Global Cancer Statistics 2018: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries

Freddie Bray, BSc, MSc, PhD[1]; Jacques Ferlay, ME[2]; Isabelle Soerjomataram, MD, MSc, PhD[3]; Rebecca L. Siegel, MPH[4]; Lindsey A. Torre, MSPH[5]; Ahmedin Jemal, PhD, DVM[6]

[1] Head, Section of Cancer Surveillance, International Agency for Research on Cancer, Lyon, France; [2] Informatics Officer, Section of Cancer Surveillance, International Agency for Research on Cancer, Lyon, France; [3] Deputy Head, Section of Cancer Surveillance, International Agency for Research on Cancer, Lyon, France; [4] Scientific Director, Surveillance and Health Services Research, American Cancer Society, Atlanta, GA; [5] Scientist, Surveillance and Health Services Research, American Cancer Society, Atlanta, GA; [6] Scientific Vice President, Surveillance and Health Services Research, American Cancer Society, Atlanta, GA.

Corresponding author: Freddie Bray, BSc, MSc, PhD, Section of Cancer Surveillance, International Agency for Research on Cancer, 150, cours Albert Thomas, F-69372 Lyon Cedex 08, France; brayf@iarc.fr

DISCLOSURES: Lindsey A. Torre, Ahmedin Jemal, and Rebecca L. Siegel are employed by the American Cancer Society, which received a grant from Merck Inc for intramural research outside the submitted work; however, their salaries are solely funded through American Cancer Society funds. The remaining authors report no conflicts of interest.

doi: 10.3322/caac.21492. Available online at cacancerjournal.com

Abstract: This article provides a status report on the global burden of cancer worldwide using the GLOBOCAN 2018 estimates of cancer incidence and mortality produced by the International Agency for Research on Cancer, with a focus on geographic variability across 20 world regions. There will be an estimated 18.1 million new cancer cases (17.0 million excluding nonmelanoma skin cancer) and 9.6 million cancer deaths (9.5 million excluding nonmelanoma skin cancer) in 2018. In both sexes combined, lung cancer is the most commonly diagnosed cancer (11.6% of the total cases) and the leading cause of cancer death (18.4% of the total cancer deaths), closely followed by female breast cancer (11.6%), prostate cancer (7.1%), and colorectal cancer (6.1%) for incidence and colorectal cancer (9.2%), stomach cancer (8.2%), and liver cancer (8.2%) for mortality. Lung cancer is the most frequent cancer and the leading cause of cancer death among males, followed by prostate and colorectal cancer (for incidence) and liver and stomach cancer (for mortality). Among females, breast cancer is the most commonly diagnosed cancer and the leading cause of cancer death, followed by colorectal and lung cancer (for incidence), and vice versa (for mortality); cervical cancer ranks fourth for both incidence and mortality. The most frequently diagnosed cancer and the leading cause of cancer death, however, substantially vary across countries and within each county depending on the degree of economic development and associated social and life style factors. It is noteworthy that high-quality cancer registry data, the basis for planning and implementing evidence-based cancer control programs, are not available in most low- and middle income countries. The Global Initiative for Cancer Registry Development is an international partnership that supports better estimation, as well as the collection and use of local data, to prioritize and evaluate national cancer control efforts. **CA: A Cancer Journal for Clinicians 2018;0:1-31.**

Keywords: cancer, epidemiology, incidence, survival

Introduction

Noncommunicable diseases (NCDs) are now responsible for the majority of global deaths,[1] and cancer is expected to rank as the leading cause of death and the single most important barrier to increasing life expectancy in every country of the world in the 21st century. According to estimates from the World Health Organization (WHO) in 2015, cancer is the first or second leading cause of death before age 70 years in 91 of 172 countries, and it ranks third or fourth in an additional 22 countries (Fig. 1).

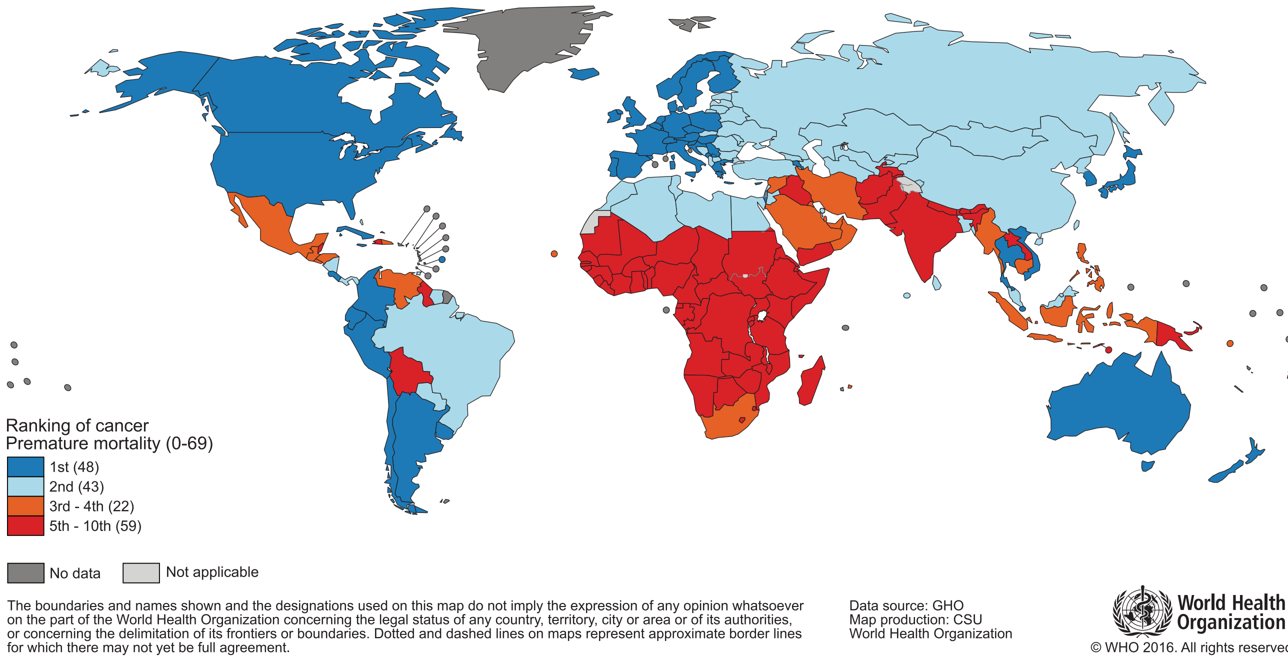

FIGURE 1. Global Map Presenting the National Ranking of Cancer as a Cause of Death at Ages Below 70 Years in 2015. The numbers of countries represented in each ranking group are included in the legend. Source: World Health Organization.

Cancer incidence and mortality are rapidly growing worldwide. The reasons are complex but reflect both aging and growth of the population, as well as changes in the prevalence and distribution of the main risk factors for cancer, several of which are associated with socioeconomic development.[2,3] With rapid population growth and aging worldwide, the rising prominence of cancer as a leading cause of death partly reflects marked declines in mortality rates of stroke and coronary heart disease, relative to cancer, in many countries. The extent to which cancer's position as a cause of premature death reflects national levels of social and economic development can be seen by comparing the maps in Figures 1 and 2A (the latter map depicts the 4-tier Human Development Index [HDI]).

Cancer transitions are most striking in emerging economies, where an increasing magnitude of the disease is paralleled by a changing profile of common cancer types. A recurring observation is the ongoing displacement of infection-related and poverty-related cancers by those cancers that already are highly frequent in the most developed countries (eg, in Europe, North America, and high-income countries in Asia and Oceania). These cancers are often ascribed to a so-called *westernization* of lifestyle,[3–5] yet the differing cancer profiles in individual countries and between regions signify that marked geographic diversity still exists, with a persistence of local risk factors in populations at quite different phases of social and economic transition. This is illustrated by the prominent differences in rates of infection-associated cancers, including cervix, stomach, and liver, observed in countries at opposite ends of the human development spectrum.[4]

Against this backdrop, the current article provides a status report on the cancer burden worldwide in 2018, based on the *GLOBOCAN 2018* estimates of cancer incidence and mortality produced by the International Agency for Research on Cancer (IARC).[6] As in previous reports for 2002,[7] 2008,[8] and 2012,[9] the primary focus is on a description of cancer incidence and mortality at the global level and an assessment of the geographic variability observed across 20 predefined world regions. We describe the magnitude and distribution of the disease overall and for the major cancer types, commenting briefly on the associated risk factors and prospects for prevention of the major cancers observed worldwide. We conclude by stating the limitations of the exercise and the need for population-based national and subnational cancer surveillance data to improve the accuracy of the GLOBOCAN estimates and inform on-the-ground initiatives in cancer control.

Data Sources and Methods

The sources and methods used in compiling the estimates in GLOBOCAN 2018 are described in detail elsewhere[6] and also are available online at the Global Cancer Observatory (gco.iarc.fr). The Global Cancer Observatory website includes facilities for the tabulation and graphical visualization of the GLOBOCAN database for 185 countries and 36 cancers (as well as all cancers combined) by age and sex.

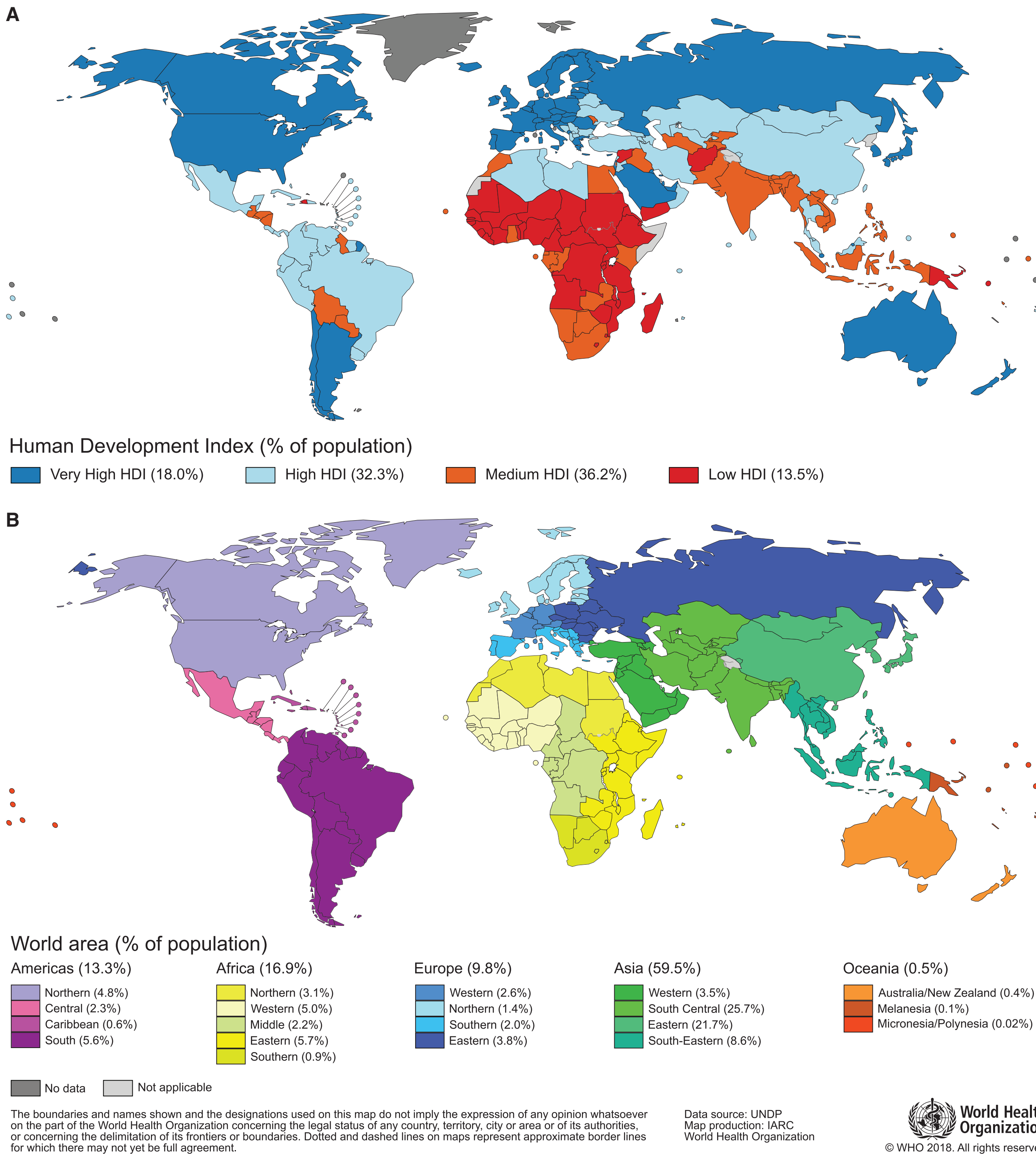

FIGURE 2. Global Maps Present (A) the 4-Tier Human Development Index and (B) 20 Areas of the World. The sizes of the respective populations are included in the legend. Source: United Nations Procurement Division/United Nations Development Program.

The profile of cancer, globally and by world region, is built up in GLOBOCAN using the best available sources of cancer incidence and mortality data within a given country; therefore, validity of the national estimates depends on the degree of representativeness and the quality of source information. The methods used to compile the 2018 estimates are largely based on those developed previously, with an emphasis on the use of short-term predictions and modeling of incidence-to-mortality ratios, where applicable. The list of cancer sites, however, has been extended to 36 cancer types in GLOBOCAN 2018, with one of the major additions being estimates of the incidence of, and mortality from, nonmelanoma skin cancer (NMSC) (excluding basal-cell carcinomas).[6] Together with all cancers combined, cancer-specific estimates are provided for 185 countries or territories worldwide by sex and for 18 age groups (ages birth-4, 5-9, …, 80-84, and >85 years).

The numbers of new cancer cases and cancer deaths were extracted from the GLOBOCAN 2018 database for all cancers combined (International Statistical Classification of Diseases and Related Health Problems-10th Revision codes C00-C97) and for 36 cancer types: lip, oral cavity (C00-C06); salivary glands (C07-C08); oropharynx (C09-C10); nasopharynx (C11); hypopharynx (C12-C13); esophagus (C15); stomach (C16); colon (C18); rectum (C19-C20); anus (C21); liver (C22, including intrahepatic bile ducts); gallbladder (C23-C24, including extrahepatic ducts); pancreas (C25); larynx (C32); lung (C33-C34, including trachea and bronchus); melanoma of the skin (C43); NMSC (C44, excluding basal cell carcinoma for incidence); mesothelioma (C45); Kaposi sarcoma (C46); female breast (C50); vulva (C51); vagina (C52); cervix uteri (C53); corpus uteri (C54); ovary (C56); penis (C60); prostate (C61); testis (C62); kidney (C64-C65, including renal pelvis); bladder (C67); brain, central nervous system (C70-C72); thyroid (C73); Hodgkin lymphoma (C81); non-Hodgkin lymphoma (C82-C86 and C96); multiple myeloma (C88 and C90, including immunoproliferative diseases); and leukemia (C91-C95). For the purposes of consistency with previous exercises,[10] we combine cancers of the colon, rectum, and anus as colorectal cancer (codes C18-C21) and exclude NMSC (C44) when making global comparisons of the magnitude of different cancers; however, NMSC is included in the overall estimation of the total cancer burden, unless otherwise stated.

