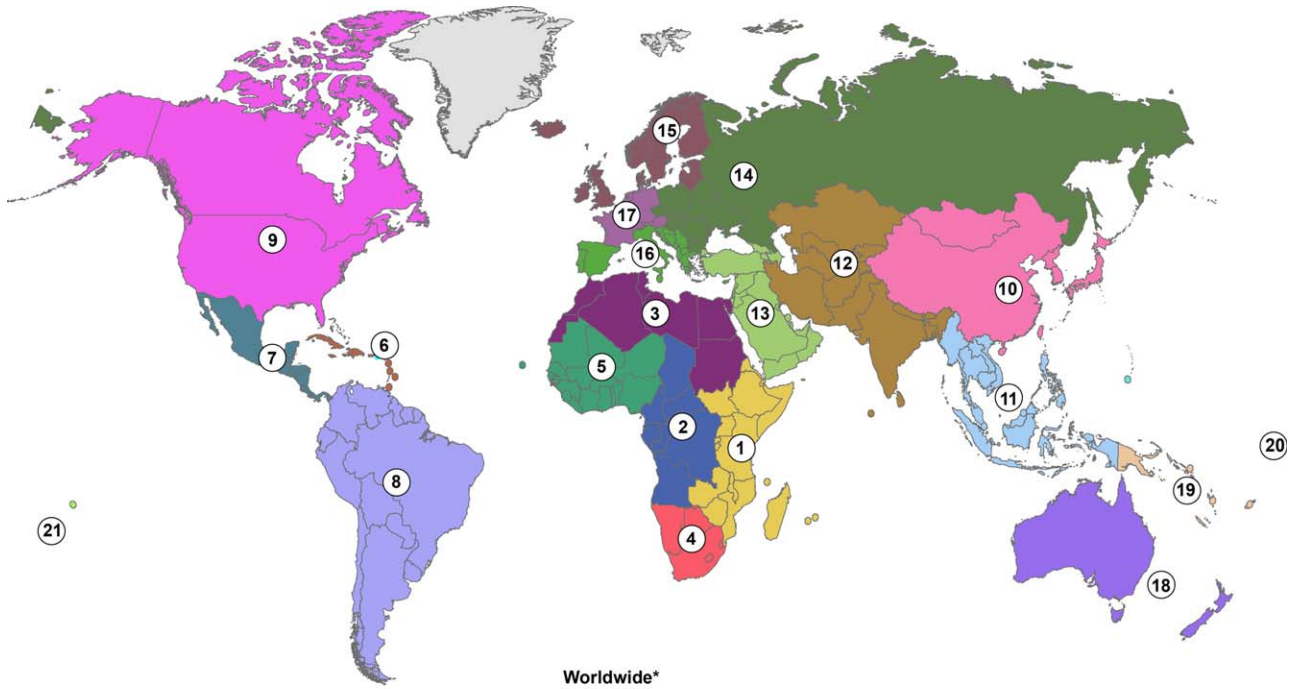

FIGURE 1. Estimated Number of New Cancer Cases in 21 World Areas, 2012.
*Region estimates do not sum to the worldwide estimate due to calculation method.
Source: GLOBOCAN 2012.

the all-sites cancer incidence rate for both sexes combined in Western Europe is more than twice as high as that in Eastern Africa (Table 2).

Although incidence rates for all cancers combined are twice as high in more developed compared with less developed countries, mortality rates are only 8% to 15% higher in more developed countries. This disparity primarily reflects differences in cancer profiles and/or the availability of treatment. For example, liver cancer, a highly fatal cancer, is much more common in less developed countries, thus contributing disproportionately to the overall cancer mortality rate in these countries. Similarly, cancers are more often detected at a later stage in less developed countries (Fig. 3), which contributes to the disparity.

Selected Cancers

Female breast cancer

Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death among females worldwide, with an estimated 1.7 million cases and 521,900 deaths in 2012 (Fig. 2). Breast cancer alone accounts for 25% of all cancer cases and 15% of all cancer deaths among females. More developed countries account for about one-half of all breast cancer cases and 38% of deaths. Rates are generally high in Northern America, Australia/New Zealand, and Northern and Western Europe; intermediate in Central and Eastern Europe, Latin America, and the Caribbean; and low in most of Africa and Asia (Fig. 4). International variation in breast cancer incidence rates reflects differences in the availability of early detection as well as risk factors. Risk factors for breast cancer include reproductive and hormonal factors such as a long menstrual history, recent use of oral contraceptives, and never having children.[12] Giving birth to children and breastfeeding decrease the risk of breast cancer.[12] Potentially modifiable risk factors include weight gain after age 18 years, being overweight or obese (for postmenopausal breast cancer), use of menopausal hormone therapy (combined estrogen and progestin), physical inactivity, and alcohol consumption.[12,13]

Between 1980 and the late 1990s, breast cancer incidence rates rose approximately 30% in Western countries, likely because of changes in reproductive factors and the use of menopausal hormone therapy and more recently because of increased screening.[14] Declining incidence rates in the early 2000s have been attributed to the reduced use of menopausal

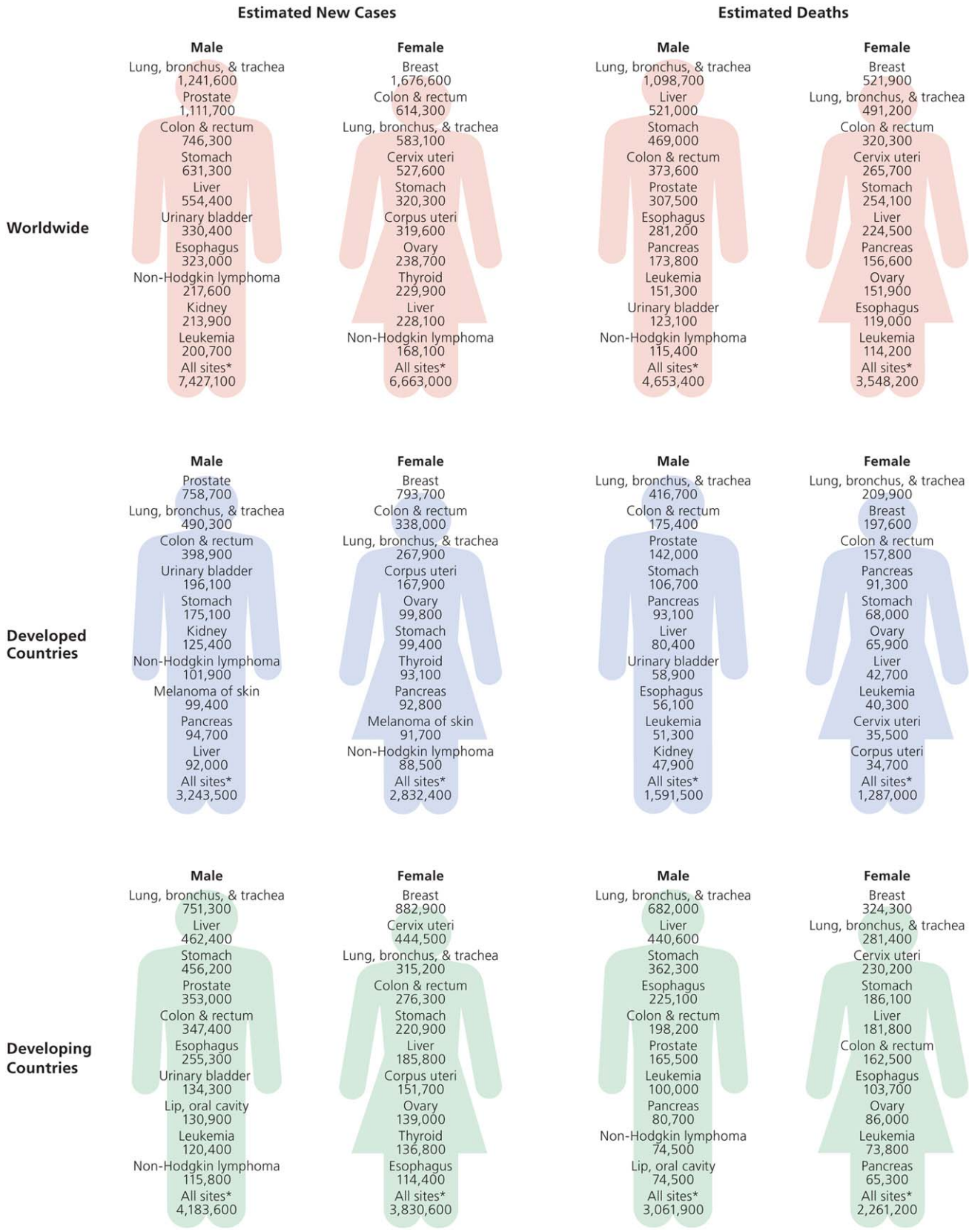

FIGURE 2. Estimated New Cancer Cases and Deaths Worldwide by Sex and Level of Economic Development.
*Excluding non-melanoma skin cancers.
Source: GLOBOCAN 2012.

hormone therapy in countries where it was formerly common, such as the United States, the United Kingdom, France, and Australia.[15-20] Beyond changes in menopausal hormone therapy use, declining or stable incidence rates in Western countries may also be due to plateaus in participation in mammographic screening.[21] In contrast, breast cancer death rates have been stable or decreasing since around 1990 in Northern America and higher-resource European countries. These reductions have been attributed to early detection through mammography and improved treatment,[14] although the respective contributions of each are unclear.[22-24] Breast cancer incidence rates have been rising

TABLE 1. Incidence and Mortality Rates and Cumulative Probability of Developing Cancer by Age 75 Years by Sex and Cancer Site for More Developed and Less Developed Areas, 2012