Incidence is the number of new cases occurring in a specified period and geographic area, conveyed either as an absolute number of cases per annum or as a rate per 100,000 persons per year. Rates are used to approximate the average risk of developing a cancer in the year 2018 and allow comparisons between countries and world regions. Primary prevention strategies aim to reduce this measure, although increasing incidence rates do not necessarily reflect failure in this domain, given that early detection (tests or programs) can result in a transient rise in incidence rates as subclinical cancer cases are discovered. This increase, however, will be maintained if some of the detected cases represent *overdiagnosis* (those cancers that would not otherwise have been diagnosed in an individual's lifetime). Recent illustrations of this phenomenon include prostate cancer in the era of prostate-specific antigen (PSA) testing and thyroid cancer after the introduction of new diagnostic techniques,[11] including ultrasonography.[12]

Incidence data are produced by population-based cancer registries (PBCRs). Although PBCRs may cover national populations, more often they cover subnational areas, such as selected urban areas, particularly in countries undergoing economic development. According to the most recent data compiled in Volume XI of the IARC's *Cancer Incidence in Five Continents*,[13] approximately 15% of the world population was covered by high-quality cancer registries around 2010, with lower registration in South America (7.5% of the total population), Asia (6.5%), and Africa (1%). The coverage in Africa rises to 13% when we consider additional PBCR data from Sub-Saharan African registries in the African Cancer Registry Network (afrcn.org/) that did not meet the criteria for inclusion in *Cancer Incidence in Five Continents*.[13] However, such recorded data from lower resource countries are the only relatively unbiased source of information on the distribution of common cancer types in a defined population and are vital for planning local cancer prevention and control as well as developing national estimates.

Similarly, *mortality* is the number of deaths occurring in a specified region and period, and the mortality rate is the number of deaths per 100,000 persons per year. Mortality is the product of the incidence and the fatality rate (the proportion of patients who die); thus, the mortality rates given in this report measure the average risk of death in the population from a specific cancer in 2018. Mortality data are available in many countries through the WHO, although the degree of detail and quality of the data (both the accuracy of the recorded cause of death and the completeness of registration) vary considerably; currently, only about 1 in 5 countries can report high-quality death registrations. Mortality rates are often used (instead of incidence) as a proxy measure of the risk of acquiring the disease across populations, but this assumes that survival is constant between the populations being compared. This still may be the case for cancers associated with poor prognoses, but it is much less likely for cancers that can be detected early and treated successfully in view of significant variations in the availability of, and access to, cancer care services among populations.

A novel feature of GLOBOCAN 2018 is the inclusion of 95% uncertainty intervals (95% UIs) for the estimated sex-specific and site-specific, all-ages number of new cancer cases and cancer deaths.[6] The 95% UIs take into account uncertainties linked to the extent of geographic coverage of the cancer registry and death registration (because the data used in the estimation may be subregional rather than national), the timeliness of data reporting (because the data come from years before 2018), and the quality of data (because the completeness and accuracy of the data are variable, depending on the source).

Age-standardized rates (ASRs) per 100,000 person-years are calculated using the direct method and the world standard population.[14] The cumulative risk of developing or dying from cancer before age 75 years, assuming the absence of competing causes of death, also was calculated using the age-specific rates and is expressed as a percentage. Both of these indicators allow comparisons between populations that are not influenced by differences in their age structures.

We present the incidence and mortality rates globally and for 20 aggregated regions, as defined by the United Nations Population Division (Fig. 2B). We also characterize the burden according to the HDI, which was created by the United Nations Development Program to highlight the importance of national policy decisions beyond economic growth in assessing development outcomes.[10] As noted, the HDI can help identify cancer transitions, and we use the 4-tier HDI (Fig. 2A) to further assess the cancer burden according to a binary proxy of development (low and medium HDI vs high and very-high HDI).

We summarize the estimated numbers of new cases and deaths by cancer type and point to the variations in the incidence and mortality rates observed in the world regions and individual countries. We use the terms *developing*, *transitioning*, *emerging*, and *lower HDI countries/economies* as synonyms for countries classified as low or medium HDI, and we use *developed*, *transitioned*, or *higher HDI countries/economies* for countries classified as high or very-high HDI.

Results

Distribution of Cases and Deaths by World Region and Cancer Types

We estimate that there will be 18.1 million new cases (17.0 million excluding NMSC) and 9.6 million cancer deaths (9.5 million excluding NMSC) worldwide in 2018 (Table 1). Figure 3 presents the distribution of all-cancer incidence and mortality according to world area for both sexes combined and separately for men and women. For both sexes combined, it is estimated that nearly one-half of the cases and over one-half of the cancer deaths in the world will occur in Asia in the year 2018, in part because close to 60% of the global population resides there (Fig. 2B). Europe accounts for 23.4% of the total cancer cases and 20.3% of the cancer deaths, although it represents only 9% of the global population, followed by the Americas' 21% of incidence and 14.4% of mortality worldwide. In contrast to other regions, the shares of cancer deaths in Asia (57.3%) and Africa (7.3%) are higher than the shares of incidence (48.4% and

TABLE 1. New Cases and Deaths for 36 Cancers and All Cancers Combined in 2018

CANCER SITE	NO. OF NEW CASES (% OF ALL SITES)	NO. OF DEATHS (% OF ALL SITES)
Lung	2,093,876 (11.6)	1,761,007 (18.4)
Breast	2,088,849 (11.6)	626,679 (6.6)
Prostate	1,276,106 (7.1)	358,989 (3.8)
Colon	1,096,601 (6.1)	551,269 (5.8)
Nonmelanoma of skin	1,042,056 (5.8)	65,155 (0.7)
Stomach	1,033,701 (5.7)	782,685 (8.2)
Liver	841,080 (4.7)	781,631 (8.2)
Rectum	704,376 (3.9)	310,394 (3.2)
Esophagus	572,034 (3.2)	508,585 (5.3)
Cervix uteri	569,847 (3.2)	311,365 (3.3)
Thyroid	567,233 (3.1)	41,071 (0.4)
Bladder	549,393 (3.0)	199,922 (2.1)
Non-Hodgkin lymphoma	509,590 (2.8)	248,724 (2.6)
Pancreas	458,918 (2.5)	432,242 (4.5)
Leukemia	437,033 (2.4)	309,006 (3.2)
Kidney	403,262 (2.2)	175,098 (1.8)
Corpus uteri	382,069 (2.1)	89,929 (0.9)
Lip, oral cavity	354,864 (2.0)	177,384 (1.9)
Brain, nervous system	296,851 (1.6)	241,037 (2.5)
Ovary	295,414 (1.6)	184,799 (1.9)
Melanoma of skin	287,723 (1.6)	60,712 (0.6)
Gallbladder	219,420 (1.2)	165,087 (1.7)
Larynx	177,422 (1.0)	94,771 (1.0)
Multiple myeloma	159,985 (0.9)	106,105 (1.1)
Nasopharynx	129,079 (0.7)	72,987 (0.8)
Oropharynx	92,887 (0.5)	51,005 (0.5)
Hypopharynx	80,608 (0.4)	34,984 (0.4)
Hodgkin lymphoma	79,990 (0.4)	26,167 (0.3)
Testis	71,105 (0.4)	9,507 (0.1)
Salivary glands	52,799 (0.3)	22,176 (0.2)
Anus	48,541 (0.3)	19,129 (0.2)
Vulva	44,235 (0.2)	15,222 (0.2)
Kaposi sarcoma	41,799 (0.2)	19,902 (0.2)
Penis	34,475 (0.2)	15,138 (0.2%)
Mesothelioma	30,443 (0.2)	25,576 (0.3)
Vagina	17,600 (0.1)	8,062 (0.1)
All sites excluding skin	17,036,901	9,489,872
All sites	**18,078,957**	**9,555,027**

Source: GLOBOCAN 2018.

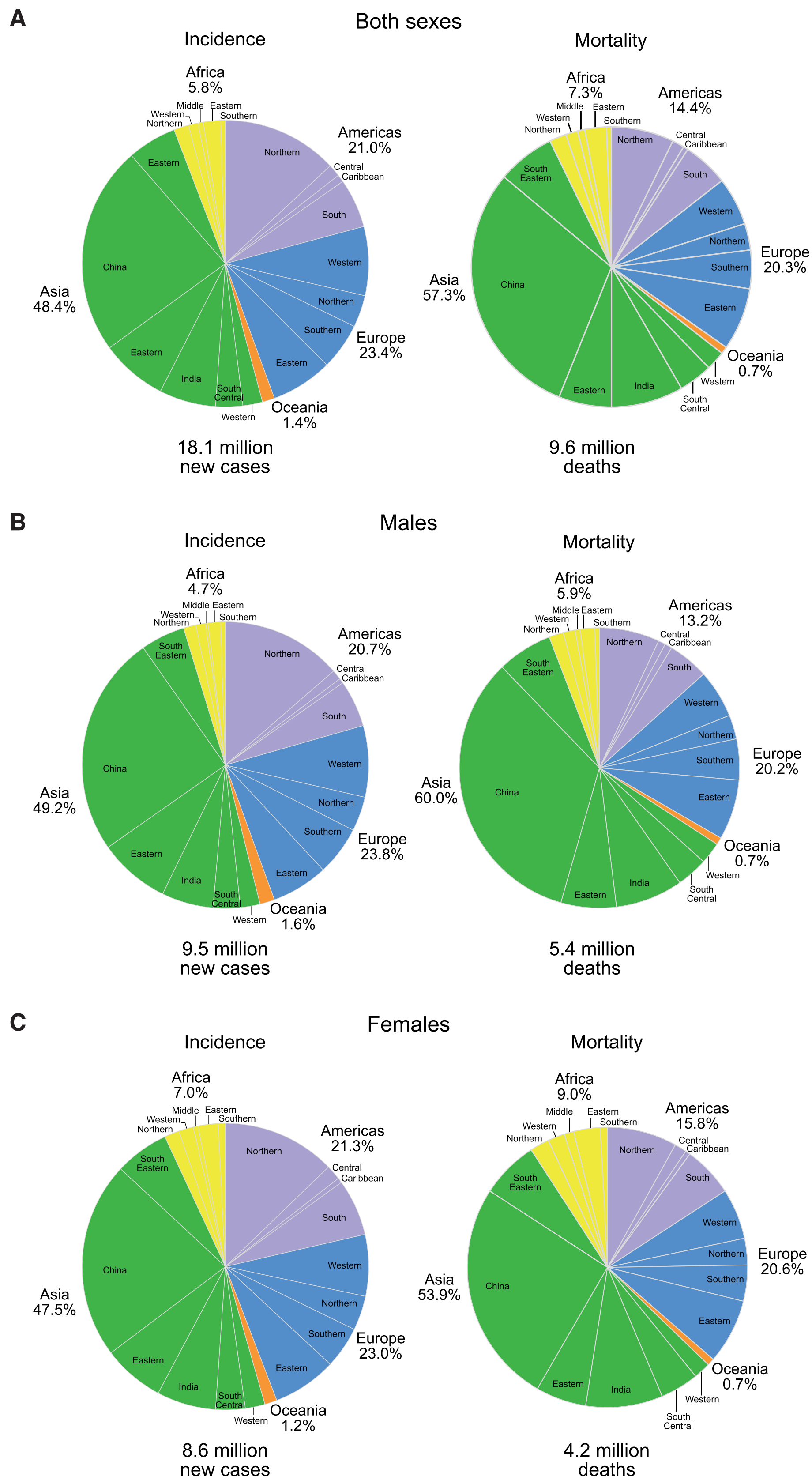

FIGURE 3. Pie Charts Present the Distribution of Cases and Deaths by World Area in 2018 for (A) Both Sexes, (B) Males, and (C) Females. For each sex, the area of the pie chart reflects the proportion of the total number of cases or deaths. Source: GLOBOCAN 2018.

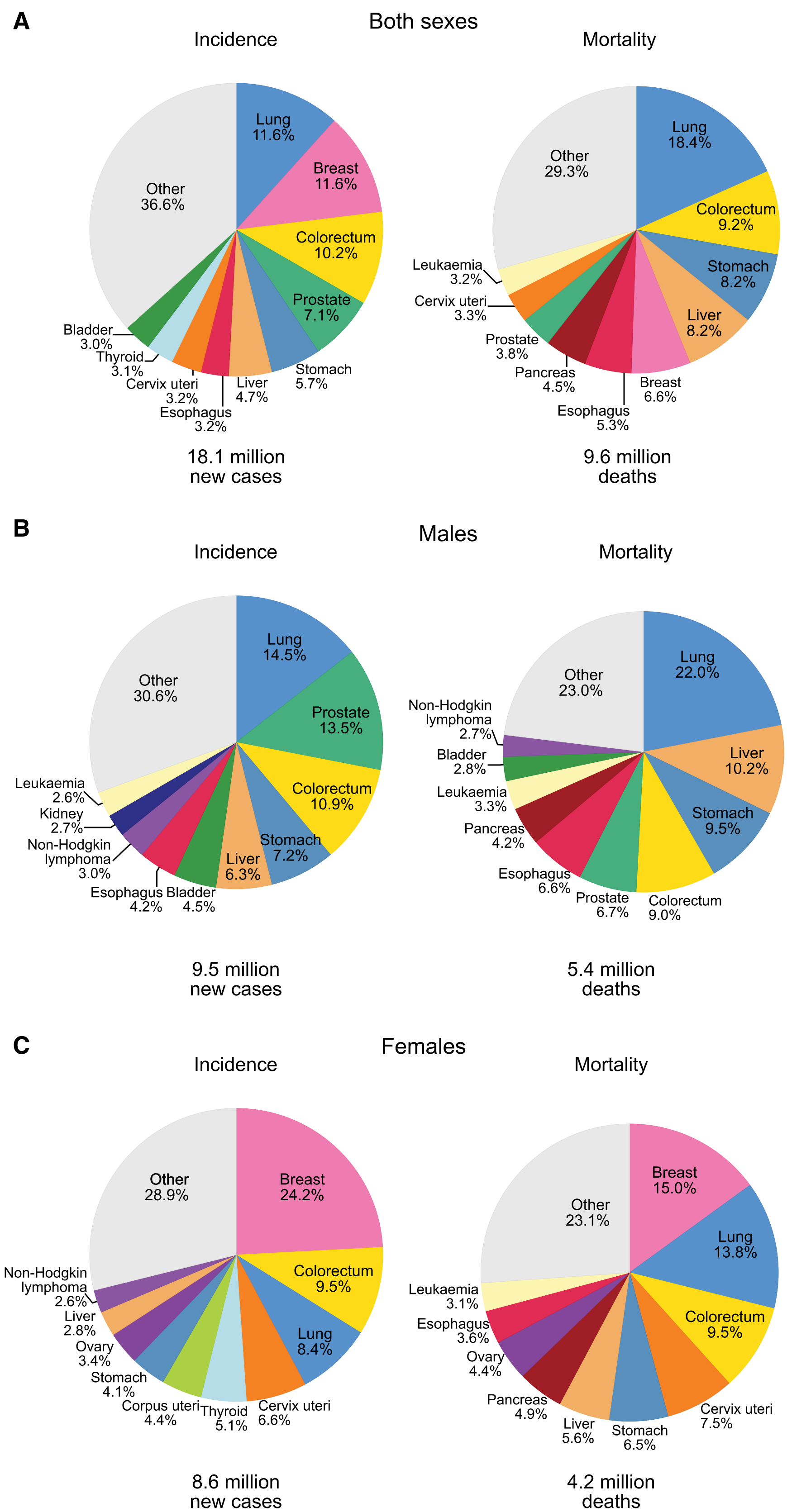

FIGURE 4. Pie Charts Present the Distribution of Cases and Deaths for the 10 Most Common Cancers in 2018 for (A) Both Sexes, (B) Males, and (C) Females. For each sex, the area of the pie chart reflects the proportion of the total number of cases or deaths; nonmelanoma skin cancers are included in the "other" category. Source: GLOBOCAN 2018.

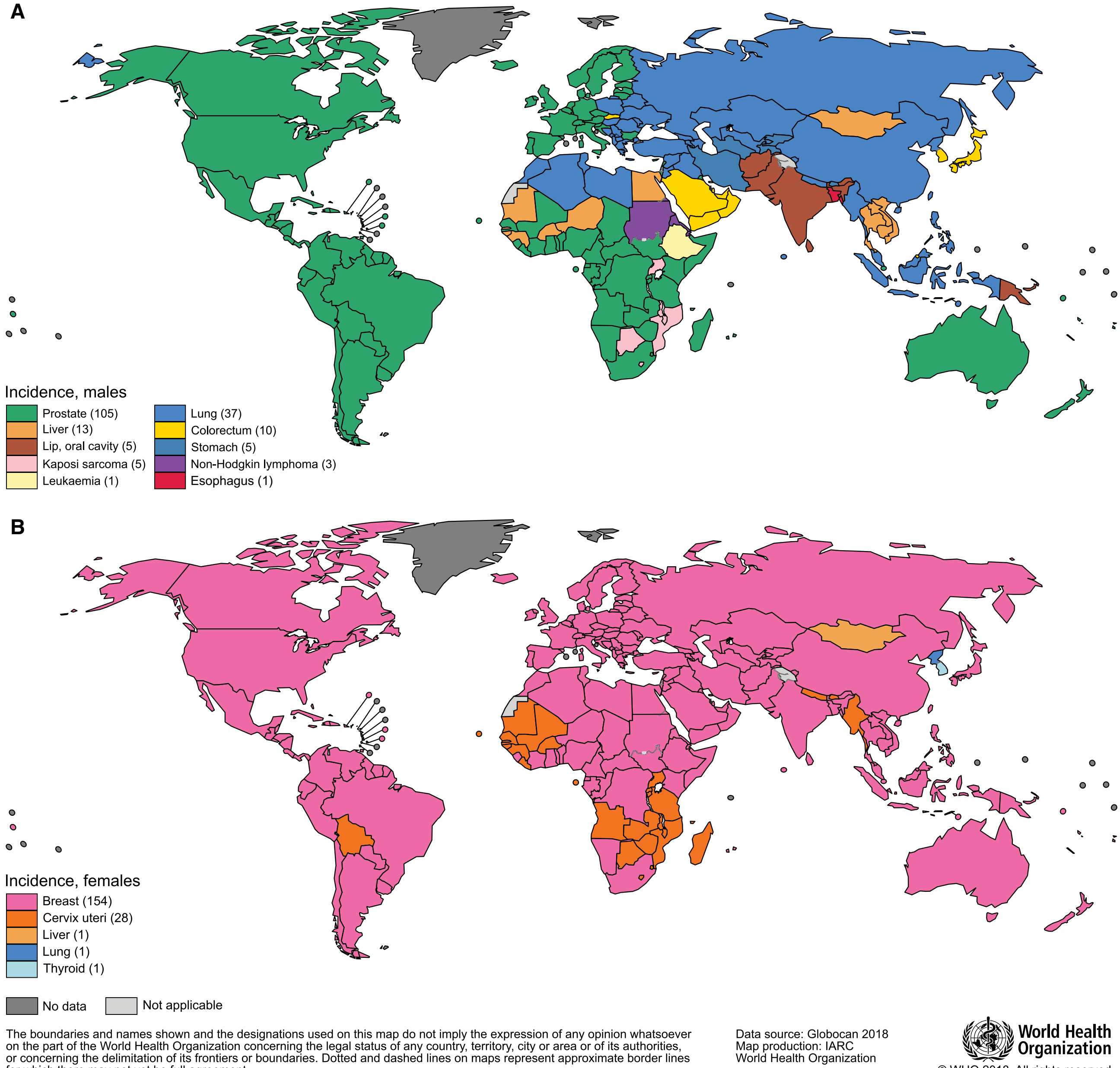

FIGURE 5. Global Maps Presenting the Most Common Type of Cancer Incidence in 2018 in Each Country Among (A) Men and (B) Women. The numbers of countries represented in each ranking group are included in the legend. Source: GLOBOCAN 2018.

5.8%, respectively) because of the different distribution of cancer types and higher case fatality rates in these regions.

Figure 4 shows the top 10 cancer types for estimated cases and deaths worldwide for men and women, combined and separately, with NMSC included within the *other* category. For both sexes combined, lung cancer is the most commonly diagnosed cancer (11.6% of the total cases) and the leading cause of cancer death (18.4% of the total cancer deaths), closely followed by female breast cancer (11.6%), colorectal cancer (10.2%), and prostate cancer (7.1%) for incidence and colorectal cancer (9.2%), stomach cancer (8.2%), and liver cancer (8.2%) for mortality. By sex, lung cancer is the most commonly diagnosed cancer and the leading cause of cancer death in males, followed by prostate and colorectal cancer for incidence, and liver and stomach cancer for mortality. Among females, breast cancer is the most commonly diagnosed cancer and the leading cause of cancer death, followed by colorectal and lung cancer for incidence, and vice versa for mortality; cervical cancer ranks fourth for both incidence and mortality. Overall, the top 10 cancer types account for over 65% of newly diagnosed cancer cases and deaths.

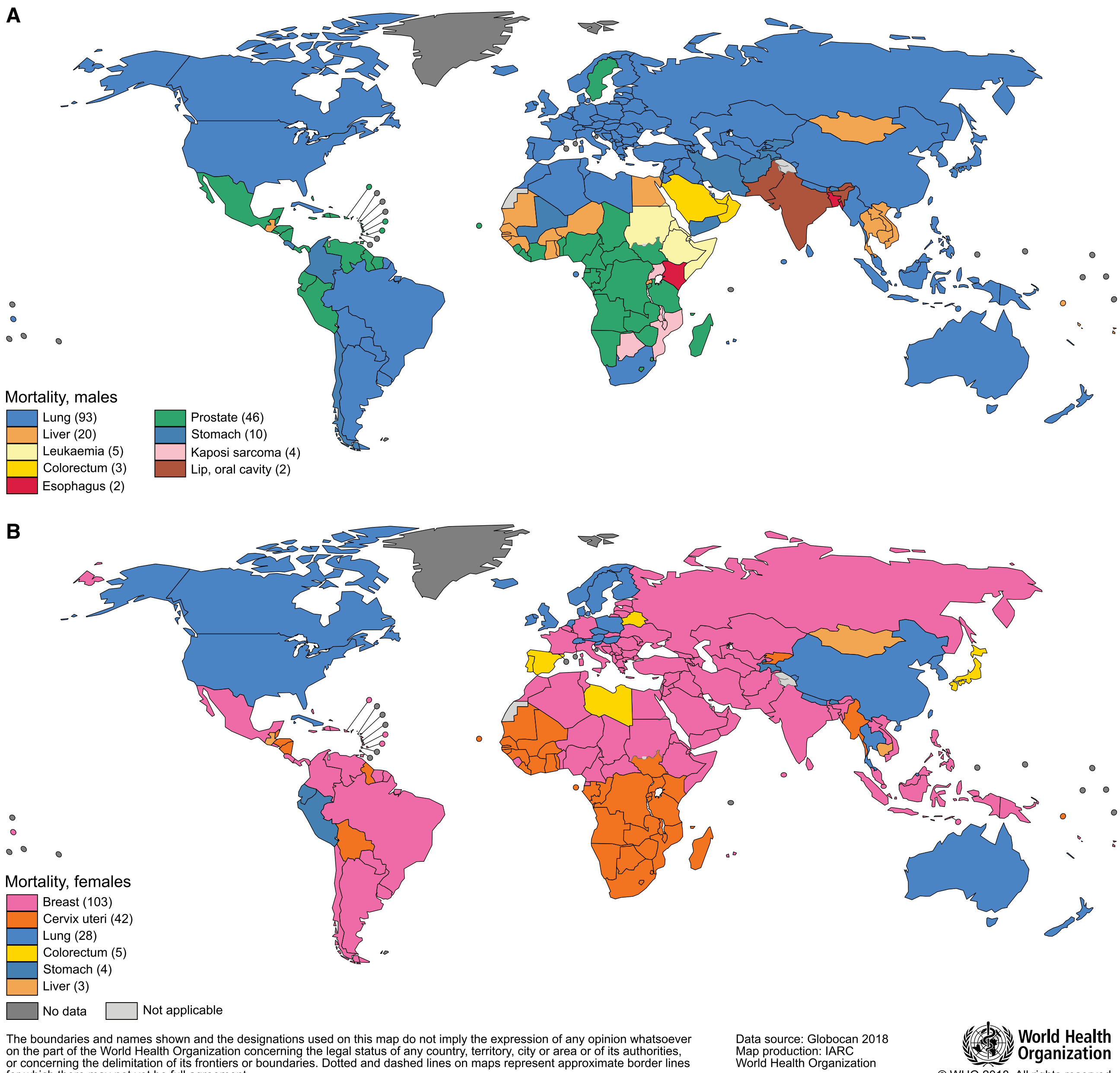

FIGURE 6. Global Maps Presenting the Most Common Type of Cancer Mortality by Country in 2018 Among (A) Men and (B) Women. The numbers of countries represented in each ranking group are included in the legend. Source: GLOBOCAN 2018.

Global Cancer Patterns

Figures 5 and 6, respectively, show the most commonly diagnosed cancer and leading causes of cancer death at the national level in males (Fig. 5A) and females (Fig. 5B). The maps reveal substantial global diversity in leading cancer types, particularly for incidence in men (10 different cancer types) and mortality in both men (9 types) and women (6 types). Prostate cancer is the most frequently diagnosed cancer in 105 countries, followed by lung cancer in 37 countries, and liver cancer in 13 countries (Fig. 5A). Some cancers represent the most frequent type in geographically heterogeneous regions (eg, liver cancer), whereas others tend to cluster in certain high-risk regions (eg, cancers of lip and oral cavity in South Asia, Kaposi sarcoma in Eastern Africa). With regard to mortality (Fig. 6A), lung cancer is the leading cause of cancer death among men in 93 countries, in part because of its high fatality rate, followed by prostate cancer (46 countries) and liver cancer (20 countries).

In women, the profile of the most commonly diagnosed cancers across countries is marked by its dichotomous nature, with female breast cancer most frequent in terms of new cases in the majority (154 countries) of countries and with cervical cancer leading in most (28 of 31 countries)

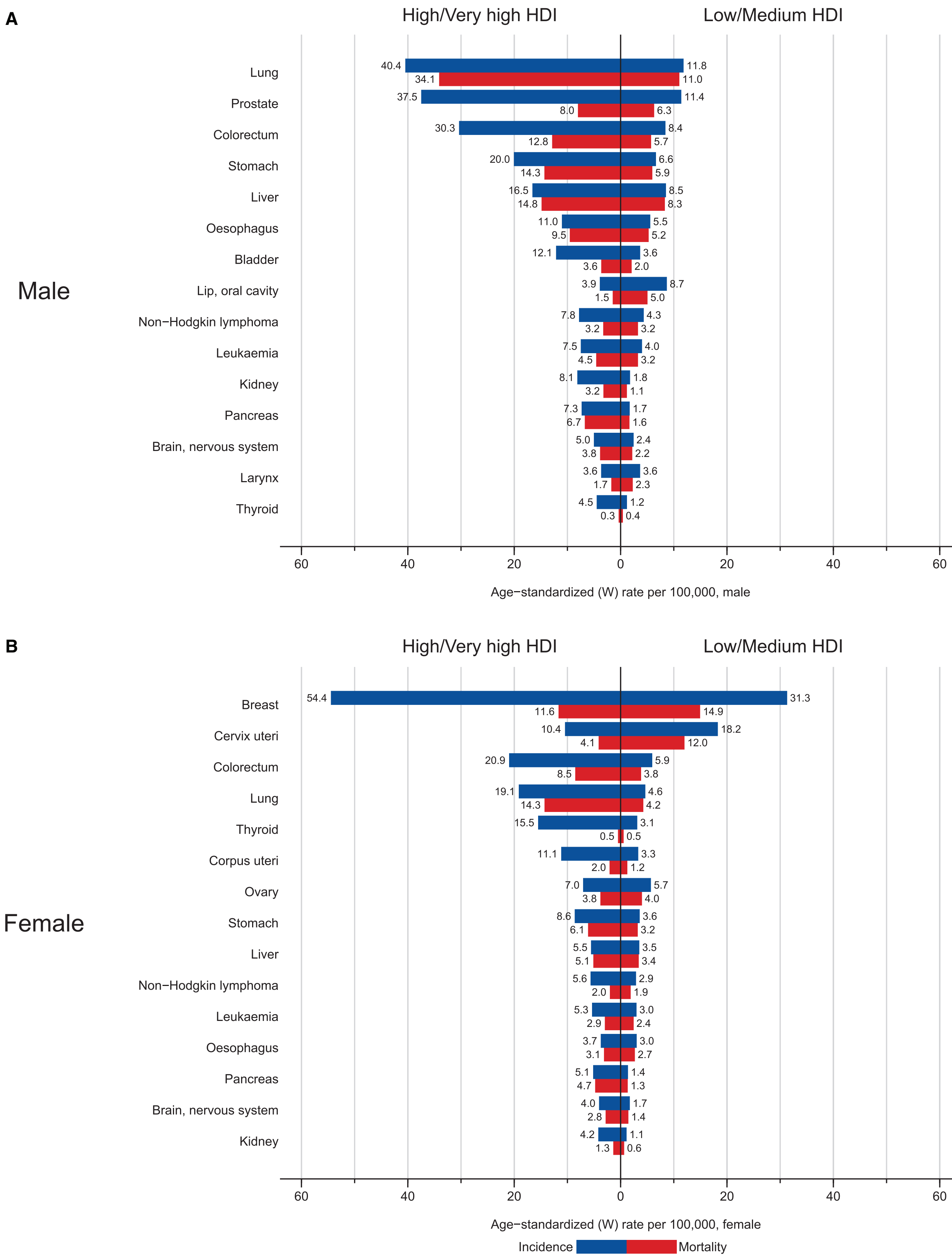

FIGURE 7. Bar Charts of Incidence and Mortality Age-Standardized Rates in High/Very-High Human Development Index (HDI) Regions Versus Low/Medium HDI Regions Among (A) Men and (B) Women in 2018. The 15 most common cancers world (W) in 2018 are shown in descending order of the overall age-standardized rate for both sexes combined. Source: GLOBOCAN 2018.

of the remaining countries (Fig. 5B). The mortality profile among women is more heterogeneous (Fig. 7B), with breast and cervical cancer as the leading causes of cancer death in 103 and 42 countries, respectively, followed by lung cancer in 28 countries.

Cancer Incidence and Mortality Patterns by the 4-Tier HDI

Figures 7A and 7B show cancer incidence and mortality ASRs in high/very-high HDI regions versus low/medium HDI regions for men and women, respectively, in 2018. For many cancers, incidence rates are generally 2-fold to 3-fold higher in transitioned compared with transitioning economies. However, the differences in mortality between these 2 regions are smaller, in part because of a higher case fatality for many cancer types in lower HDI countries. In men (Fig. 6A), lung cancer ranks first and prostate cancer ranks second in both high/very-high and low/medium HDI countries despite considerable variations in the magnitude of the incidence rates between the 2 regions. These cancers are followed by colorectal cancer in transitioned countries and lip and oral cavity cancer in transitioning countries, in part because of the high burden of the disease in India, which accounts for 36% of the population among lower HDI countries. In women (Fig. 7B), incidence rates for breast cancer far exceed those for other cancers in both transitioned and transitioning countries, followed by colorectal cancer in transitioned countries, and cervical cancer in transitioning countries.