	MORE DEVELOPED AREAS				LESS DEVELOPED AREAS			
	INCIDENCE		MORTALITY		INCIDENCE		MORTALITY	
	ASR	CUMULATIVE RISK, % (AGED BIRTH TO 74 YEARS)	ASR	CUMULATIVE RISK, % (AGED BIRTH TO 74 YEARS)	ASR	CUMULATIVE RISK, % (AGED BIRTH TO 74 YEARS)	ASR	CUMULATIVE RISK, % (AGED BIRTH TO 74 YEARS)
Males								
All cancers* (C00-97, but C44)	308.7	30.9	138.0	14.3	163.0	16.6	120.1	12.0
Bladder (C67)	16.9	2.0	4.5	0.4	5.3	0.6	2.6	0.3
Brain, nervous system (C70-72)	5.9	0.6	4.0	0.4	3.3	0.3	2.6	0.3
Colorectum (C18-21)	36.3	4.3	14.7	1.6	13.7	1.6	7.8	0.8
Esophagus (C15)	6.4	0.8	5.2	0.6	10.1	1.2	9.0	1.0
Gallbladder (C23-24)	2.3	0.3	1.5	0.2	2.0	0.2	1.6	0.2
Hodgkin lymphoma (C81)	2.3	0.2	0.4	0.0	0.8	0.1	0.4	0.0
Kaposi sarcoma (C46)	0.3	0.0	0.0	0.0	0.9	0.1	0.6	0.1
Kidney (C64-66)	12.6	1.5	4.2	0.5	3.4	0.4	1.7	0.2
Larynx (C32)	5.1	0.6	2.2	0.3	3.5	0.4	2.0	0.2
Leukemia (C91-95)	8.8	0.9	4.6	0.5	4.4	0.4	3.7	0.3
Lip, oral cavity (C00-08)	7.0	0.8	2.3	0.3	5.0	0.6	2.8	0.3
Liver (C22)	8.6	1.0	7.1	0.8	17.8	2.0	17.0	1.8
Lung (C33-34)	44.7	5.4	36.8	4.4	30.0	3.3	27.2	2.9
Melanoma of skin (C43)	10.2	1.1	2.0	0.2	0.8	0.1	0.4	0.0
Multiple myeloma (C88, C90)	3.3	0.4	1.8	0.2	1.0	0.1	0.8	0.1
Nasopharynx (C11)	0.6	0.1	0.2	0.0	2.0	0.2	1.3	0.2
Non-Hodgkin lymphoma (C82-85, C96)	10.3	1.1	3.5	0.4	4.3	0.5	2.8	0.3
Other pharynx (C09-10, C12-14)	4.7	0.6	2.2	0.3	2.8	0.3	2.2	0.3
Pancreas (C25)	8.6	1.0	8.3	1.0	3.3	0.4	3.2	0.4
Prostate (C61)	69.5	8.8	10.0	0.8	14.5	1.7	6.6	0.6
Stomach (C16)	15.6	1.9	9.2	1.0	18.1	2.1	14.4	1.6
Testis (C62)	5.2	0.4	0.3	0.0	0.7	0.1	0.3	0.0
Thyroid (C73)	3.6	0.4	0.3	0.0	1.4	0.1	0.4	0.0

TABLE 1. Continued

	MORE DEVELOPED AREAS				LESS DEVELOPED AREAS			
	INCIDENCE		MORTALITY		INCIDENCE		MORTALITY	
	ASR	CUMULATIVE RISK, % (AGED BIRTH TO 74 YEARS)	ASR	CUMULATIVE RISK, % (AGED BIRTH TO 74 YEARS)	ASR	CUMULATIVE RISK, % (AGED BIRTH TO 74 YEARS)	ASR	CUMULATIVE RISK, % (AGED BIRTH TO 74 YEARS)
Females								
All cancers* (C00-97, but C44)	240.6	23.3	86.2	9.0	135.8	13.4	79.8	8.1
Bladder (C67)	3.7	0.4	1.1	0.1	1.5	0.2	0.7	0.1
Brain, nervous system (C70-72)	4.4	0.4	2.7	0.3	2.7	0.3	1.9	0.2
Breast (C50)	74.1	8.0	14.9	1.6	31.3	3.3	11.5	1.2
Cervix uteri (C53)	9.9	0.9	3.3	0.3	15.7	1.6	8.3	0.9
Colorectum (C18-21)	23.6	2.7	9.3	1.0	9.8	1.1	5.6	0.6
Corpus uteri (C54)	14.7	1.8	2.3	0.3	5.5	0.6	1.5	0.2
Esophagus (C15)	1.2	0.1	0.9	0.1	4.1	0.5	3.6	0.4
Gallbladder (C23-24)	2.0	0.2	1.4	0.1	2.4	0.3	2.0	0.2
Hodgkin lymphoma (C81)	1.9	0.2	0.3	0.0	0.5	0.0	0.3	0.0
Kaposi sarcoma (C46)	0.1	0.0	0.0	0.0	0.5	0.0	0.3	0.0
Kidney (C64-66)	6.2	0.7	1.7	0.2	1.8	0.2	0.9	0.1
Larynx (C32)	0.6	0.1	0.2	0.0	0.4	0.1	0.3	0.0
Leukemia (C91-95)	5.8	0.5	2.8	0.3	3.2	0.3	2.6	0.3
Lip, oral cavity (C00-08)	2.6	0.3	0.6	0.1	2.5	0.3	1.4	0.2
Liver (C22)	2.7	0.3	2.5	0.3	6.6	0.7	6.4	0.7
Lung (C33-34)	19.6	2.4	14.3	1.7	11.1	1.2	9.8	1.0
Melanoma of skin (C43)	9.3	0.9	1.2	0.1	0.7	0.1	0.3	0.0
Multiple myeloma (C88, C90)	2.2	0.3	1.2	0.1	0.7	0.1	0.6	0.1
Nasopharynx (C11)	0.2	0.0	0.1	0.0	0.8	0.1	0.5	0.1
Non-Hodgkin lymphoma (C82-85, C96)	7.1	0.8	2.0	0.2	2.8	0.3	1.8	0.2
Other pharynx (C09-10, C12-14)	0.8	0.1	0.3	0.0	0.7	0.1	0.5	0.1
Ovary (C56)	9.1	1.0	5.0	0.6	5.0	0.5	3.1	0.4
Pancreas (C25)	5.9	0.7	5.5	0.6	2.4	0.3	2.3	0.3
Stomach (C16)	6.7	0.8	4.2	0.4	7.8	0.9	6.5	0.7
Thyroid (C73)	11.1	1.1	0.4	0.0	4.7	0.5	0.7	0.1

ASR indicates age-standardized rate per 100,000. Rates are standardized to the World Standard Population.

*Excludes nonmelanoma skin cancer.

Source: GLOBOCAN 2012.

TABLE 2. Estimated Age-Standardized Incidence and Mortality Rates Per 100,000 by World Area, 2012*

	INCIDENCE			MORTALITY		
	MALE	FEMALE	OVERALL	MALE	FEMALE	OVERALL
Eastern Africa	120.7	154.7	137.8	103.8	110.5	106.5
Middle Africa	91.8	110.7	100.8	82.3	82.3	81.2
Northern Africa	133.5	127.7	129.7	99.9	75.7	86.8
Southern Africa	210.3	161.1	177.5	136.5	98.7	112.5
Western Africa	78.7	112.4	95.3	68.5	75.7	71.6
Eastern Asia	225.4	151.9	186.0	159.3	80.2	117.7
South-Central Asia	98.4	103.3	100.1	74.8	64.7	69.3
South-Eastern Asia	147.6	132.6	138.2	114.1	79.5	94.8
Western Asia	192.8	150.2	168.2	129.3	81.3	103.0
Caribbean	207.7	168.0	185.4	119.8	87.7	102.0
Central America	125.8	141.9	133.6	76.6	72.1	73.7
North America	344.2	295.4	315.6	123.2	91.7	105.5
South America	206.7	180.6	190.6	118.0	88.4	101.2
Central and Eastern Europe	260.0	193.5	216.1	173.4	91.6	123.4
Northern Europe	298.4	263.9	277.4	126.2	94.4	108.2
Southern Europe	297.6	220.4	253.6	137.9	78.9	105.2
Western Europe	343.7	263.7	298.7	131.3	83.6	105.0
Australia/New Zealand	365.3	277.9	318.5	115.3	82.6	97.6
Melanesia	152.1	182.1	164.7	117.9	118.5	116.4
Micronesia	202.1	146.3	171.4	106.8	55.8	79.7
Polynesia	226.4	181.6	200.7	125.7	93.3	108.1

*Excludes nonmelanoma skin cancer

Source: GLOBOCAN 2012.

in many countries in South America, Africa, and Asia.[25] The reasons are not completely understood but likely reflect changing reproductive patterns, increasing obesity, decreasing physical activity,[26] and some breast cancer screening activity.[14] Mortality rates in these countries are also increasing,[27] most likely due to lifestyle changes associated with westernization compounded by the delayed introduction of effective breast cancer screening programs and, in some cases, limited access to treatment.[27,28]

Maintaining a healthy body weight, increasing physical activity, and minimizing alcohol intake are the best available strategies to reduce the risk of developing breast cancer.[29] Mammography can often detect breast cancer at an early stage, when treatment is more effective and a cure is more likely. However, mammography screening is not perfect. Not all breast cancers will be detected by a mammogram, and some breast cancers that are screen-detected still have a poor prognosis. Sometimes mammography results in false-positive results, as well as overdiagnosis and overtreatment of some breast cancers. In spite of these limitations, numerous studies have shown that early detection with mammography saves lives and increases treatment options. However, implementation of population-based, organized mammography screening programs may be cost-prohibitive in many less developed countries and is only recommended for those countries with a good health infrastructure that can afford long-term screening programs. Otherwise, the recommended early detection strategies are awareness of early signs and symptoms and screening by clinical breast examination.[30]

Colorectal cancer

Colorectal cancer is the third most commonly diagnosed cancer in males and the second in females, with an estimated 1.4 million cases and 693,900 deaths occurring in 2012 (Fig. 2). The highest incidence rates are in Australia/New Zealand, Europe, and Northern America (Fig. 5). Rates are low in Africa and South-Central Asia. Rates are higher in men than in women in most parts of the world.