Cancer Incidence and Death Rates by World Region

Worldwide, the incidence rate for all cancers combined was about 20% higher in men (ASR, 218.6 per 100,000) than in women (ASR, 182.6 per 100,000), with the incidence rates varying across regions in both males and females. Among males, incidence rates across regions varied almost 6-fold, from 571.2 per 100,000 in Australia/New Zealand to 95.6 per 100,000 in Western Africa (Table 2). Among females, incidence rates varied nearly 4-fold, from 362 per 100,000 in Australia/New Zealand to 96.2 per 100,000 in South-Central Asia. These variations largely reflect differences in the type of exposures and associated cancers (cancer mix) and in the availability

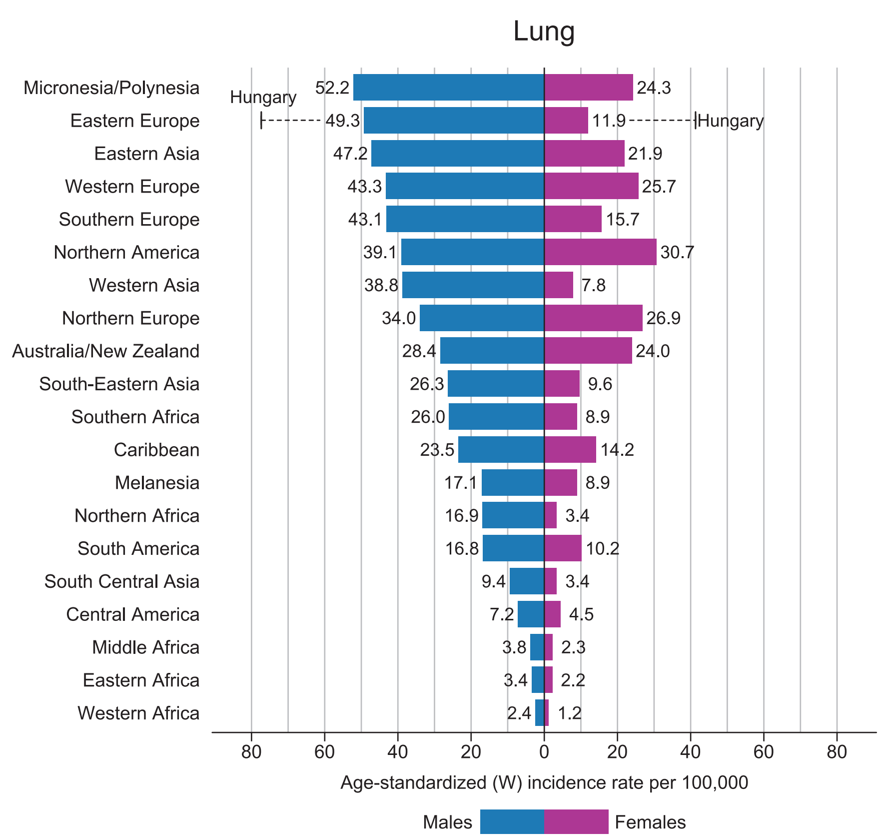

FIGURE 8. Bar Chart of Region-Specific Incidence Age-Standardized Rates by Sex for Cancers of the Lung in 2018. Rates are shown in descending order of the world (W) age-standardized rate among men, and the highest national rates among men and women are superimposed. Source: GLOBOCAN 2018.

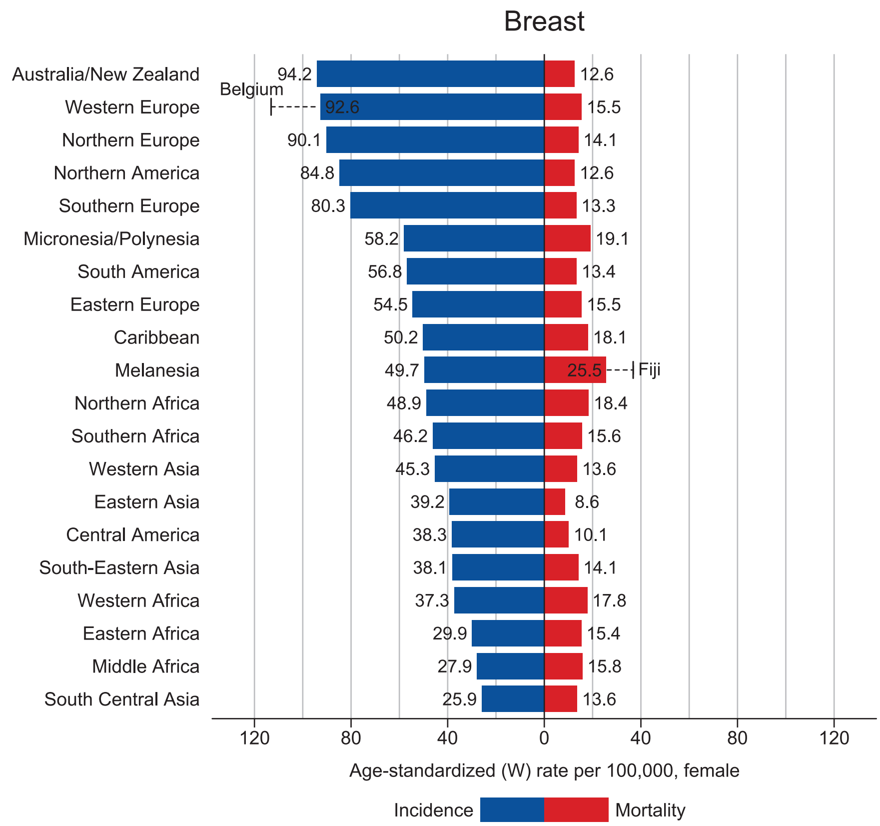

FIGURE 9. Bar Chart of Region-Specific Incidence and Mortality Age-Standardized Rates for Cancers of the Female Breast in 2018. Rates are shown in descending order of the world (W) age-standardized rate, and the highest national age-standardized rates for incidence and mortality are superimposed. Source: GLOBOCAN 2018.

and use of screening services and diagnostic imaging. For example, the highest overall incidence rates among both men and women are found in Australia/New Zealand, in part because of an elevated risk, but also resulting from an increased detection of skin cancers, particularly NMSC, in these countries; the possibility that the latter site may be inadequately captured in certain regions despite markedly increasing the global cancer incidence burden overall, must be also considered.

Similar to incidence rates, death rates for all cancers combined worldwide are nearly 50% higher in males than in females and, within each sex, the rates vary across regions (Table 2). Death rates per 100,000 persons varied from 171.0 in Eastern Europe to 67.4 in Central America among males and from 120.7 in Melanesia to 64.2 in Central America and Eastern Asia (excluding China). Notably, the estimated cumulative risk of dying from cancer among women in 2018 is higher in East Africa (11.4%) than the corresponding risks estimated in North America (8.6%), Northern Europe (9.1%), and Australia/New Zealand (8.1%).

Table 3 shows the total number of newly diagnosed cancer cases and deaths, the incidence and mortality ASRs, and the lifetime risk of developing/dying from cancer overall and for the 36 cancer types separately in men and women. With cumulative risks of 21.4% for developing cancer and 17.7% for dying from it before age 75 years globally for both sexes combined, 1 in 5 men and 1 in 6 women will develop the disease and 1 in 8 men and 1 in 10 women will die from it. Below, we describe the variations in sex-specific incidence and mortality rates by world region for 16 of these cancer types (Figs. 8–21).

Lung cancer

Worldwide, lung cancer remains the leading cause of cancer incidence and mortality, with 2.1 million new lung cancer cases and 1.8 million deaths predicted in 2018, representing close to 1 in 5 (18.4%) cancer deaths (Table 1) (Fig. 4). Among males, lung cancer is the leading cause of death in most countries in Eastern Europe, Western Asia (notably in the former Soviet Union), Northern Africa, and specific countries in Eastern Asia (China) and South-Eastern Asia (eg, Myanmar, the Philippines, and Indonesia). The highest incidence rates among men are observed in Micronesia/Polynesia, in Eastern Asia (rates are above 40 per 100,000 in China, Japan, and the Republic of Korea), and in much of Europe, especially in Eastern Europe, with an ASR in Hungary as high as 77.4 per 100,000 males (Fig. 8). Incidence rates among males remain generally low in Africa, although

TABLE 2. Incidence and Mortality Rates (Age-Standardized Rate, Cumulative Risk) for 24 World Areas and Sex for All Cancers Combined (Including Nonmelanoma Skin Cancer) in 2018

	INCIDENCE				MORTALITY			
	MALES		FEMALES		MALES		FEMALES	
WORLD AREA	ASR (WORLD)	CUMULATIVE RISK, AGES BIRTH TO 74 YEARS, %	ASR (WORLD)	CUMULATIVE RISK, AGES BIRTH TO 74 YEARS, %	ASR (WORLD)	CUMULATIVE RISK, AGES BIRTH TO 74 YEARS, %	ASR (WORLD)	CUMULATIVE RISK, AGES BIRTH TO 74 YEARS, %
Eastern Africa	112.4	11.6	150.7	15.2	87.0	8.9	107.6	11.4
Middle Africa	101.8	10.6	109.2	11.2	79.5	8.0	80.9	8.7
Northern Africa	138.9	14.7	137.3	13.9	102.1	10.6	76.9	8.2
Southern Africa	230.5	22.4	196.1	18.5	142.4	13.5	98.3	9.8
Western Africa	95.6	10.1	122.0	12.7	72.1	7.4	83.6	9.1
Caribbean	213.1	22.4	182.9	18.3	117.4	11.7	89.5	9.3
Central America	139.3	14.5	149.7	14.9	67.4	6.8	64.2	6.9
South America	220.0	22.4	195.2	19.1	107.3	10.8	81.1	8.4
Northern America	387.6	36.3	322.1	30.3	104.2	10.8	80.7	8.6
Eastern Asia	238.4	24.2	192.0	18.9	159.6	16.4	89.7	9.4
All but China	293.8	29.1	237.8	22.2	116.9	11.3	64.2	6.2
China	223.0	23.0	182.6	18.3	166.6	17.3	95.2	10.0
South-Eastern Asia	156.1	16.3	142.5	14.5	113.8	12.0	79.7	8.6
South Central Asia	97.5	10.6	95.9	10.0	70.9	7.8	60.6	6.6
All but India	117.6	12.6	111.0	11.5	84.4	9.2	68.7	7.5
India	89.8	9.8	90.0	9.4	65.8	7.3	57.5	6.3
Western Asia	190.1	19.9	154.6	15.6	120.5	12.8	74.3	7.8
Eastern Europe	280.1	29.4	216.5	22.0	171.0	18.8	92.0	10.2
Northern Europe	344.6	33.1	295.0	28.0	118.4	11.6	88.7	9.1
Southern Europe	319.5	31.8	247.0	23.7	131.5	13.5	76.2	7.9
Western Europe	363.5	34.9	292.1	27.7	130.0	13.3	84.4	8.8
Australia/New Zealand	571.2	49.1	362.2	33.3	109.8	10.8	78.4	8.1
Melanesia	197.3	20.8	203.6	19.8	133.3	13.9	120.7	12.5
Micronesia/ Polynesia	224.0	24.2	184.9	19.1	142.8	15.1	95.2	10.2
Low HDI	101.6	10.5	128.4	13.0	78.2	7.9	91.1	9.7
Medium HDI	114.2	12.3	112.8	11.7	83.4	9.1	68.6	7.4
High HDI	214.6	22.2	178.3	17.9	147.7	15.5	87.8	9.4
Very high HDI	335.1	32.7	269.5	25.9	124.2	12.7	80.9	8.5
World	**218.6**	**22.4**	**182.6**	**18.3**	**122.7**	**12.7**	**83.1**	**8.7**

Abbreviations: ASR, age-standardized risk; HDI, Human Development Index.

Source: GLOBOCAN 2018.

TABLE 3. Incidence (Cases, Age-Standardized Rate, Cumulative Risk) and Mortality (Deaths, ASR, Cumulative Risk) for 36 Cancers and All Cancers Combined (Including Nonmelanoma Skin Cancer) by Sex in 2018

	INCIDENCE						MORTALITY					
	MALES			FEMALES			MALES			FEMALES		
CANCER SITE	CASES	ASR (WORLD)	CUMULATIVE RISK, AGES BIRTH TO 74 YEARS, %	CASES	ASR (WORLD)	CUMULATIVE RISK, AGES BIRTH TO 74 YEARS, %	DEATHS	ASR (WORLD)	CUMULATIVE RISK, AGES BIRTH TO 74 YEARS, %	DEATHS	ASR (WORLD)	CUMULATIVE RISK, AGES BIRTH TO 74 YEARS, %
Lip, oral cavity	246,420	5.8	0.66	108,444	2.3	0.26	119,693	2.8	0.32	57,691	1.2	0.14
Salivary glands	29,256	0.7	0.07	23,543	0.5	0.05	13,440	0.3	0.03	8,736	0.2	0.02
Oropharynx	74,472	1.8	0.21	18,415	0.4	0.05	42,116	1.0	0.12	8,889	0.2	0.02
Nasopharynx	93,416	2.2	0.24	35,663	0.8	0.09	54,280	1.3	0.15	18,707	0.4	0.05
Hypopharynx	67,496	1.6	0.19	13,112	0.3	0.03	29,415	0.7	0.08	5,569	0.1	0.01
Esophagus	399,699	9.3	1.15	172,335	3.5	0.43	357,190	8.3	1.00	151,395	3.0	0.36
Stomach	683,754	15.7	1.87	349,947	7.0	0.79	513,555	11.7	1.36	269,130	5.2	0.57
Colon	575,789	13.1	1.51	520,812	10.1	1.12	290,509	6.4	0.66	260,760	4.6	0.44
Rectum	430,230	10.0	1.20	274,146	5.6	0.65	184,097	4.2	0.46	126,297	2.4	0.26
Anus	20,196	0.5	0.05	28,345	0.6	0.07	9,618	0.2	0.03	9,511	0.2	0.02
Liver	596,574	13.9	1.61	244,506	4.9	0.57	548,375	12.7	1.46	233,256	4.6	0.53
Gallbladder	97,396	2.2	0.25	122,024	2.4	0.26	70,168	1.6	0.17	94,919	1.8	0.19
Pancreas	243,033	5.5	0.65	215,885	4.0	0.45	226,910	5.1	0.59	205,332	3.8	0.41
Larynx	154,977	3.6	0.45	22,445	0.5	0.06	81,806	1.9	0.23	12,965	0.3	0.03
Lung	1,368,524	31.5	3.80	725,352	14.6	1.77	1,184,947	27.1	3.19	576,060	11.2	1.32
Melanoma of skin	150,698	3.5	0.39	137,025	2.9	0.31	34,831	0.8	0.08	25,881	0.5	0.05
Nonmelanoma of skin	637,733	13.9	1.31	404,323	7.0	0.67	38,345	0.8	0.08	26,810	0.5	0.04
Mesothelioma	21,662	0.5	0.05	8,781	0.2	0.02	18,332	0.4	0.04	7,244	0.1	0.02
Kaposi sarcoma	28,248	0.7	0.06	13,551	0.3	0.03	13,117	0.3	0.03	6,785	0.2	0.01
Breast				2,088,849	46.3	5.03				626,679	13.0	1.41
Vulva				44,235	0.9	0.09				15,222	0.3	0.03
Vagina				17,600	0.4	0.04				8,062	0.2	0.02
Cervix uteri				569,847	13.1	1.36				311,365	6.9	0.77
Corpus uteri				382,069	8.4	1.01				89,929	1.8	0.21

TABLE 3. CONTINUED

	INCIDENCE						MORTALITY					
	MALES			FEMALES			MALES			FEMALES		
CANCER SITE	CASES	ASR (WORLD)	CUMULATIVE RISK, AGES BIRTH TO 74 YEARS, %	CASES	ASR (WORLD)	CUMULATIVE RISK, AGES BIRTH TO 74 YEARS, %	DEATHS	ASR (WORLD)	CUMULATIVE RISK, AGES BIRTH TO 74 YEARS, %	DEATHS	ASR (WORLD)	CUMULATIVE RISK, AGES BIRTH TO 74 YEARS, %
Ovary				295,414	6.6	0.72				184,799	3.9	0.45
Penis	34,475	0.8	0.09				15,138	0.3	0.04			
Prostate	1,276,106	29.3	3.73				358,989	7.6	0.60			
Testis	71,105	1.7	0.14				9,507	0.2	0.02			
Kidney	254,507	6.0	0.69	148,755	3.1	0.35	113,822	2.6	0.28	61,276	1.1	0.12
Bladder	424,082	9.6	1.08	125,311	2.4	0.27	148,270	3.2	0.29	51,652	0.9	0.08
Brain, nervous system	162,534	3.9	0.40	134,317	3.1	0.31	135,843	3.2	0.35	105,194	2.3	0.25
Thyroid	130,889	3.1	0.33	436,344	10.2	1.03	15,557	0.4	0.04	25,514	0.5	0.05
Hodgkin lymphoma	46,559	1.1	0.10	33,431	0.8	0.07	15,770	0.4	0.04	10,397	0.2	0.02
Non-Hodgkin lymphoma	284,713	6.7	0.72	224,877	4.7	0.51	145,969	3.3	0.35	102,755	2.0	0.21
Multiple myeloma	89,897	2.1	0.24	70,088	1.4	0.17	58,825	1.3	0.15	47,280	0.9	0.10
Leukemia	249,454	6.1	0.57	187,579	4.3	0.40	179,518	4.2	0.40	129,488	2.8	0.26
All sites excluding skin	8,818,685	204.7	21.38	8,218,216	175.6	17.71	5,347,295	121.9	12.65	4,142,577	82.7	8.66
All sites	**9,456,418**	**218.6**	**22.41**	**8,622,539**	**182.6**	**18.25**	**5,385,640**	**122.7**	**12.71**	**4,169,387**	**83.1**	**8.70**

Abbreviation: ASR, age-standardized risk.

Source: GLOBOCAN 2018.

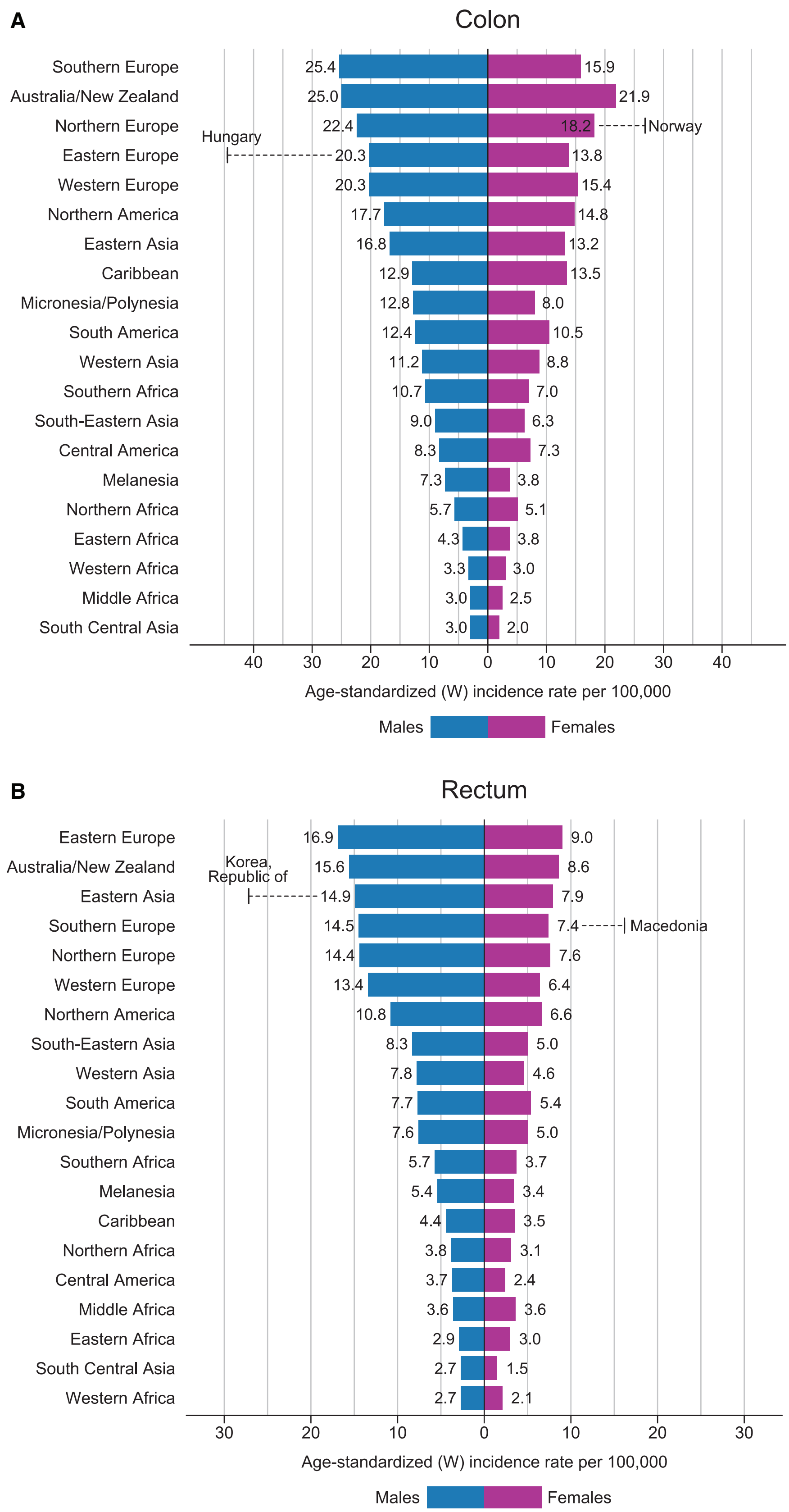

FIGURE 10. Bar Chart of Region-Specific Incidence Age-Standardized Rates by Sex for Cancers of the (A) Colon and (B) Rectum in 2018. Rates for cancers of the colon and rectum are shown in descending order of the world (W) age-standardized rate among men, and the highest national rates among men and women are superimposed. Source: GLOBOCAN 2018.

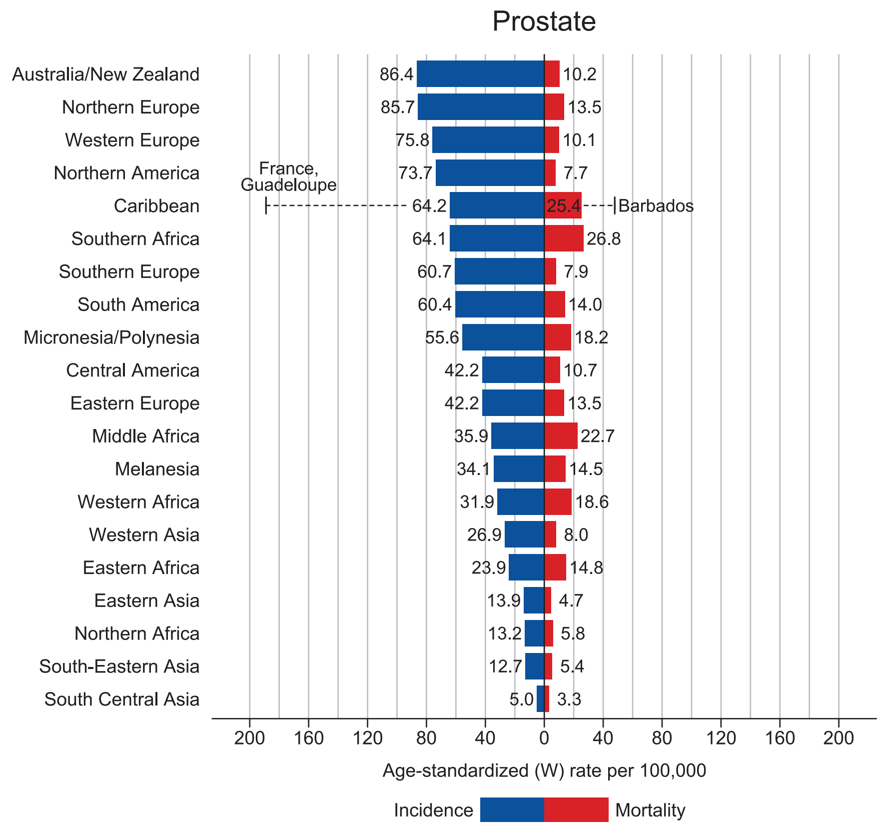

FIGURE 11. Bar Chart of Region-Specific Incidence and Mortality Age-Standardized Rates for Cancers of the Prostate in 2018. Rates are shown in descending order of the world (W) age-standardized rate, and the highest national age-standardized rates for incidence and mortality are superimposed. Source: GLOBOCAN 2018.

they range from intermediate to high in several countries in both Northern and Southern regions, notably in Morocco (31.9 per 100,000) and South Africa (28.2 per 100,000).

Among females, lung cancer is the leading cause of cancer death in 28 countries (Fig. 6B). The highest incidence rates are seen in North America, Northern and Western Europe (notably in Denmark and the Netherlands), and Australia/New Zealand, with Hungary topping the list (Fig. 8). It is of note that the incidence rates among Chinese women (22.8 per 100,000) are not dissimilar to those observed among females in several Western European countries (eg, in France [22.5 per 100,000], despite substantial differences in smoking prevalence between the 2 populations). The high lung cancer incidence rates in Chinese women, despite their low smoking prevalence, are thought to reflect increased exposures to smoke from burning of charcoal for heating and cooking.

There is a 20-fold variation in lung cancer rates by region, which largely reflects the maturity of the tobacco epidemic and differentials in the historic patterns of tobacco exposure, including intensity and duration of smoking, type of cigarettes, and degree of inhalation. Among men, a diminution in smoking prevalence, followed by a peak and decline in lung cancer rates in the same generations, was first observed in several high-income countries where smoking was first established, including the United Kingdom, the United States, Finland, Australia, New Zealand, the Netherlands, Singapore, and (more recently) Germany, Uruguay, and the remaining Nordic countries.[15,16] A recent analysis of incidence trends in 26 European countries revealed that rates in men aged 35 to 64 years have been decreasing in recent years, including Eastern European countries, although rates were still increasing in Bulgaria.[17]

Among women, the epidemic is less advanced and, in contrast to men, most countries are still observing a rising trend in incidence,[17,18] and only a relatively few populations (eg, the United States [whites] and possibly the United Kingdom) are showing signs of a peak and decline among recent birth cohorts. Given the differential trends by sex, rates in men and women are converging in several European countries, and it is postulated that this is the result of sex-specific differences in the distribution of histologic subtypes as well as smoking prevalence.[17] In the United States, lung cancer incidence rates are now higher among young women than among young men, with the pattern confined to non-Hispanic whites and Hispanics;

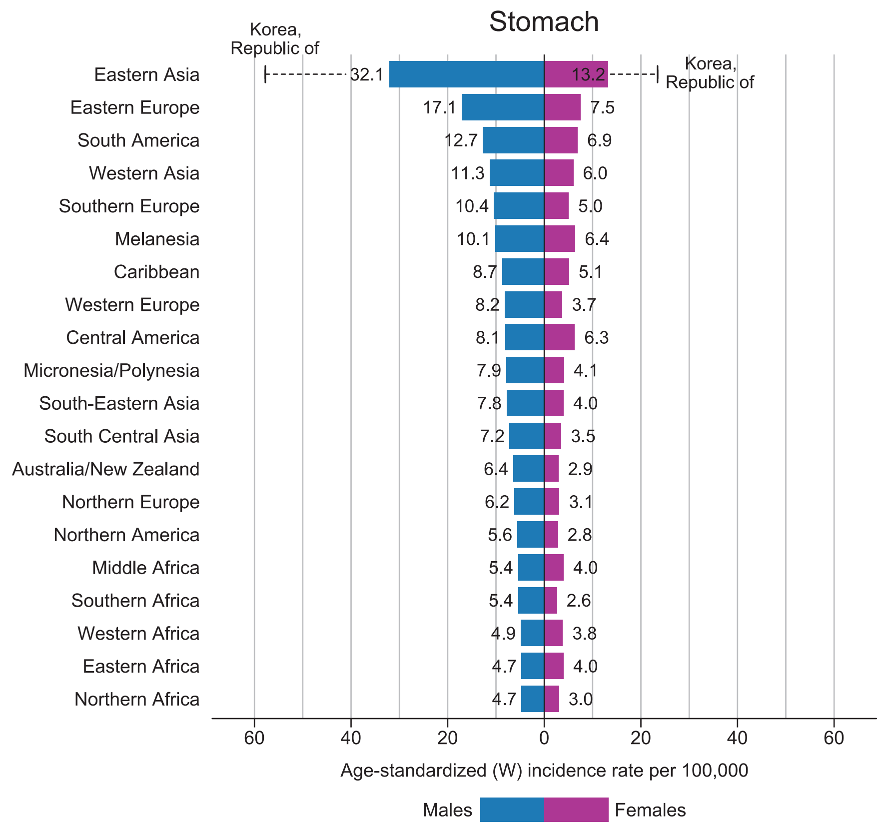

FIGURE 12. Bar Chart of Region-Specific Incidence Age-Standardized Rates by Sex for Cancers of the Stomach in 2018. Rates are shown in descending order of the world (W) age-standardized rate among men, and the highest national rates among men and women are superimposed. Source: GLOBOCAN 2018.

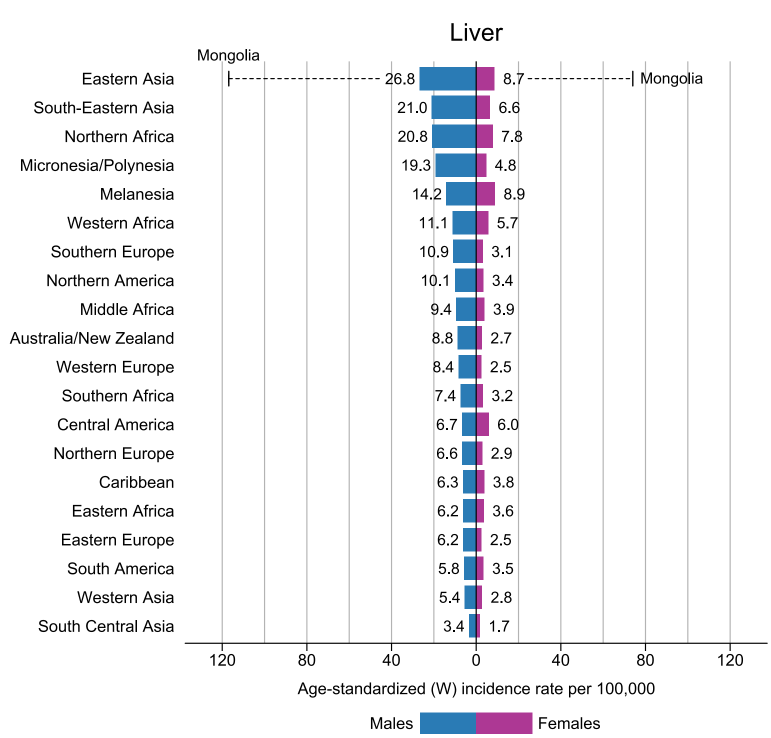

FIGURE 13. Bar Chart of Region-Specific Incidence Age-Standardized Rates by Sex for Cancers of the Liver in 2018. Rates are shown in descending order of world (W) age-standardized rates among men, and the highest national rates among men and women are superimposed. Source: GLOBOCAN 2018.