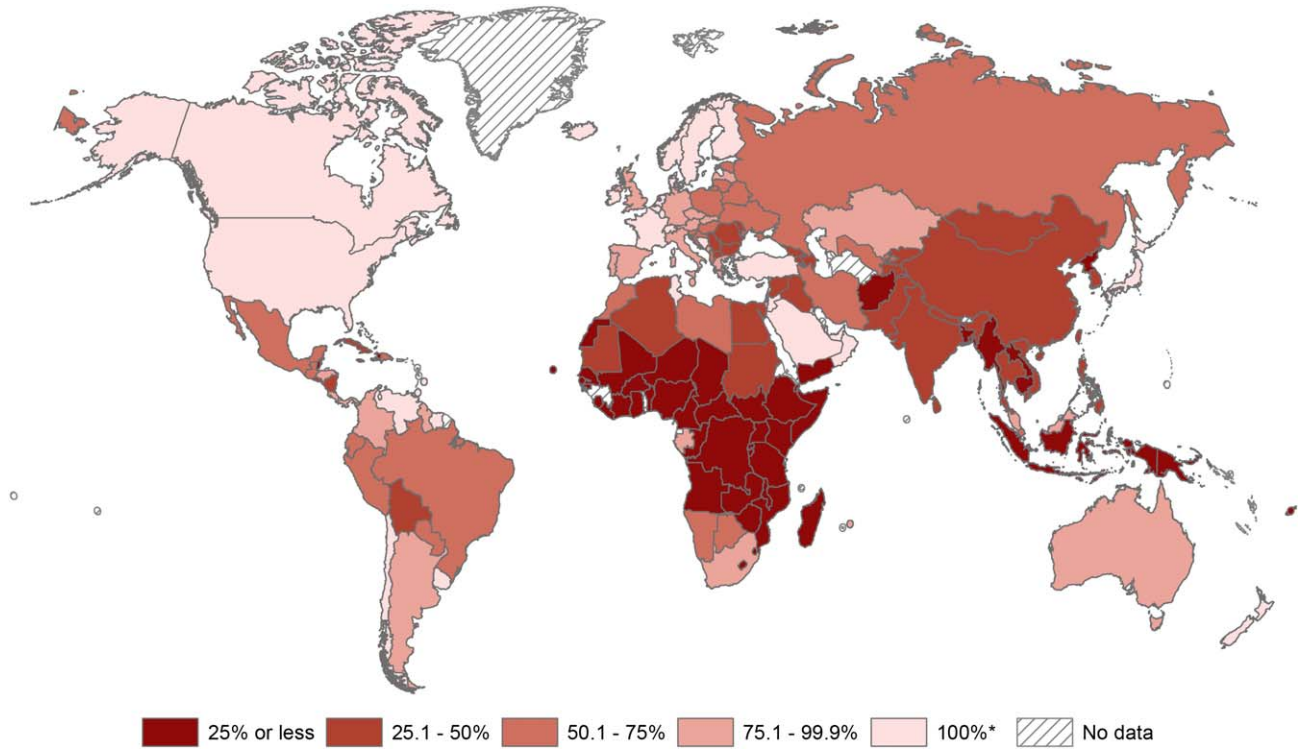

FIGURE 3. Estimated Percentage of Patients Able to Access Radiotherapy, 2013.
*Countries with 100% of patients able to access radiotherapy may also include countries where radiotherapy supply is greater than demand, although disparities in access may still exist within these countries.
Source: The Cancer Atlas, second edition, as obtained from the International Atomic Energy Agency.

The incidence of colorectal cancer is increasing in certain countries where risk has been historically low, most notably in Western Asia (Kuwait and Israel) and Eastern Europe (Czech Republic and Slovakia).[31] Trends in high-risk/high-income countries have varied over the past 20 years; for example, rates gradually increased in Finland and Norway, stabilized in France and Australia, and declined in the United States. The decrease in colorectal cancer incidence in the United States is confined to those aged 50 years and older, which primarily reflects the increase in screening and removal of precancerous adenomas.[32] The increase in several Asian and Eastern European countries may reflect an increased prevalence of risk factors for colorectal cancer, including unhealthy diet, obesity, and smoking.[33]

In contrast to incidence trends, decreasing colorectal cancer mortality rates have been observed in a large number of countries worldwide and are most likely attributed to colorectal cancer screening, reduced prevalence of risk factors, and/or improved treatments.[32,34] However, increases in mortality rates are still occurring in countries that have more limited resources and increasing incidence, including Brazil and Chile in South America and Romania and Russia in Eastern Europe.[35,36]

Preventive measures for colorectal cancer include maintaining a healthy body weight, being physically active, minimizing consumption of red and processed meat and alcohol, and avoidance of smoking.[37-39] Screening can detect colorectal polyps that can be removed before they become cancerous, as well as detect cancer at an early stage when treatment is usually less extensive and more successful. There are several accepted screening options (eg, the guaiac-based fecal occult blood test [FOBT], the immunochemical FOBT [or fecal immunochemical test], flexible sigmoidoscopy, stool DNA test, computed tomography [CT] colonography ["virtual colonoscopy"], double-contrast barium enema, and colonoscopy), although some of these options are less feasible for lower-resource areas. Although colonoscopy is a highly sensitive screening method, it requires a skilled examiner, involves greater cost, is less convenient, and has more risk for the patient compared with other tests.[40] FOBT, which is inexpensive and easy to perform, is a more practical screening option in many parts of the world.[33] Population-based colorectal screening programs may not be recommended in many less developed countries where the incidence of the disease is not yet sufficiently high to merit screening programs.[43] However, future attention should also be focused on the many areas of the developing world with a growing and aging population and an increasingly westernized lifestyle. For example, a colorectal cancer screening program using

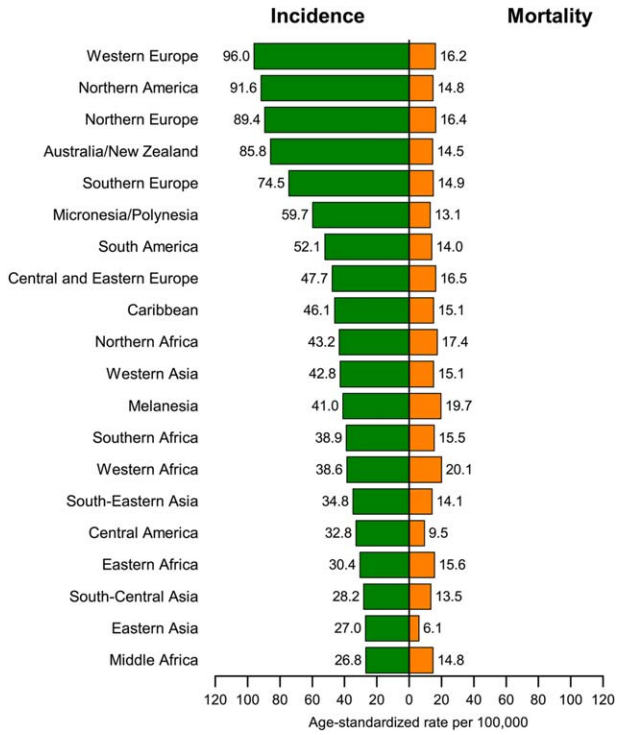

FIGURE 4. Breast Cancer Incidence and Mortality Rates by World Area.

the fecal immunochemical test was recently piloted in Thailand, where colorectal cancer incidence is increasing.[44]

Lung cancer

An estimated 1.8 million new lung cancer cases occurred in 2012, accounting for about 13% of total cancer diagnoses. Lung cancer was the most frequently diagnosed cancer and the leading cause of cancer death among males in 2012 (Fig. 2). Among females, lung cancer was the leading cause of cancer death in more developed countries, and the second leading cause of cancer death in less developed countries. In men, the highest lung cancer incidence rates were in Europe, Eastern Asia, and Northern America, and the lowest rates were in sub-Saharan Africa (Fig. 6). Among women, the highest lung cancer rates were in Northern America, Northern and Western Europe, Australia/New Zealand, and Eastern Asia (Fig. 6). Lung cancer rates in Chinese women (20.4 cases per 100,000 women) were higher than rates among women in some European countries despite a lower prevalence of smoking. This is thought to reflect indoor air pollution from unventilated coal-fueled stoves and cooking fumes.[45] Other known risk factors for lung cancer include exposure to occupational and environmental carcinogens such as asbestos, arsenic, radon, and polycyclic aromatic hydrocarbons.[46] Recently, outdoor pollution has also been determined to cause lung cancer.[47] More than one-half of the lung cancer deaths attributable to ambient fine particles were projected to have been in China and other East Asian countries.[48]

International variations in lung cancer rates and trends largely reflect differences in the stage and degree of the tobacco epidemic.[49-51] In several Western countries, such as the United States, the United Kingdom, and Denmark, where the tobacco epidemic began earliest and peaked around the middle of the last century, lung cancer mortality rates have been decreasing in men and plateauing in women.[52-55] Lung cancer rates are also decreasing in men, but continuing to increase in women, in countries where the tobacco epidemic peaked later, such as Spain and Hungary.[55] In contrast, in countries where the epidemic has been established more recently and smoking has just peaked or continues to increase, such as China, Indonesia, and several countries in Africa, lung cancer rates are likely to continue to increase at least for the next few decades, barring interventions to accelerate smoking cessation and avoid initiation.[51,56,57]

Lung cancer is one of the most preventable cancers. Most lung cancers could be avoided by eliminating smoking initiation and increasing smoking cessation among current smokers. This requires a comprehensive tobacco control program that includes raising the price of tobacco products through excise taxes, banning smoking in public places and tobacco sales to minors, restricting tobacco advertising and promotion, counteradvertising, and providing treatment and counseling for tobacco dependence. In the United States, comprehensive tobacco control programs in many states, including California and New York, have markedly decreased smoking rates and accelerated the reduction in

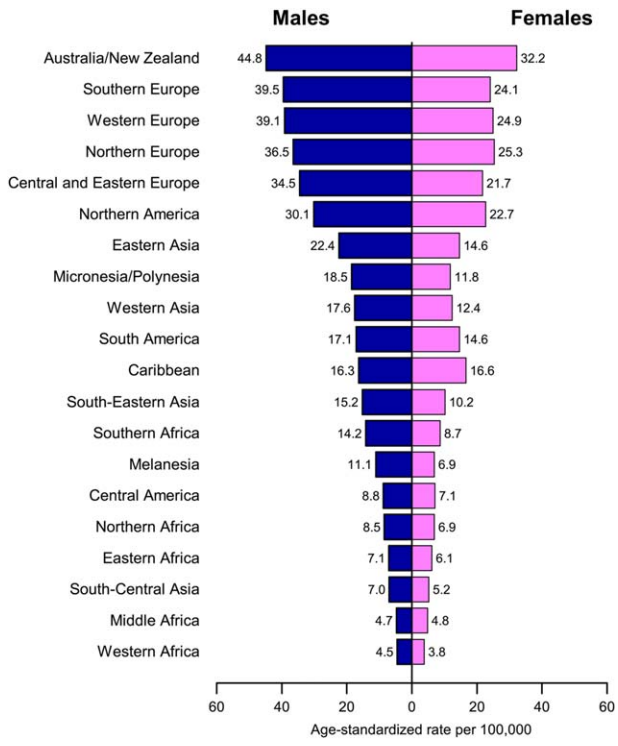

FIGURE 5. Colorectal Cancer Incidence Rates by Sex and World Area.