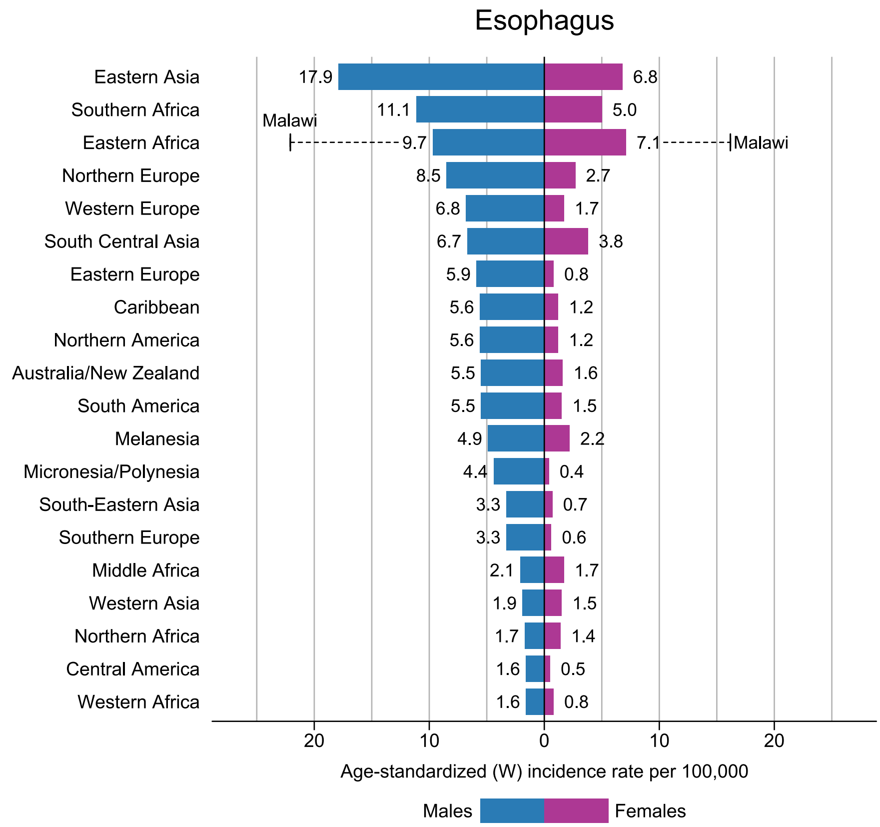

FIGURE 14. Bar Chart of Region-Specific Incidence Age-Standardized Rates by Sex for Cancers of the Esophagus in 2018. Rates are shown in descending order of the world (W) age-standardized rate among men, and the highest national rates among men and women are superimposed. Source: GLOBOCAN 2018.

intriguingly, a sex-specific difference in smoking behavior is not considered a likely explanatory factor.[19]

In countries where the epidemic is at an earlier stage, surveillance data are more limited. In China and Indonesia, smoking has either peaked or continues to increase[20] and, in several African countries, lung cancer rates are likely to continue to increase at least for the next few decades, barring interventions to accelerate smoking cessation or reduce initiation.[21] In India, bidi smoking confers a risk close to that of cigarette smoking, yet no significant changes in lung cancer incidence rates (ie, among males, in whom prevalence is high) have been observed in either sex, at least in the urban areas with long-standing and robust incidence data.[22]

With greater than 80% of lung cancers in Western populations attributed to smoking, the disease largely can be prevented through tobacco control. Best-practice measures that effectively reduce active smoking and prevent involuntary exposure to tobacco smoke—particularly increasing excise taxes and prices on tobacco products, as well as implementing plain packaging and graphic health warnings on tobacco products and enforcing comprehensive bans on tobacco advertising—are embedded in the WHO Framework Convention on Tobacco Control and, after its adoption in 2003, 168 signatories have ratified the agreement.

Female breast cancer

Worldwide, there will be about 2.1 million newly diagnosed female breast cancer cases in 2018, accounting for almost 1 in 4 cancer cases among women (Table 1) (Fig. 4). The disease is the most frequently diagnosed cancer in the vast majority of the countries (154 of 185) and is also the leading cause of cancer death in over 100 countries (Figs. 5B and 6B); the main exceptions are Australia/New Zealand, Northern Europe, Northern America (where it is preceded by lung cancer), and many countries in Sub-Saharan Africa (because of elevated cervical cancer rates). Breast cancer incidence rates are highest in Australia/New Zealand, Northern Europe (eg, the United Kingdom, Sweden, Finland, and Denmark), Western Europe (Belgium [with the highest global rates], the Netherlands, and France), Southern Europe (Italy), and Northern America (Fig. 9). In terms of mortality, breast cancer rates show less variability, with the highest mortality estimated in Melanesia, where Fiji has the highest mortality rates worldwide.

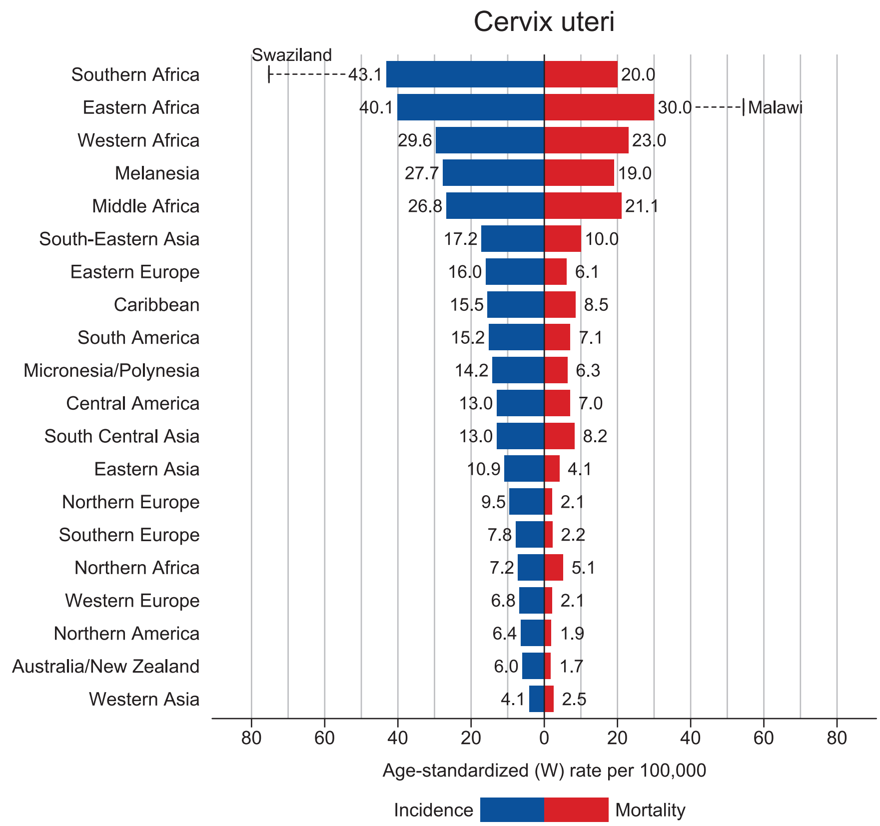

FIGURE 15. Bar Chart of Region-Specific Incidence and Mortality Age-Standardized Rates for Cancers of the Cervix in 2018. Rates are shown in descending order of the world (W) age-standardized rate, and the highest national age-standardized rates for incidence and mortality are superimposed. Source: GLOBOCAN 2018.

Although hereditary and genetic factors, including a personal or family history of breast or ovarian cancer and inherited mutations (in *BRCA1*, *BRCA2*, and other breast cancer susceptibility genes), account for 5% to 10% of breast cancer cases, studies of migrants have shown that non-hereditary factors are the major drivers of the observed international and interethnic differences in incidence. Comparisons of low-risk populations migrating to high-risk populations have revealed that breast cancer incidence rates rise in successive generations.[23] Elevated incidence rates in higher HDI countries are attributed to a higher prevalence of known risk factors and the elevated incidence rates in transitioned countries are the consequence of a higher prevalence of known risk factors related to menstruation (early age at menarche, later age at menopause), reproduction (nulliparity, late age at first birth, and fewer children), exogenous hormone intake (oral contraceptive use and hormone replacement therapy), nutrition (alcohol intake), and anthropometry (greater weight, weight gain during adulthood, and body fat distribution); whereas breastfeeding and physical activity are known protective factors.[24]

However, knowledge is still limited about how geographic or temporal variations in rates relate to specific etiologic factors. Incidence rates of breast cancer have been rising for most countries in transition over the last decades, with some of the most rapid increases occurring where rates have been historically relatively low, in transitioning countries in South America, Africa, and Asia.[25] These trends likely reflect a combination of demographic factors allied to social and economic development, including the postponement of childbearing and having fewer children, greater levels of obesity and physical inactivity, and increases in breast cancer screening and awareness. In several developed countries, including the United States, Canada, the United Kingdom, France, and Australia, the fall in incidence in the early 2000s was partly attributable to declines in the use of postmenopausal hormonal treatment after publication of the Women's Health Initiative trial linking postmenopausal hormone use to increased breast cancer risk,[26] as first reported in the United States.[27] The primary risk factors for breast cancer are not easily modifiable because they stem from prolonged, endogenous hormonal exposures, although prevention through the promotion of breastfeeding, particularly with longer duration, may be beneficial.[24]

Colorectal cancer

Over 1.8 million new colorectal cancer cases and 881,000 deaths are estimated to occur in 2018, accounting for about

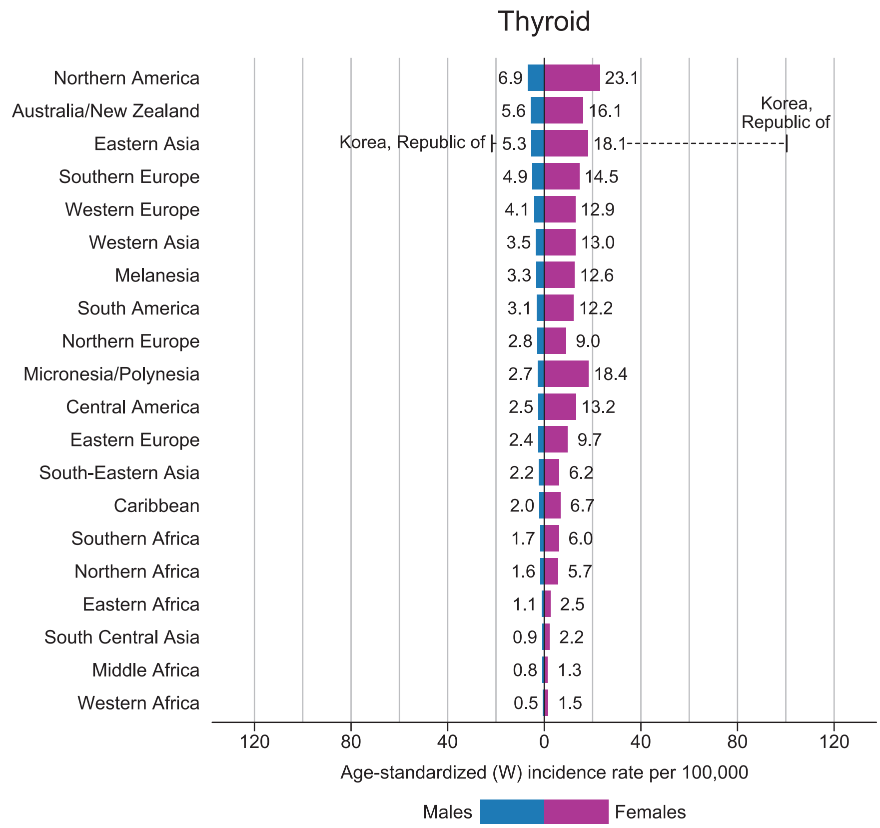

FIGURE 16. Bar Chart of Region-Specific Incidence Age-Standardized Rates by Sex for Cancers of the Thyroid in 2018. Rates are shown in descending order of the world (W) age-standardized rate among men, and the highest national rates among men and women are superimposed. Source: GLOBOCAN 2018.

1 in 10 cancer cases and deaths (Table 1). Overall, colorectal cancer ranks third in terms of incidence but second in terms of mortality (Fig. 4). Colorectal cancer incidence rates are about 3-fold higher in transitioned versus transitioning countries; however, with average case fatality higher in lower HDI settings, there is less variation in the mortality rates (Fig. 7).

The highest colon cancer incidence rates are found in parts of Europe (eg, in Hungary, Slovenia, Slovakia, the Netherlands, and Norway), Australia/New Zealand, Northern America, and Eastern Asia (Japan and the Republic of Korea, Singapore [in females]), with Hungary and Norway ranking first among males and females, respectively (Fig. 10A). Rates also are elevated in Uruguay among both men and women. Rectal cancer incidence rates have a similar regional distribution, although the highest rates are seen in the Republic of Korea among males and in Macedonia among females (Fig. 10B). Rates of both colon and rectal cancer incidence tend to be low in most regions of Africa and in Southern Asia.

Colorectal cancer incidence rates vary widely, with 8-fold and 6-fold variations in colon and rectal cancer, respectively, by world region; the disease can be considered a marker of socioeconomic development and, in countries undergoing major development transition, incidence rates tend to rise uniformly with increasing HDI.[4,28] Assessing incidence and mortality trends, Arnold et al[29] identified 3 distinct global temporal patterns linked to development levels: 1) increases in both incidence and mortality in the most recent decade (including the Baltic countries, Russia, China, and Brazil); 2) increasing incidence but decreasing mortality (Canada, the United Kingdom, Denmark, and Singapore); and 3) both decreasing incidence and decreasing mortality (the United States, Japan, and France).

The rises in incidence—particularly the generational changes detected in most age-period-cohort analyses—point to the influence of dietary patterns, obesity, and lifestyle factors, whereas the mortality declines seen in more developed countries reflect improvements in survival through the adoption of best practices in cancer treatment and management in developed countries.[29] Longer standing screening and early detection programs, such as those in the United States and Japan implemented in the 1990s,[30] have also had an impact. Although the results from studies assessing colorectal cancer risk and single foods or nutrients have tended to be inconsistent,[31] the revised World Cancer Research Fund/American Institute for Cancer Research report notes convincing evidence that processed meat, alcohol

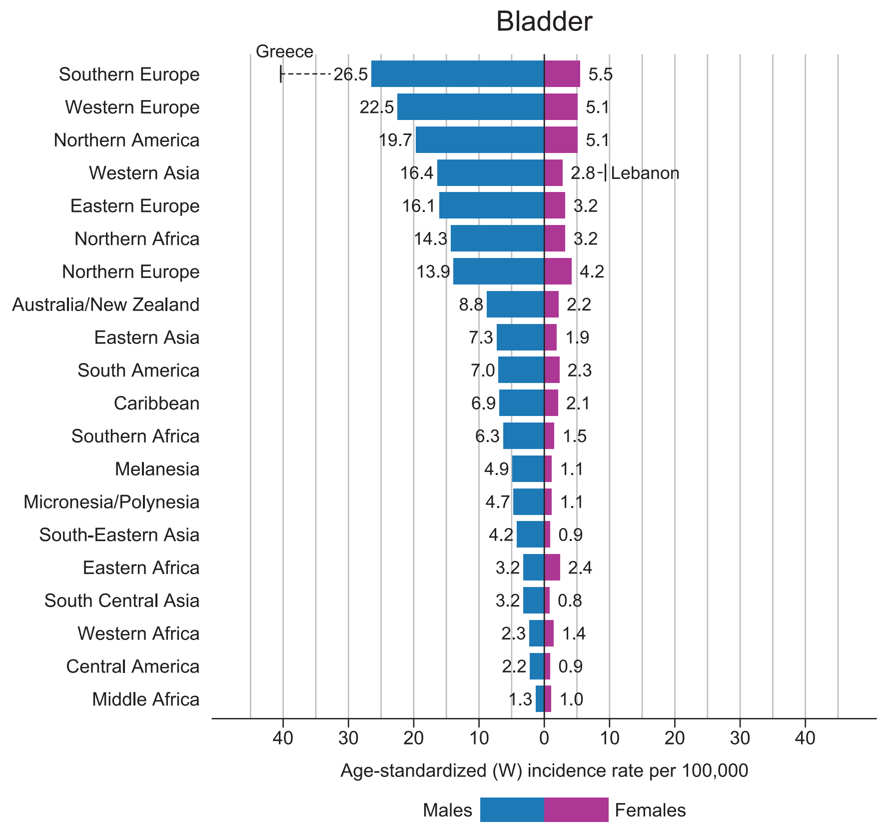

FIGURE 17. Bar Chart of Region-Specific Incidence Age-Standardized Rates by Sex for Cancers of the Bladder in 2018. Rates are shown in descending order of the world (W) age-standardized rate among men, and the highest national rates among men and women are superimposed. Source: GLOBOCAN 2018.

drinks, and body fatness increase risk, whereas physical activity is protective (colon only).[32] A diet high in the consumption of red or processed meats has been associated with an increased risk of colon cancer, but not rectal cancer.[33]

Prostate cancer

It is estimated that there will be almost 1.3 million new cases of prostate cancer and 359,000 associated deaths worldwide in 2018, ranking as the second most frequent cancer and the fifth leading cause of cancer death in men (Table 1) (Fig. 4B). It is the most frequently diagnosed cancer among men in over one-half (105 of 185) of the countries of the world (Fig. 6A), notably in the Americas, Northern and Western Europe, Australia/New Zealand, and much of Sub-Saharan Africa. It is the leading cause of cancer death among men in 46 countries, particularly in Sub-Saharan Africa and the Caribbean. The highest incidence and mortality rates globally are seen in Guadeloupe and Barbados (Fig. 11), respectively. Although incidence rates are high in Australia/New Zealand, Northern and Western Europe (eg, Norway, Sweden, Ireland), and North America (particularly in the United States), mortality rates do not follow those of incidence, with mortality rates elevated in the Sub-Saharan Africa regions (eg, Benin, South Africa, Zambia, and Zimbabwe) as well as the Caribbean (Barbados, Jamaica, and Haiti).

For a disease as common as prostate cancer, relatively little is known about its etiology. The rates are highest among men of African descent in the United States and the Caribbean, reflecting ethnic and genetic predisposition,[34] but there are few additional risk factors for advanced prostate cancer other than body fatness, for which there is convincing evidence of an association.[35] Prostate cancer incidence in recent decades has been heavily influenced by the diagnosis of latent cancers either by PSA testing of asymptomatic individuals or by the detection of latent cancer in tissue removed during prostatectomy or at autopsy. The commercial availability of PSA testing from the middle to late 1980s led to intensive use of the test for early detection and diagnostics, and incidence rates rapidly increased, first in the United States[26] and, within a few years, in greater Europe, notably in several Nordic countries,[36] Australia, and Canada.[37,38] These trends have been followed by declines as the pool of prevalent cases diminishes; in the United States, the 2012 recommendation against the routine use of PSA testing by the US Preventive Services Task Force may have partly driven trends downward in recent years (although this organization

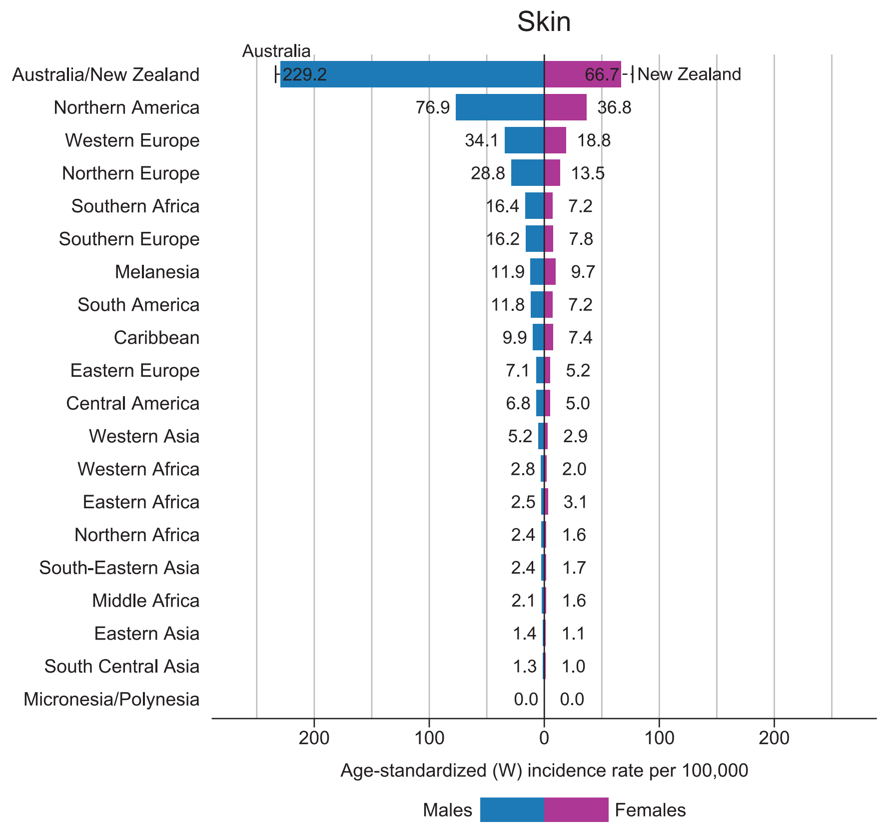

FIGURE 18. Bar Chart of Region-Specific Incidence Age-Standardized Rates by sex for Nonmelanoma Skin Cancer. Rates are shown in descending order of the world (W) age-standardized rate among men, and the highest national rates among men and women are superimposed. Source: GLOBOCAN 2018.

currently recommends that this decision should be an individual one),[39] whereas incidence in the Nordic countries has either declined (Denmark, Finland, and Sweden) or has been stable (Norway) since the middle 2000s.[40] However, rates are on the rise in countries where PSA testing became more widely used later, including the United Kingdom, Japan, Brazil, Costa Rica, and Thailand.[37,38,41] Incidence is also rising in several African populations, including Kampala (Uganda) and in the black population of Harare (Zimbabwe), although, because the registry catchment areas comprise urban populations, it remains difficult to attribute the trends to changes in risk or to enhanced diagnostic capabilities and increased PSA testing.[42,43]

Death rates for prostate cancer have been decreasing in many countries, including those in Northern America, Oceania, Northern and Western Europe, developed countries of Asia,[38,41,44] and the United States, which has been linked to earlier diagnosis because of screening and improved treatment, resulting in a genuine postponement of death for some men with metastatic disease, as well as changes in the attribution of cause of death.[45] In contrast, the rising mortality rates in several Central and South American, Asian, and Central and Eastern European countries, including Cuba, Brazil, the Philippines, Singapore, Bulgaria, Belarus, and Russia, may partly reflect underlying incidence trends and a changing distribution of risk factors, possibly linked to a more Westernized lifestyle, in combination with limited access to effective treatment.[35,38]

Stomach cancer

Stomach cancer (cardia and noncardia gastric cancer combined) remains an important cancer worldwide and is responsible for over 1,000,000 new cases in 2018 and an estimated 783,000 deaths (equating to 1 in every 12 deaths globally), making it the fifth most frequently diagnosed cancer and the third leading cause of cancer death (Table 1) (Fig. 4A). Rates are 2-fold higher in men than in women. Among men, it is the most commonly diagnosed cancer and the leading cause of cancer death in several Western Asian countries, including Iran, Turkmenistan, and Kyrgyzstan (Figs. 5A and 6A). Incidence rates are markedly elevated in Eastern Asia (eg, in Mongolia, Japan and the Republic of Korea [the country with the highest rates worldwide in both sexes]), whereas the rates in Northern America and Northern Europe are generally low and are equivalent to those seen across the African regions (Fig. 12).

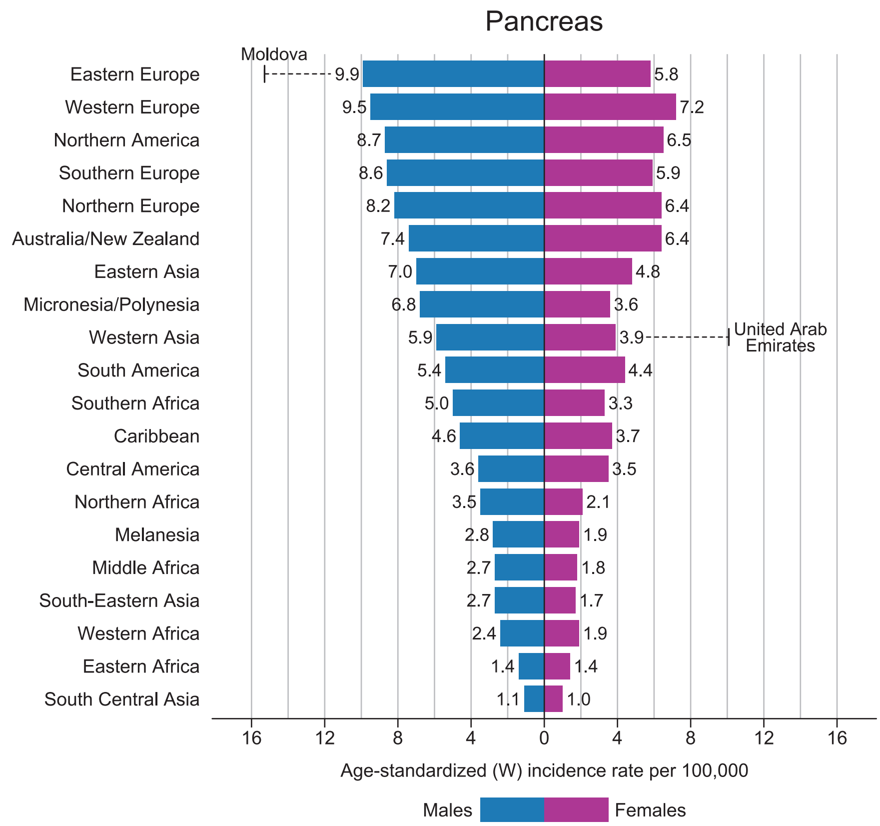

FIGURE 19. Bar Chart of Region-Specific Incidence Age-Standardized Rates by Sex for Pancreatic Cancer in 2018. Rates are shown in descending order of the world (W) age-standardized rate among men, and the highest national rates among men and women are superimposed. Source: GLOBOCAN 2018.

Several migrant studies have documented a strong environmental component in explaining the regional variation in stomach cancer incidence rates. Stomach cancer incidence rates among first-generation Japanese migrants to Hawaii were observed to be lower than the rates among Japanese living in Japan, and the second-generation, Hawaiian-born Japanese experienced a further diminution in rates, although they still were higher than the rates among whites in the host population.[46]

Helicobacter pylori is the main risk factor for stomach cancer, with almost 90% of new cases of noncardia gastric cancer attributed to this bacterium.[47,48] Although international variation in *H. pylori* prevalence correlates reasonably with that of stomach cancer incidence, factors other than *H. pylori* also are likely of major importance. There is a dietary component, with foods preserved by salting and low fruit intake increasing risk, and both alcohol consumption and active tobacco smoking are also established risk factors.[49,50]

Although they often are reported as a single entity, gastric cancers can generally be classified into 2 topographical categories. Rates of noncardia gastric cancer (arising from more distal regions) have been steadily declining over the last one-half century in most populations. The trends are attributed to the *unplanned triumph* of prevention,[51] including a decreased prevalence of *H. pylori* and improvements in the preservation and storage of foods. Cancers of the gastric cardia (arising in the area adjoining the esophageal-gastric junction) have epidemiological characteristics more similar to those of esophageal adenocarcinoma (AC), and important risk factors include obesity and gastroesophageal reflux disease (GERD), with Barrett esophagus (a condition resulting from GERD) also thought to increase risk; the incidence of these cancers has been increasing particularly in high-income countries.[52]

Liver cancer

Liver cancer is predicted to be the sixth most commonly diagnosed cancer and the fourth leading cause of cancer death worldwide in 2018, with about 841,000 new cases and 782,000 deaths annually (Table 1) (Fig. 4). Rates of both incidence and mortality are 2 to 3 times higher among men in most world regions (Fig. 13); thus liver cancer ranks fifth in terms of global cases and second in terms of deaths for males (Fig. 4A). Incidence rates are 2-fold greater among men in transitioned countries (Fig. 7), but the highest rates are observed mainly in lower HDI settings, with liver cancer the most common cancer in 13 geographically diverse countries that include several in Northern and Western Africa (Egypt, the Gambia, Guinea) and Eastern and

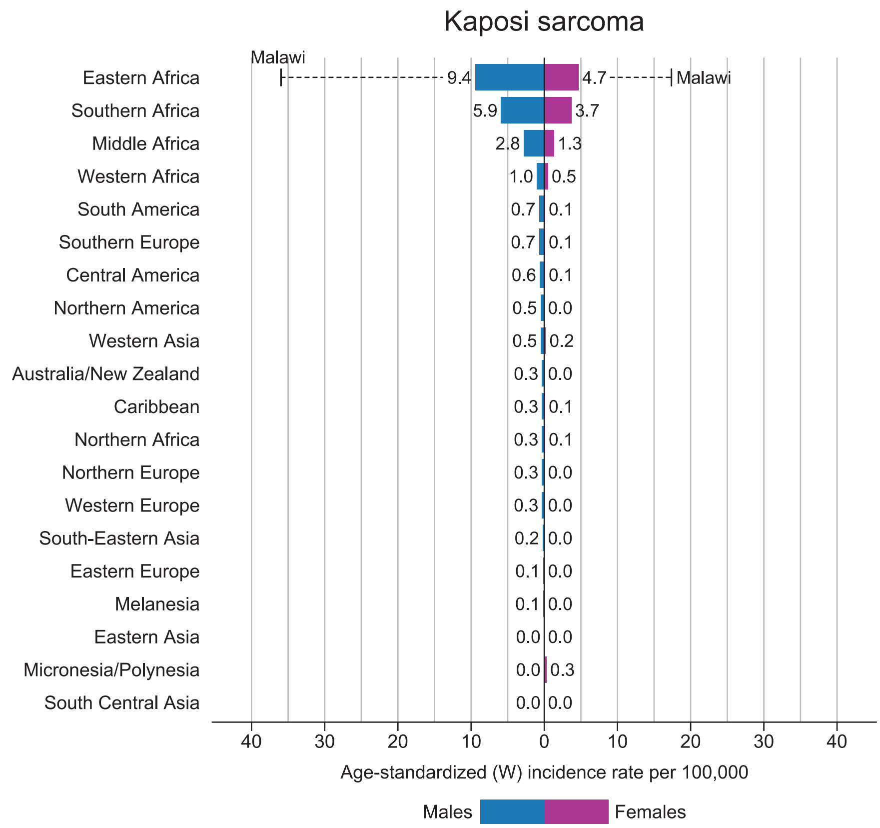

FIGURE 20. Bar Chart of Region-Specific Incidence Age-Standardized Rates by Sex for Kaposi Sarcoma in 2018. Rates are shown in descending order of the world (W) age-standardized rate among men, and the highest national rates among men and women are superimposed. Source: GLOBOCAN 2018.

South-Eastern Asia (Mongolia, Cambodia, and Vietnam). Liver cancer incidence rates in Mongolia far exceed those of any other country (Fig. 13), with estimated 2018 rates 4 times higher than those estimated among men in China and the Republic of Korea, for example.