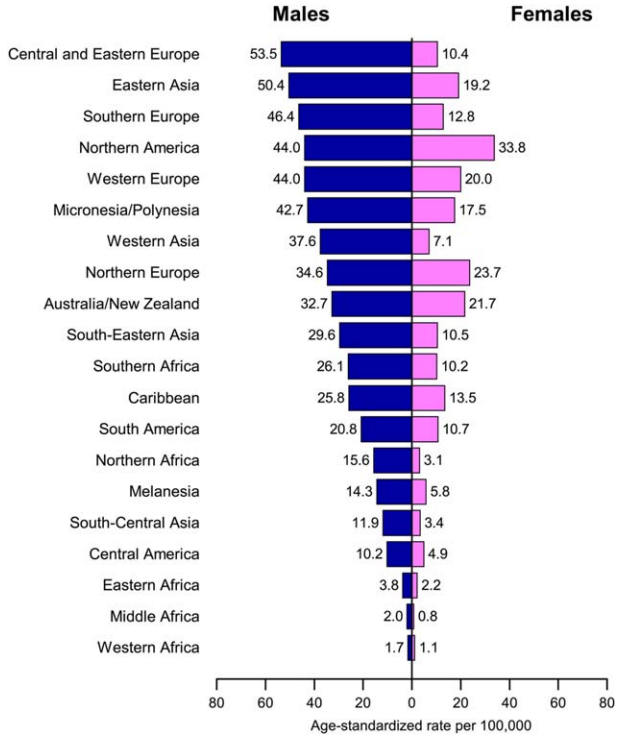

FIGURE 6. Lung Cancer Incidence Rates by Sex and World Area.

lung cancer occurrence.[58,59] In the developing world, many of the most populous countries, such as China and India, are in the earlier stages of the tobacco epidemic.[60] If these and other less developed countries take swift action to promote smoking cessation and prevent initiation, they can attenuate future lung cancer rates and avoid the extraordinary burden of smoking-related diseases experienced in more developed countries.

Results from the National Lung Screening Trial, a clinical trial in the United States designed to determine the effectiveness of lung cancer screening in high-risk individuals, showed 16% to 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.[61] However, it is unknown whether these results are relevant for individuals who have smoked less. In addition, there are limitations and risks associated with screening, including a high rate of false-positive results, cumulative radiation exposure from multiple CT scans, and unnecessary lung biopsy and surgery. These potential harms may be substantially greater in settings that lack access to high-quality screening.[62] The WHO also recommends that effective treatment capable of reducing morbidity and mortality should be available if screening is implemented.[63] As a result, screening likely will not benefit those in low-resource countries in the near future.

Prostate cancer

Prostate cancer is the second most frequently diagnosed cancer in men worldwide, with 1.1 million new cases estimated to have occurred in 2012 (Fig. 2). It is the most frequently diagnosed cancer among men in more developed countries, where about two-thirds of all prostate cancer cases occur among just 17% of the world's male population. Incidence rates vary by more than 25-fold worldwide, and are highest in Australia/New Zealand, Northern America, Northern and Western Europe, and some Caribbean nations, and lowest in Asia (Fig. 7). Much of the variation reflects differences in the use of prostate-specific antigen (PSA) testing.[64] Prostate cancer is the fifth leading cause of cancer death worldwide, with the highest mortality rates found in the Caribbean and Southern and Middle Africa. The reason for the high prostate cancer risk among some populations of African descent is still poorly understood, although it may in part reflect differences in genetic susceptibility.[64,65]

Incidence trends in countries with higher uptake of PSA testing, such as Australia, Canada, and the United States, follow a consistent pattern, with a rapid rise in the incidence of prostate cancer noted in the early 1990s, soon after the introduction of PSA testing, followed by a sharp decline.[64,66] In other high-income countries with more gradual adoption of PSA testing, such as many countries in Western Europe, the dramatic peak in incidence is not observed, although rates continue to increase.[64] Rates are also increasing in some countries where PSA testing began later or remains uncommon, such as the United Kingdom, Japan, and Thailand.[64]

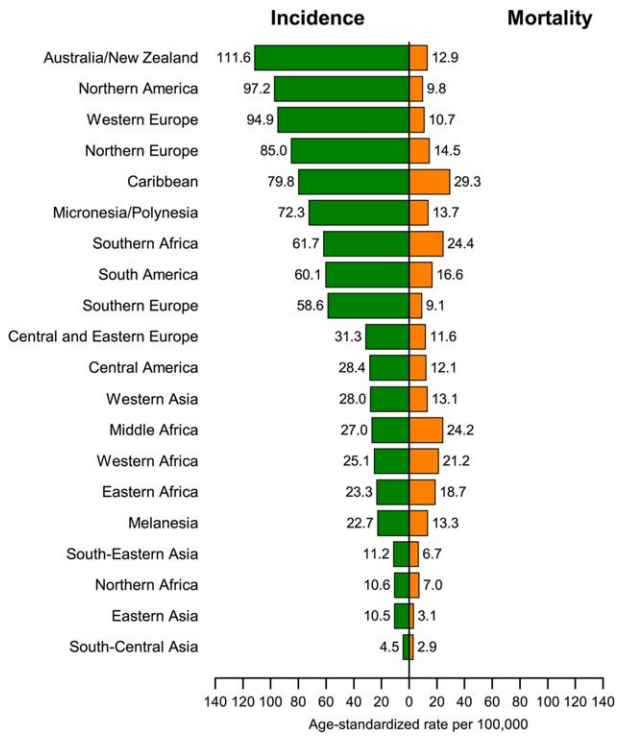

FIGURE 7. Prostate Cancer Incidence and Mortality Rates by World Area.

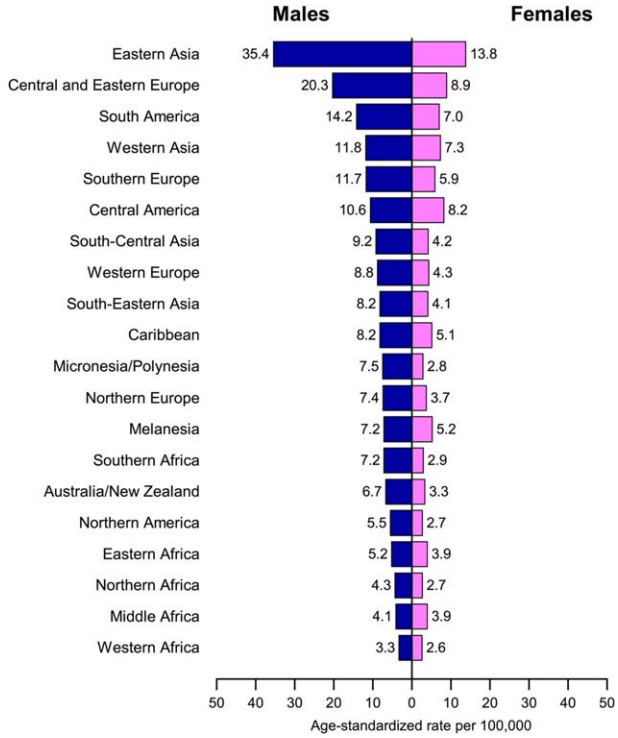

FIGURE 8. Stomach Cancer Incidence Rates by Sex and World Area.

Death rates for prostate cancer have been decreasing in the majority of more developed countries, including those in Northern America, Oceania, and Northern and Western Europe.[64] This decrease has been attributed mainly to improved treatment and/or early detection, although the specific contribution of PSA testing is debated.[64] Studies are ongoing to clarify the impact of PSA screening on prostate cancer death rates.[67] In contrast, mortality rates are rising in some Asian and Central and Eastern European countries, such as Korea, China (Hong Kong), and Russia.[64] The increase is postulated to reflect risk factors associated with economic development, including an increased consumption of animal fat, obesity, and physical inactivity.[64]

There are few known modifiable risk factors for prostate cancer. The chemoprevention of prostate cancer is an active area of research.[68] Routine PSA screening is no longer recommended for men at average risk given the large potential for serious side effects associated with prostate cancer treatment and concerns about frequent overdiagnosis, estimated at 23% to 42% for screen-detected cancers.[69] Studies are underway to evaluate new tests for prostate cancer that could distinguish more aggressive cancers from those less likely to be lethal, to identify men at higher risk of developing prostate cancer, and to enable more efficient use of PSA testing.[67] For example, a recent study found that stopping screening at age 70 years prevents approximately one-half of avoidable deaths from prostate cancer, while greatly reducing the rate of overdiagnosis.[70]

Stomach cancer

An estimated 951,600 new stomach cancer cases and 723,100 deaths occurred in 2012 (Fig. 2). Stomach cancer rates are generally about twice as high in men as in women and vary widely across countries. In general, incidence rates are highest in Eastern Asia (particularly in Korea, Mongolia, Japan, and China), Central and Eastern Europe, and South America and lowest in Northern America and most parts of Africa (Fig. 8). Regional variations in part reflect differences in dietary patterns, food storage, and the availability of fresh produce, as well as the prevalence of *Helicobacter pylori* infection.[71] Chronic infection with *H. pylori* is the strongest identified risk factor for stomach cancer, with about 90% of new cases of noncardia gastric cancer worldwide attributed to this bacteria.[72]

A steady decline in stomach cancer incidence and mortality rates has been observed in the majority of more developed countries in Northern America and Europe since the middle of the 20th century.[73,74] Similar decreasing trends have been noted in more recent years in areas with historically high rates, including several countries in Asia (Japan, China, and Korea), Latin America (Colombia and Ecuador), and Europe (Ukraine).[75] Factors that have contributed to these declines are thought to include the increased availability of fresh fruits and vegetables, decreased reliance on salt-preserved foods, and reduction in chronic *H. pylori* infection due to improved sanitation and antibiotics.[71] In more developed countries, decreases in smoking prevalence may also account for some of the decline.[27,75] Although stomach cancer is declining overall, adenocarcinoma of the gastric cardia is increasing in North America and Europe and is thought to be related to increased obesity and perhaps improvement in classification.[27]

The primary prevention strategies for stomach cancer include reducing intake of foods preserved by salting, pickling, or smoking; increasing consumption of fresh fruits and vegetables; not smoking; and reducing the prevalence of *H. pylori* infection through the improvement of socioeconomic conditions. Screening for and eradication of *H. pylori* using antibiotics has been shown to reduce the risk of stomach cancer in recent randomized trials.[76] Although this approach requires further study in additional settings and populations, it could represent a promising intervention for the prevention of stomach cancer.

Liver cancer

Liver cancer is much more common in men than in women. In men, it is the second leading cause of cancer death worldwide and in less developed countries (Fig. 2). In more developed countries, it is the sixth leading cause of cancer death among men. An estimated 782,500 new liver cancer cases and 745,500 deaths occurred worldwide during 2012, with China alone accounting for about 50% of the total

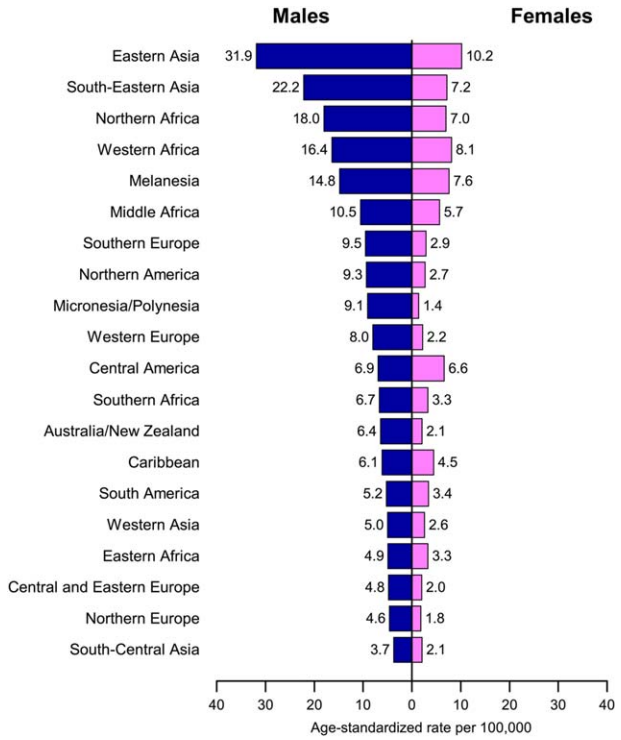

FIGURE 9. Liver Cancer Incidence Rates by Sex and World Area.

number of cases and deaths. Liver cancer rates are the highest in East and South-East Asia and Northern and Western Africa and lowest in South-Central Asia and Northern, Central, and Eastern Europe (Fig. 9). Most (70% to 90%) primary liver cancers occurring worldwide are hepatocellular carcinoma.[77] Cholangiocarcinomas that arise primarily from the epithelial lining of the bile duct (intra- and extrahepatic bile duct) are rare in most parts of the world, but have high incidence rates in Thailand and other parts of Asia due to the high prevalence of liver fluke infection.[78]

The high hepatocellular carcinoma rates in parts of Asia and sub-Saharan Africa largely reflect the elevated prevalence of chronic hepatitis B virus (HBV) infection, with over 5% of the populations in these regions chronically infected with the virus.[79] HBV and hepatitis C virus (HCV) account for an estimated 32% of infection-related cancer cases, mostly liver cancer, in less developed countries and 19% in more developed countries.[11] 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), is also a risk factor in less developed countries; however, the contribution of aflatoxin exposure to the liver cancer burden in these countries is unknown.[80] Other risk factors that are more common in Western countries include obesity, type 2 diabetes, cirrhosis related to heavy alcohol consumption, nonalcoholic fatty liver disease (associated with obesity), and smoking.[81,82]

Liver cancer incidence is increasing in areas with historically low rates, including parts of Oceania, Western Europe, and Northern America. In the United States, age-adjusted incidence rates of liver cancer more than tripled between 1975 and 2011, rising from 2.6 per 100,000 to 8.6 per 100,000 (adjusted to the 2000 US standard population).[83] This increase is thought to be attributable to increases in chronic HCV infection due to injection drug abuse, which was common in the 1960s and 1970s, or possibly increases in the prevalence of obesity and diabetes mellitus.[82,84] In contrast, liver cancer rates are decreasing in some historically high-risk areas, including China and Japan, most likely due to reductions in HCV infection in Japan and HBV infection in China through improved hygiene and sanitation.[85] A more than 80% decline in liver cancer incidence rates among youth and young adults in Taiwan has been reported as a result of a universal HBV childhood vaccination program that began in 1984.[86] However, HBV vaccination programs cannot be responsible for the decreasing liver cancer rates noted among adults in most parts of Asia because of their relatively recent implementation.

The primary causes of liver cancer can be prevented through public health measures, including vaccination, sanitary medical practices, healthy lifestyle choices, and environmental management strategies. A vaccine that protects against HBV has been available since 1982. The WHO recommends that all countries include the HBV vaccine in routine infant immunization programs. By the end of 2012, a total of 183 countries had introduced the HBV vaccine into their national infant immunization schedules, with many countries achieving more than 80% coverage for the full recommended dose (Fig. 10). In contrast, no vaccine is available against HCV, although new antiviral therapies may prevent chronic infection among those with acute infection. 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 less developed countries due to resource constraints. Among individuals who are already infected with HBV or HCV, a reduction in the risk of liver cancer has been shown with the use of antiviral treatments.[82,87] However, these treatments may be costly and unfeasible in many low-resource countries.[82] The US Centers for Disease Control and Prevention recommends a one-time test for HCV infection for all adults born between 1945 and 1965 because this birth cohort accounts for three-quarters of both HCV-infected individuals and HCV-related deaths in the United States.[88]

Effective preventive strategies also include limiting alcohol consumption and avoiding smoking. Other approaches to reduce liver cancer in less economically developed countries include reducing aflatoxin contamination of foods and

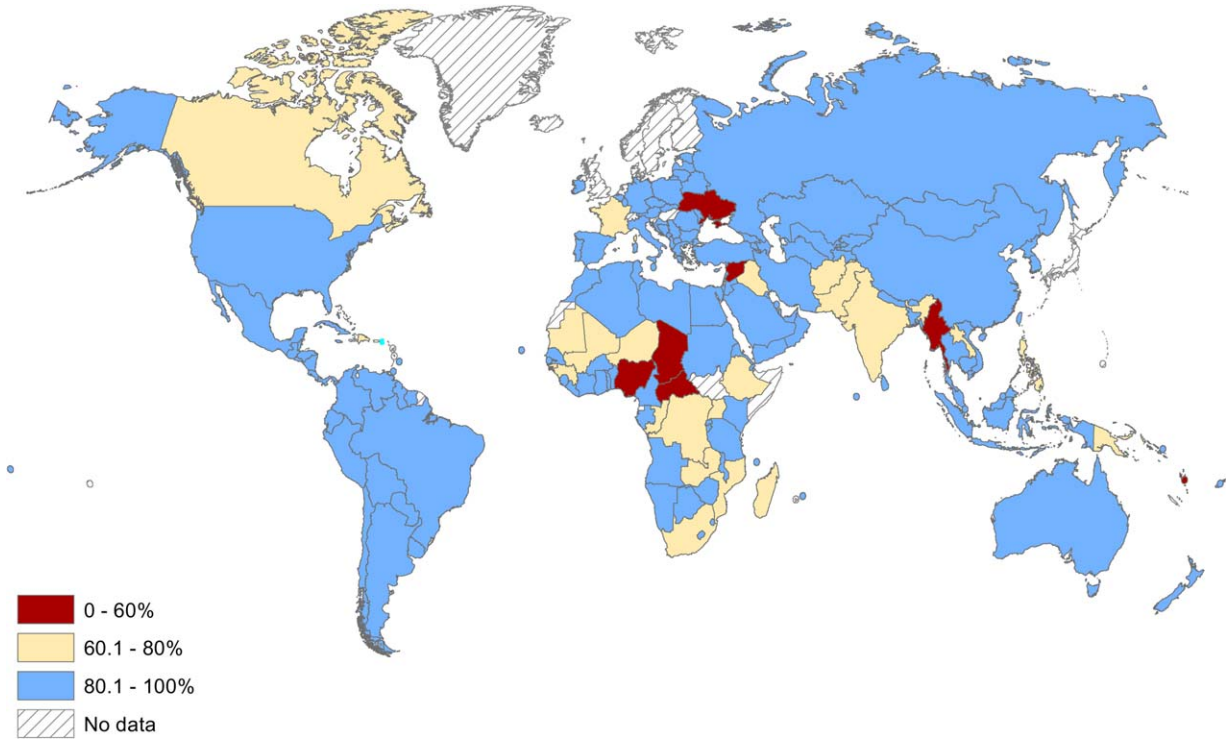

FIGURE 10. Percentage of One-Year-Olds Given the Three-Series Hepatitis B Vaccination*, 2012.
*Countries with no data may represent countries where hepatitis B is not endemic (e.g., Scandinavian countries) and national hepatitis B vaccination programs have not been introduced.
Source: World Health Organization. Global Health Observatory Data Repository, Hepatitis B (HepB3) Immunization Coverage of 1-year-olds, Data by Country, 1985-2013 [online database]. Available from: apps.who.int/ghodata/. Accessed November 14, 2014.

preventing and treating parasitic liver fluke infections. Crop substitution and improved grain storage practices have been used to reduce contamination with aflatoxin in areas such as sub-Saharan Africa. Mass drug administration for liver fluke infection and public health campaigns may contribute to the prevention of cholangiocarcinoma.[89,90]

Cervical cancer

There were an estimated 527,600 new cervical cancer cases and 265,700 deaths worldwide in 2012 (Fig. 2). It is the second most commonly diagnosed cancer and third leading cause of cancer death among females in less developed countries. Incidence rates are highest in sub-Saharan Africa, Latin America and the Caribbean, and Melanesia and lowest in Western Asia, Australia/New Zealand, and Northern America (Fig. 11). Nearly 90% of cervical cancer deaths occurred in developing parts of the world: 60,100 deaths in Africa, 28,600 in Latin America and the Caribbean, and 144,400 in Asia. India, the second most populous country in the world, accounted for 25% of cervical cancer deaths (67,500 deaths). In Eastern, Middle, and Southern Africa, as well as Melanesia, cervical cancer is the leading cause of cancer death in females. The large geographic variation in cervical cancer rates reflects differences in the availability of screening, which allows for the detection and

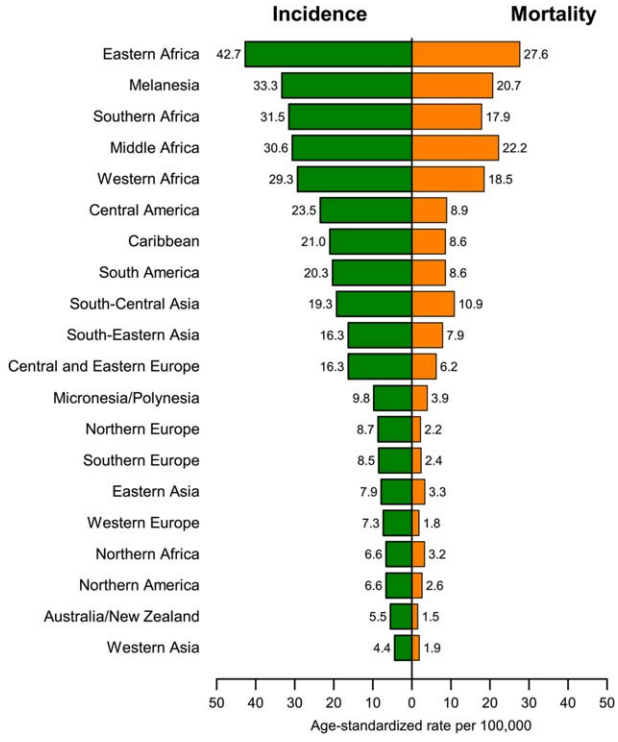

FIGURE 11. Cervical Cancer Incidence and Mortality Rates by World Area.

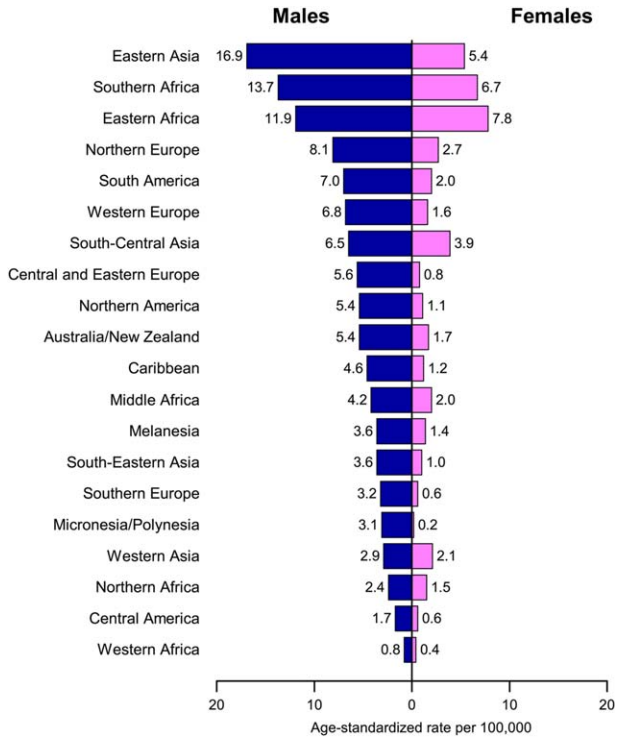

FIGURE 12. Esophageal Cancer Incidence Rates by Sex and World Area.

removal of precancerous lesions, and human papillomavirus (HPV) infection prevalence.[91-93] HPV infection prevalence (all types) varies widely, from as high as 21% in Africa and 16% in Latin America and the Caribbean to 9% in Asia and 5% in Northern America.[92]

In several Western countries, where screening programs have long been established, cervical cancer rates have decreased by as much as 65% over the past 40 years. For example, in Norway, cervical cancer incidence rates decreased from 18.7 per 100,000 in 1970 to 9.6 per 100,000 in 2011.[94] Rates have also decreased in some high-incidence areas, including Colombia, the Philippines, and India, likely due to increased awareness and improved socioeconomic conditions.[93] In contrast to favorable overall trends, cervical cancer rates are reported to be rising in Uganda and in some countries of Eastern Europe (Estonia, Lithuania, and Bulgaria).[93] Most affected are younger women in several countries, including many in Europe, Central Asia, Japan, and China[91,95]; this cohort-driven trend is thought to reflect increases in high-risk HPV prevalence from changing sexual behaviors.[93]

There are 2 vaccines (Gardasil [Merck and Company, Whitehouse Station, NJ] and Cervarix [GlaxoSmithKline, Brentford, UK]) available for protection against the 2 types of HPV that cause most (70%) cervical cancers. In economically less developed countries, the major barrier to widespread use is the high cost of the vaccine; however, GAVI, the Vaccine Alliance, has negotiated lower prices for these countries and began rolling out HPV vaccination demonstration projects in supported countries in 2013.[96] It is extremely important that all women, even those who have been vaccinated, continue to be screened, because HPV vaccines cannot protect against established infections, nor do they protect against all of the types of HPV that cause cervical cancer.

Many low-resource countries do not have the technical and public health infrastructure to support Papanicolaou testing, the most common screening tool for cervical cancer in more developed countries. The most efficient and cost-effective screening techniques in low-resource countries include visual inspection using acetic acid and HPV tests.[97] A clinical trial in rural India found that a single round of HPV testing reduced the number of cervical cancer deaths by about 50%.[98]

Esophageal cancer

An estimated 455,800 new esophageal cancer cases and 400,200 deaths occurred in 2012 worldwide (Fig. 2). Esophageal cancer incidence rates vary internationally by more than 21-fold. The highest rates are found in Eastern Asia and in Eastern and Southern Africa and the lowest rates are found in Western Africa (Fig. 12). Esophageal cancer is usually 3 to 4 times more common among men than women. The 2 main types of esophageal cancer are squamous cell carcinoma and adenocarcinoma. In the highest-risk area, often referred to as the "esophageal cancer belt," which stretches from Northern Iran through the Central Asian republics to North-Central China, 90% of cases are squamous cell carcinomas, compared with about 26% in the United States (among white individuals).[83,99,100] In high-risk areas such as Golestan (Iran) and Linxan (China), contributing risk factors are not well understood, but are thought to include poor nutritional status, low intake of fruits and vegetables, and drinking beverages at high temperatures.[101-104] HPV infection has been detected in squamous cell carcinomas, particularly in high-risk areas in Asia. However, more research is needed to determine whether HPV or other infectious agents increase risk.[105-108] The primary risk factors for squamous cell carcinoma in Western countries are alcohol and tobacco use, which account for almost 90% of total cases.

The main known risk factors for esophageal adenocarcinoma are overweight and obesity and chronic gastroesophageal reflux disease (GERD). GERD can cause metaplastic changes to the esophagus, referred to as Barrett esophagus, that predispose to dysplasia and adenocarcinoma. However, only a small percentage of those with Barrett esophagus go on to develop esophageal cancer.[109] GERD is most common in overweight men and women. Smoking and low intake of fruits and vegetables are also risk factors for adenocarcinoma of the esophagus.

Temporal trends in esophageal cancer vary greatly. For example, although incidence rates of esophageal squamous cell carcinoma have been increasing in some Asian countries,

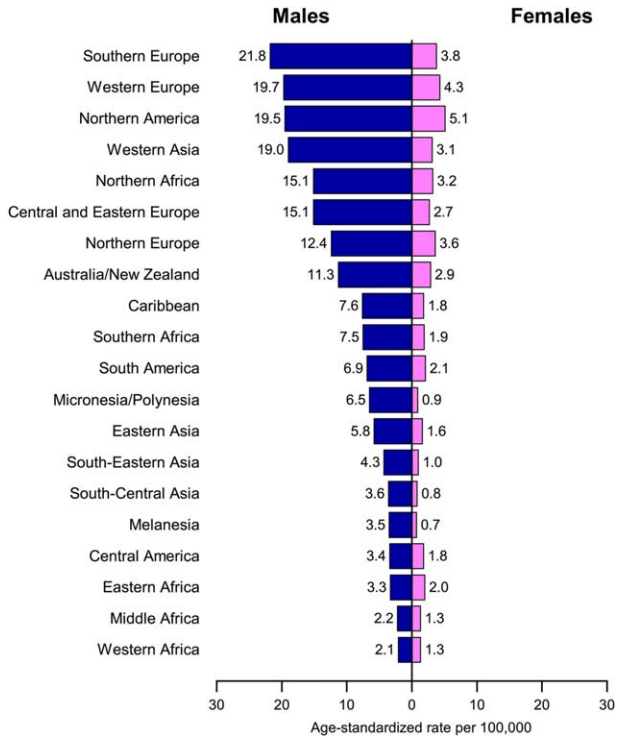

FIGURE 13. Urinary Bladder Cancer Incidence Rates by Sex and World Area.

such as Taiwan,[110] they have been steadily declining in Northern America and Europe due to reductions in alcohol and tobacco use.[111-113] In contrast, the incidence of adenocarcinoma of the esophagus has been increasing rapidly in Western countries such as the United States, Australia, France, and England in recent decades, most likely as a result of increases in the prevalence of overweight/obesity, chronic GERD, and Barrett esophagus.[114] This trend may also be related to the declining prevalence of *H. pylori* infection, which may protect against esophageal adenocarcinoma.[115-117]

Preventive measures for esophageal cancer include maintaining a healthy body weight, eliminating the use of tobacco, reducing alcohol consumption, and being physically active. 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 esophagus is a feasible method to reduce esophageal cancer mortality.[118,119] Treating gastric reflux with proton pump inhibitor drugs or surgery may prevent Barrett esophagus and esophageal cancer, although once Barrett esophagus has developed, preventive measures have not been shown to prevent esophageal cancer.[114] Further risk factor studies are necessary to elucidate primary prevention measures in high-risk areas (Northern Iran and Central Asia) because the prevalence of established major risk factors for esophageal cancer is low in those regions.

Urinary Bladder cancer

An estimated 429,800 new cases of bladder cancer and 165,100 deaths occurred in 2012 worldwide (Fig. 2). The majority of bladder cancer occurs in men, and there is about a 10-fold variation in incidence rates internationally. Incidence rates are highest in Europe, Northern America, Western Asia, and Northern Africa, and lowest in Eastern, Middle, and Western Africa (Fig. 13). Some of the geographic variation is due to differences in the reporting of low-grade tumors (ie, noninvasive lesions detected with endoscopy).[120] The highest mortality among men is in Turkey, where the estimated death rate in 2012 (12.8 per 100,000) was 50% higher than the highest rates in Europe (8.3 in Latvia and 8.0 in Poland) and 3 times as high as that in the United States (4.0). Smoking is the most well-established risk factor for bladder cancer, with the risk among smokers reported to be approximately 2-fold to 6-fold that among nonsmokers.[121] Smoking is estimated to cause about 31% of bladder cancer deaths among men and 14% of deaths among women worldwide.[122] In the developing world, particularly Africa and Western Asia, chronic infection with *Schistosoma hematobium* (a parasitic worm that causes urinary schistosomiasis) is associated with an increased risk of bladder cancer. This parasite, which is transmitted through contaminated water, is responsible for an estimated 50% of bladder cancers in some parts of Africa and about 3% of cases worldwide.[71] Bladder cancers caused by schistosomiasis usually have a different histology (squamous cell carcinoma) compared with those associated with smoking (transitional cell carcinoma).

Bladder cancer incidence rates have been declining or stable in most Western countries over the past decades after a prior period of increase. International incidence patterns across countries are difficult to interpret due to differences in the reporting of low-grade tumors. In the United States, mortality rates in males decreased from 1975 through 1987 and have subsequently stabilized, whereas in females rates have been decreasing since 1975.[123] In most countries of Europe and in urban China, declines have been observed since the 1990s.[35,124] In Latin America and the Caribbean, mortality has been largely stable.[120] Decreasing mortality trends in Western countries largely reflect reductions in smoking prevalence.[120]

The best measures for bladder cancer prevention are not smoking, increasing the intake of fruits and vegetables, and schistosomiasis control and treatment. In Egypt, schistosomiasis control has substantially reduced the burden of bladder cancer, which was once the most common cancer in Egyptian men.[120] There is currently no screening method recommended for individuals at average risk.

Non-Hodgkin lymphoma

An estimated 385,700 new cases of non-Hodgkin lymphoma (NHL) and 199,700 deaths occurred in 2012 (Fig. 2). NHL encompasses a wide variety of disease subtypes for which incidence patterns vary. NHL is more common in more developed areas, with the highest incidence rates found

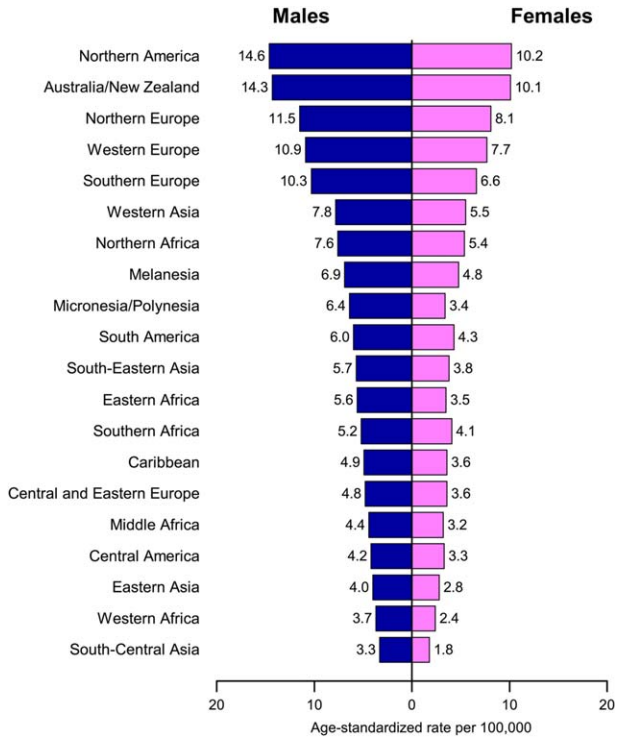

FIGURE 14. Non-Hodgkin Lymphoma Incidence Rates by Sex and World Area.

in Australia, Western and Northern Europe, and Northern America. The lowest rates are found in Asia and Eastern Europe (Fig. 14). In general, the incidence of NHL is low in Africa, with the exception of some sub-Saharan areas (particularly East Africa) because of the high incidence of Burkitt lymphoma (a subtype of NHL) among children. Most of the few known risk factors for lymphoma are associated with altered immune function. NHL risk is elevated in individuals who receive immune suppressants to prevent organ transplant rejection; those with severe autoimmune conditions; and individuals infected with the human immunodeficiency virus (HIV), human T-cell leukemia virus type I, and probably HCV. NHL is classified as an acquired immune deficiency syndrome (AIDS)- defining illness, and the risk is 60 times greater among patients with AIDS compared with the general population.[125] Epstein-Barr virus (EBV) is linked causally to Burkitt lymphoma and a number of autoimmune-related NHLs.

The incidence of NHL increased in the majority of more developed countries up to around 1990 and leveled off thereafter.[123,126] Although the increase may be due in part to improvements in diagnostic procedures and changes in classification, much of the trend may reflect a true increase in disease occurrence.[127] In the United States, some of the NHL increase noted throughout the 1980s, particularly among white males, has been attributed to the onset of the AIDS epidemic, whereas the decline after 1990 likely reflects the declining incidence of HIV infection and the success of antiretroviral therapies (ART). Non-AIDS-associated NHL subtypes continued to increase or stabilize during this time period.[128] In less developed countries, the incidence of NHL is increasing in some populations, also likely due in part to the AIDS epidemic. Recent decreases among young adults in these same populations may also reflect the use of ART.[129,130]

Cancers of the lip and oral cavity

An estimated 300,400 new cases and 145,400 deaths from oral cavity cancer (including lip cancer) occurred in 2012 worldwide (Fig. 2). The highest rates are found in Melanesia, South-Central Asia, and Central and Eastern Europe, whereas the lowest are in Western Africa and Eastern Asia (Fig. 15). Smoking, alcohol use, smokeless tobacco use, and HPV infection are the major risk factors for oral cavity cancer, with smoking and alcohol having synergistic effects.[131,132] The contribution of each of these risk factors to the burden varies across regions.[45] Smoking is estimated to account for about 71% of deaths from oral cavity cancer (including pharynx) in high-income countries and 37% of deaths in low-income and middle-income countries, whereas alcohol is estimated to account for about 33% and 14% of deaths, respectively.[133] Smokeless tobacco products and betel quid with or without tobacco are the major risk factors for oral cavity cancer in Taiwan, India, and other neighboring countries.[45,134,135]

Over the past several decades, oral cavity cancer incidence rates have decreased significantly among both males and females in Asia, Northern America, and Australia, and among males in Southern and Western Europe. Rates increased among both males and females in several countries

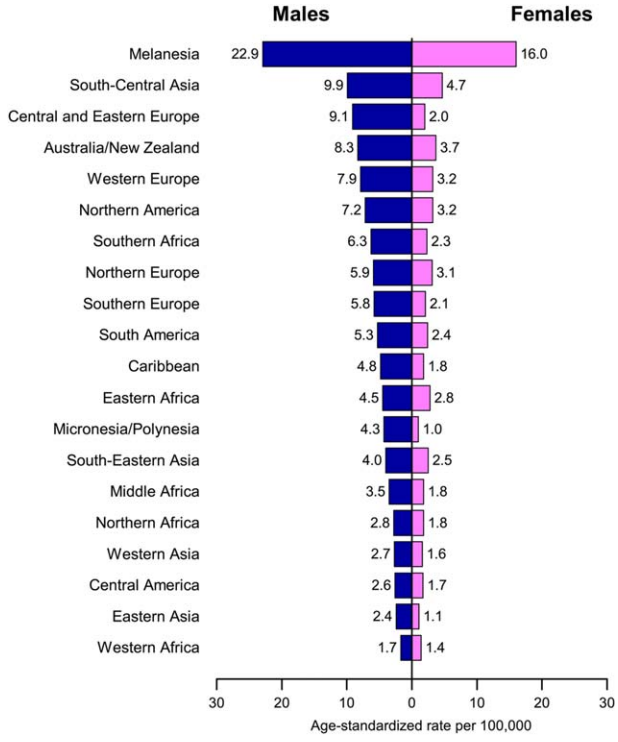

FIGURE 15. Oral Cavity Cancer Incidence Rates by Sex and World Area.

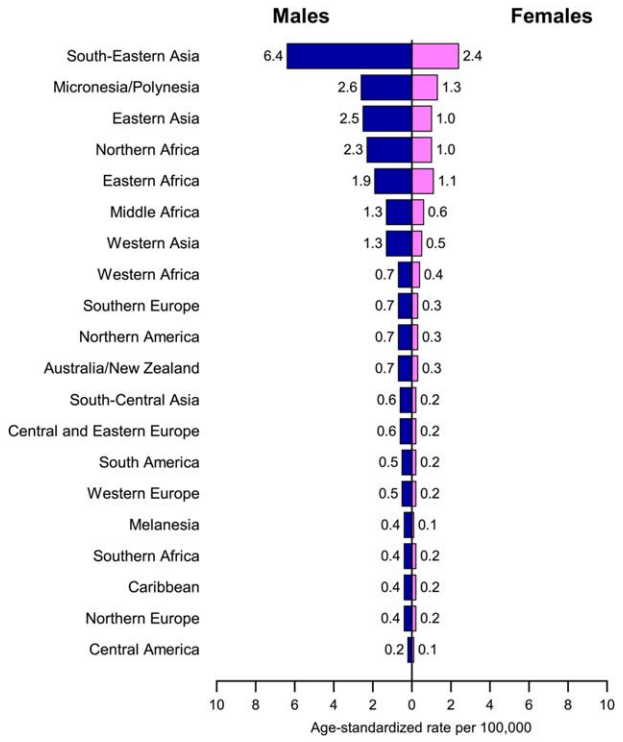

FIGURE 16. Nasopharyngeal Cancer Incidence Rates by Sex and World Area.

of Eastern and Northern Europe and among females in Southern and Western Europe,[136] which largely reflects the ongoing tobacco epidemic. This contrasts with the decreasing trends at all ages noted in both males and females in many other more developed countries, where the tobacco epidemic began and declined earlier. However, incidence rates for oral cancer sites related to HPV infections (ie, oropharynx, tonsil, and base of the tongue) are increasing in some of these countries, which is hypothesized to be in part due to changes in oral sexual behavior.[137-139]

Nasopharyngeal cancer

The term nasopharyngeal carcinoma (NPC) is used here as a surrogate for nasopharyngeal cancers (*International Classification of Diseases, 10th revision* code C11), given that carcinomas represent the vast majority of nasopharyngeal tumors. There were an estimated 86,700 new cases of NPC and 50,800 deaths in 2012 (Fig. 2). Although this disease may be considered one of the rarer forms of cancer globally, it is notable for its high incidence in select geographic and ethnic populations.

NPC is about 2 to 3 times higher in males than in females in both more and less developed countries (Table 1) (Fig. 16). The geographical disparities in the burden of NPC in relation to resource are noteworthy, with an estimated 92% of new cases occurring in economically less developed countries. Incidence rates are highest in South-Eastern Asia (at least double those in every other area) (Fig. 16); the disease is the sixth most common cancer among males in this region. Globally, the 3 highest national incidence rates are estimated to be in Malaysia, Indonesia, and Singapore, where rates are high among the Chinese and Malay populations.[4] Elsewhere in Asia, high incidence rates are observed in a number of provinces in South-Eastern China, including Guangdong and Hong Kong, and in other parts of Southern Asia (the Philippines, India, and Thailand).[40,41] Rates are also elevated in Micronesia/Polynesia, Eastern Asia, and Northern Africa (Fig. 16), particularly in Tunisia and Algeria.[141] Other populations where rates of NPC are relatively high include the Inuit populations of Alaska, Greenland, and North Canada, as well as Chinese and Filipinos living in the United States.[142] Rates of this malignancy are considerably lower in most populations living elsewhere within the Americas and Europe (Fig. 16).

The etiology of NPC appears to have viral, environmental, and genetic components.[143,144] Migrants from high- to low-risk countries retain incidence rates intermediate to natives of their host country and their country of origin,[145] implicating a role for environmental as well as genetic factors, and a possible interaction with EBV. Although the virus is considered an important step in NPC progression, only a fraction of the EBV-infected population develops the disease. Moreover, infection with the virus is considered both lifelong and ubiquitous in most areas of the world.[146]

Many studies have reported increased risks associated with certain foods eaten within high-risk areas, including salted fish, certain preserved foods, and hot spices, all of which are high in nitroso compounds and volatile nitrosamines.[143] Consumption of these foods in early life may be important because it coincides with the timing of EBV infection.[147] Although trends in NPC have been reported as reasonably stable in high-risk areas of Southern China,[148] declines have been observed in several populations of Chinese origin over the past 2 decades.[149-151] NPC in higher-resource settings is associated more with smoking and alcohol use; the decreasing smoking prevalence among US males, for example, has been postulated as a contributor to the overall decline in NPC incidence.[152]

Kaposi sarcoma

Kaposi sarcoma (KS) is a cancer of cells that line lymph and blood vessels. It differs from most other cancers in that it is multifocal in origin, growing in several areas of the body at once. Before the AIDS epidemic, KS was regarded as extremely rare with the exception of certain populations of Mediterranean, Middle Eastern, or Eastern European descent (predominantly males aged older than 50 years)[153] and, more notably, sub-Saharan African populations.[154,155] The African form of KS (sometimes termed "endemic") is diagnosed at younger ages than has been the case in European

TABLE 3. Estimated Number of Cases and Age-Standardized Incidence Rates for Kaposi Sarcoma in Regions of Sub-Saharan Africa

	MALES		FEMALES	
	NUMBER OF CASES	INCIDENCE RATE (PER 100,000)	NUMBER OF CASES	INCIDENCE RATE (PER 100,000)
Eastern Africa*	19,800	15.1	11,100	7.6
Southern Africa†	2,200	7.6	1,400	4.7
Middle Africa‡	500	1.2	200	0.4
Western Africa§	1,100	0.9	900	0.6
Sub-Saharan Africa	23,600	7.2	13,600	3.7

*Burundi, Comoros, Djibouti, Eritrea, Ethiopia, La Reunion (France), Kenya, Madagascar, Malawi, Mozambique, Rwanda, Somalia, South Sudan, Tanzania, Uganda, Zambia, and Zimbabwe.

†Botswana, Lesotho, Namibia, South Africa, and Swaziland.

‡Angola, Cameroon, Central African Republic, Chad, Democratic Republic of Congo, Republic of Congo, Republic of Equatorial Guinea, and Gabon.

§Benin, Burkina Faso, Cape Verde, Cote d'Ivoire, The Gambia, Ghana, Guinea-Bissau, Guinea, Liberia, Mali, Mauritania, Niger, Nigeria, Senegal, Sierra Leone, and Togo.

Source: GLOBOCAN 2012.

populations and affects proportionally more females, although the male-to-female ratio may still be as high as 9 to 1.[155,156] KS is also diagnosed in immunosuppressed patient populations, including transplant recipients and, especially, individuals infected with HIV. The diagnosis of KS is regarded as AIDS-defining in those who are HIV positive, and for many years KS was the most common cancer observed in patients with AIDS and, in part, initially defined the AIDS epidemic.[157] However, since the advent of ART for HIV in the 1990s, this is no longer the case. In populations where ART is readily available to those infected with HIV, KS has again become a rare diagnosis.[158] Due to the limited availability of ART, this is not the case in much of sub-Saharan Africa, where KS is one of the most common forms of cancer and is even diagnosed in young children[159]; the provision of ART to those in need is, however, improving.[160]

KS is rare in many areas of the world, but it is one of the most common cancers in sub-Saharan Africa. This region accounted for 84% of KS cases worldwide in 2012, with an estimated 23,600 cases in males and 13,600 cases in females (Table 3). The corresponding estimated age-standardized incidence rates were 7.2 and 3.7 per 100,000, respectively. The majority of cases occurred in Eastern Africa in both males (19,800 cases) and females (11,100 cases), with age-standardized incidence rates (per 100,000) of 15.1 in males and 7.6 in females. KS was, therefore, the most common cancer in males and the third most common in females (after cervical and breast cancers) in Eastern Africa. The countries of Southern Africa had the highest rates of KS (7.6 and 4.7 per 100,000, respectively) after Eastern Africa, followed by Middle Africa (1.2 and 0.4 per 100,000, respectively) and Western Africa (0.9 and 0.6 per 100,000, respectively). Outside of sub-Saharan Africa, the highest rates of KS were in Israel (1.5 cases per 100,000), French Guyana (1.3), Portugal (0.8), Colombia (0.7), and Italy (0.6).[1] The KS in these populations represents a mix of pre-AIDS era and HIV-associated forms.

It is now evident that the KS-associated herpes virus (human herpes virus type 8 [HHV-8]) is the major cause of KS but generally requires immunosuppressive conditions in which to function pathogenically.[161] HHV-8 infection is common in sub-Saharan Africa, in those European populations at higher risk of KS, and in all HIV transmission high-risk groups.[161] Dual HIV and HHV-8 positivity increases the risk of KS by more than 1000-fold.[162] Those areas of Africa where endemic KS and HHV-8 infection have been historically common have seen a rapid increase in the incidence of KS since the onset of the HIV epidemic. However, recent decreases have been documented in Uganda and Zimbabwe, especially among younger men, likely due to improvements in the provision of ART, as well as HIV prevention activities.[163]

Limitations

The global and region-specific estimates presented here are aggregated from those for 184 countries or territories, together with a set of methods based on the availability of cancer incidence and mortality data at the country or regional level. Therefore, it should be emphasized that the estimates presented in GLOBOCAN 2012 are variable in accuracy, depending on the extent and validity of available data, ranging from real and valid counts of cases and deaths to estimates based on samples or neighboring rates. Around 2005, about 21% of the world's population was covered by

PBCR[164] and one-third was covered by mortality schemes based on medically certified deaths.[6] A scoring system to indicate the accuracy and quality of the estimate has been developed to help users evaluate the data presented for each country in GLOBOCAN; these scores can be accessed on the GLOBOCAN Web site (globocan.iarc.fr). It should be noted that the quality and availability of data are improving over time, driven in many cases by initiatives to develop cancer incidence and mortality registration. Despite its limitations, the GLOBOCAN 2012 estimates are the best cancer data available and are a legitimate basis for establishing priorities for cancer control actions in different regions and countries of the world.

Conclusions

Cancer constitutes an enormous burden worldwide that is expected to increase due to the growth and aging of the population and because of the adoption of behaviors and lifestyle factors known to cause cancer. Economically less developed countries are experiencing an increased frequency of cancers with historically low rates, such as female breast, lung, and colorectal cancers, in addition to a disproportionately high burden of infection-related cancers. A substantial proportion of the worldwide burden of cancer can be prevented through the widespread application of existing cancer control knowledge, including tobacco control, vaccination (for liver and cervical cancers), early detection, and the promotion of physical activity and healthy dietary patterns. Additional suffering and premature death could be alleviated through the application of appropriate treatments and palliative care. Much remains to be learned about the causes of several major malignancies, including prostate, pancreatic, and hematopoietic cancers. A coordinated and intensified response from all sectors of society, including governments, civil society, the private sector, and individuals, is required to seize control of the growing burden of cancer. ■

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