Primary liver cancer includes hepatocellular carcinoma (HCC) (comprising 75%-85% of cases) and intrahepatic cholangiocarcinoma (comprising 10%-15% of cases) as well as other rare types. The main risk factors for HCC are chronic infection with hepatitis B virus (HBV) or hepatitis C virus (HCV), aflatoxin-contaminated foodstuffs, heavy alcohol intake, obesity, smoking, and type 2 diabetes.[53] The major risk factors vary from region to region. In most high-risk HCC areas (China, Eastern Africa), the key determinants are chronic HBV infection and aflatoxin exposure, whereas in other countries (Japan, Egypt), HCV infection is likely the predominant cause. In Mongolia, HBV and HCV virus and coinfections of HBV carriers with HCV or hepatitis δ virus, as well as alcohol abuse, all contribute to the high burden.[54] The rising obesity prevalence is considered a contributory factor to the observed increasing incidence of HCC in low-risk HCC areas.[55]

Primary prevention of the majority of liver cancer cases has been feasible through a vaccine against HBV since 1982, and future benefits of this vaccine will accrue as younger generations vaccinated in childhood reach the ages where liver cancer becomes common. The WHO recommends its inclusion in routine infant immunization programs and, by the end of 2016, 186 countries had introduced the HBV vaccine into their national immunization schedules,[56] with many countries achieving greater than 80% coverage for the full recommended dose. The vaccine has dramatically reduced the prevalence of HBV infection and the incidence of HCC at younger ages in high-risk countries in East Asia, where mass vaccination was first introduced.[57] However, currently, there is no vaccine available to prevent HCV infection. Although there have been substantive declines in HCV transmission in highly resourced countries, the continued use of contaminated needles and unsafe transfusions contribute to the spread of infection in several low-income countries.[58] Recent developments in the treatment of HBV and HCV suggest that large numbers of liver cancer cases could be avoided, although the costs are prohibitive at present.[53]

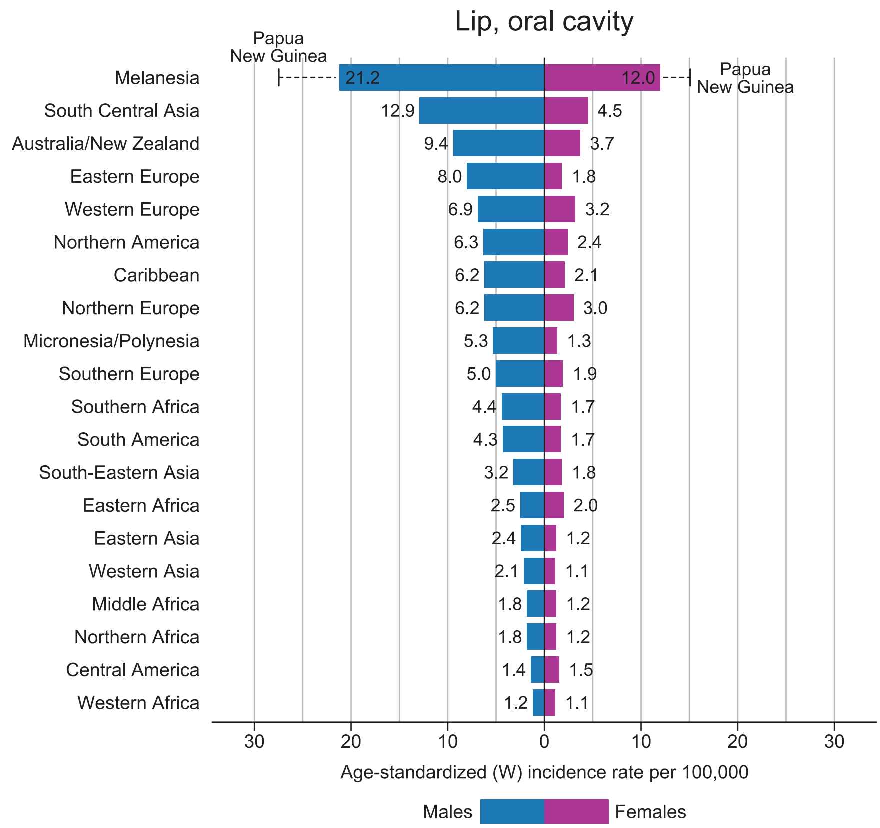

FIGURE 21. Bar Chart of Region-Specific Incidence Age-Standardized Rates by Sex for Cancers of the Lip and Oral Cavity in 2018. Rates are shown in descending order of the world (W) age-standardized rate among men, and the highest national rates among men and women are superimposed. Source: GLOBOCAN 2018.

Esophageal cancer

This disease ranks seventh in terms of incidence (572,000 new cases) and sixth in mortality overall (509,000 deaths), the latter signifying that esophageal cancer will be responsible for an estimated 1 in every 20 cancer deaths in 2018 (Table 1) (Fig. 4). Approximately 70% of cases occur in men, and there is a 2-fold to 3-fold difference in incidence and mortality rates between the sexes worldwide (Fig. 7) and between regions (Fig. 14). Among men, rates are also 2-fold greater in higher HDI countries, with mortality rates ranking fifth in these countries (Fig. 7). Esophageal cancer is common in several Eastern and Southern African countries; it is the leading cause of cancer mortality in Kenyan men (Fig. 6A), whereas Malawi exhibits the highest incidence rates globally in both men and women (Fig. 14). Incidence rates in Eastern Africa rank third by region in men, with the highest rates in Eastern Asia, where rates in Mongolia and China are in the top 5 worldwide.

The geographic variation in esophageal cancer incidence is striking, and the 2 most common histologic subtypes (squamous cell carcinoma [SCC] and AC) have quite different etiologies. Heavy drinking and smoking and their synergistic effects are the major risk factors for SCC in Western settings.[59] However, in lower income countries, such as in parts of Asia and Sub-Saharan Africa, the major risk factors for SCC (which usually comprises over 90% of all esophageal cancer cases) have yet to be elucidated. However, suspected additional risk factors for SCC in other parts of the world include betel quid chewing on the Indian subcontinent and drinking very hot mate in Southern America (eg, in Uruguay, Brazil, and Argentina).[59] Major risk factors in the high-incidence countries in Eastern and Southern Africa have yet to be elucidated, and research is needed to address the role of these factors and other dietary components (eg, nutritional deficiencies, nitrosamines).[60] AC represents the majority of esophageal cancer cases in high-income countries, with excess body weight and GERD among the key risk factors.[59] The incidence of esophageal SCC is broadly in decline and may have been preceded by economic gains and dietary improvements in certain high-risk areas in Asia, whereas in several high-income countries (eg, the United States, Australia, France, and the United Kingdom), it is believed that the reductions are caused primarily by declines in cigarette smoking.[59] In those same countries, incidence rates of AC are rising rapidly in part because of increased obesity and waist circumference, increasing GERD, and possibly decreasing levels of chronic infection with *H. pylori*.[61]

Cervical cancer

With an estimated 570,000 cases and 311,000 deaths in 2018 worldwide, this disease ranks as the fourth most frequently diagnosed cancer and the fourth leading cause of cancer death in women (Fig. 4). Cervical cancer ranks second in incidence and mortality behind breast cancer in lower HDI settings (Fig. 7); however, it is the most commonly diagnosed cancer in 28 countries (Fig. 5G) and the leading cause of cancer death in 42 countries, the vast majority of which are in Sub-Saharan Africa and South-Eastern Asia (Figs. 5B and 6B). The highest regional incidence and mortality rates are seen in Africa (Fig. 15), with rates elevated in Southern Africa (eg, Swaziland, with the highest incidence rate), Eastern Africa (Malawi, with the highest mortality rate; and Zimbabwe), and Western Africa (Guinea, Burkina Faso, and Mali). In relative terms, the rates are 7 to 10 times lower in North America, Australia/New Zealand, and Western Asia (Saudi Arabia and Iraq).

Human papillomavirus (HPV) is the virtually necessary (but not sufficient) cause of cervical cancer,[62] with 12 oncogenic types classified as group 1 carcinogens by the IARC Monographs.[63] Other important cofactors include immunosuppression (particularly human immunodeficiency virus), smoking, parity (a higher number of full-term pregnancies increases risk), and oral contraceptive use.[64] Over the last few decades, cervical cancer incidence and mortality rates reportedly have been in decline in many populations worldwide. Aside from screening (where available), these declines have been ascribed to factors linked either to increasing average socioeconomic levels or a diminishing risk of persistent infection with high-risk HPV, resulting from improvements in genital hygiene, reduced parity, and a diminishing prevalence of sexually transmitted disease.[65] The beneficial effects of population-based cytological screening programs hastened declines in cervical cancer rates upon their implementation in many European countries, Australia/New Zealand, and North America, despite the observation that, in most of these populations, successive generations of women (born during 1930-1950) were increasingly at risk of the disease because of changing sexual behavior.[66,67] In the absence of effective screening, as in Eastern Europe and Central Asia (including the former republics of the Soviet Union), there have been rapid increases in premature cervical cancer mortality in recent generations.[68] Where data are available in Sub-Saharan Africa, uniform rises also have been reported in Uganda[42] and Zimbabwe.[43]

In such high-risk countries and regions, the challenge is to ensure that resource-dependent programs of screening and vaccination are implemented to transform the situation.[69] HPV vaccination programs potentially can reduce the long-term future burden of cervical cancer, and the WHO currently recommends as *best buys* (effective and cost-effective interventions) vaccinations against HPV (2 doses) of girls aged 9 to 13 years. High-quality screening programs are also important to prevent cervical cancer among unvaccinated older women. The WHO recommends the screening of women aged 30 to 49 years—either through visual inspection with acetic acid in low-resource settings, Papanicolaou tests (cervical cytology) every 3 to 5 years, or HPV testing every 5 years—coupled with timely treatment of precancerous lesions. In recent years, clear evidence supports the use of HPV-based tests for the detection of precursor lesions of the cervix[70]; in a randomized trial in India, HPV testing offered greater protection against invasive cervical cancer than either visual inspection with acetic acid or cytology.[71] However, with increased feasibility in resource-limited countries, there is a need to identify the best triage test for HPV-positive women, given the relatively low specificity of the HPV test.[72] The effective integration of HPV vaccine programs with HPV-based testing via screening programs[73] has the potential to virtually eliminate the burden of cervical cancer in every country of the world in this century.

Thyroid cancer

Thyroid cancer is responsible for 567,000 cases worldwide, ranking in ninth place for incidence. The global incidence rate in women of 10.2 per 100,000 is 3 times higher than in men (Table 3); the disease represents 5.1% of the total estimated female cancer burden, or 1 in 20 cancer diagnoses in 2018 (Fig. 4). Mortality rates from the disease are much lower, with rates from 0.4 to 0.5 in men and women, and an estimated 41,000 deaths. Incidence rates are 4 and 5 times higher in men and women in higher HDI versus lower HDI settings, respectively, although mortality rates, in contrast, are rather similar (Fig. 7). Thyroid cancer incidence rates are highest among both men and women in the Republic of Korea (Fig. 16), where it is also the most frequently diagnosed cancer in women (Fig. 6A). Incidence rates are much higher among women than among men in high-incidence regions, including North America (notably in Canada), Australia/New Zealand, as well as Eastern Asia; female rates also are high in several countries in the Pacific, including New Caledonia and French Polynesia.

The etiology of thyroid cancer is not well understood. The only well established risk factor for thyroid cancer is ionizing radiation, particularly when exposure is in childhood, although there is evidence that other factors (obesity, smoking, hormonal exposures, and certain environmental pollutants) may play a role.[74] The incidence of thyroid cancer has been increasing in many countries since the early 1980s largely because of the increased diagnosis of papillary thyroid cancer through diagnostic changes, improvements in the detection and diagnosis of these tumors, and possibly changes in the prevalence of risk factors.[74] Pointedly, mortality has remained fairly stable over the same period. Much of the increasing incidence of thyroid cancer is thought to be caused by overdiagnosis, particularly after the introduction of new diagnostic techniques.[12] In women, overdiagnosis was estimated to account for 90% of newly diagnosed cases in South Korea; from 70% to 80% in the United States, Italy, France, and Australia; and about 50% in Japan, the Nordic countries, England, and Scotland.[12]

Bladder cancer

Bladder cancer is the 10th most common form of cancer worldwide, with an estimated 549,000 new cases and 200,000 deaths (Table 1). Bladder cancer is more common in men than in women, with respective incidence and mortality rates of 9.6 and 3.2 per 100,000 in men: about 4 times those of women globally (Table 3). Thus the disease ranks higher among men, in whom it is the sixth most common cancer and ninth leading cause of cancer death (Fig. 4). Incidence rates in both sexes are highest in Southern Europe (Greece, with the highest incidence rate in men globally; Spain; Italy), Western Europe (Belgium and the Netherlands), and Northern America, although the highest rates are estimated in Lebanon among women (Fig. 17). Other than certain occupational exposures to chemical and water contaminants, cigarette smoking is the main risk factor for bladder cancer[75] and, with the rising prevalence of smoking among women, the attributable risk, at least in the United States, has reached that among men, with 50% of bladder cancer cases attributable to smoking in both sexes.[76,77]

Other cancers common in certain regions

With over 1,000,000 new cases and 65,000 deaths estimated globally, and incidence rates around 2 times higher among men than among women, NMSC is the most frequently diagnosed cancer in North America, and in Australia and New Zealand, the countries with the highest incidence rates worldwide in men and women, respectively (Fig. 18). Because of its poor prognosis, with almost as many deaths (n = 432,000) as cases (n = 459,000), pancreatic cancer is the seventh leading cause of cancer death in both males and females (Fig. 4). Rates are 3-fold to 4-fold higher in higher HDI countries, with incidence rates highest in Europe, North America, and Australia/New Zealand (Fig. 19). In the 28 countries of the European Union, given that rates are rather stable relative to declining rates of breast cancer, it has been projected that pancreatic cancer will surpass breast cancer as the third leading cause of cancer death in the future.[78]

There are several cancers that, although not featured among the top 10 cancers, are major cancers within certain regions or specific countries. With around 42,000 new cases and 20,000 deaths, Kaposi sarcoma is a relatively rare cancer worldwide, but it is endemic in several countries in Southern and Eastern Africa and estimated to be the leading cause of both cancer incidence and mortality in 2018 in Malawi, Mozambique, Uganda, and Zambia (Figs. 5 and 6); rates in Malawi are estimated to be the highest worldwide in both sexes (Fig. 20). Cancers of the lip and oral cavity are highly frequent in Southern Asia (eg, India and Sri Lanka) as well as the Pacific Islands (Papua New Guinea, with the highest incidence rate worldwide in both sexes), and it is also the leading cause of cancer death among men in India and Sri Lanka (Figs. 6A and 21).

Summary and Conclusions

The GLOBOCAN 2018 estimates presented in this report indicate that there will be 18.1 million new cases of cancer and 9.6 million deaths from cancer in 2018. Cancer is an important cause of morbidity and mortality worldwide, in every world region, and irrespective of the level of human development. The cumulative risk of incidence, even in low-HDI settings, indicates that 1 in 8 men and 1 in 10 women will develop the disease in a lifetime, whereas, in the 5 African regions, the cumulative risk of death in women in 2018 is broadly comparable to the risks observed among women in North America and in the highest income countries of Europe.

The extraordinary diversity of cancer is captured by the variations in the magnitude and profile of the disease between and within world regions. On one hand, there are specific types of cancer that dominate globally: lung, female breast, and colorectal cancers explain one-third of the cancer incidence and mortality burden worldwide and are the respective top 3 cancers in terms of incidence and within the top 5 in terms of mortality (first, fifth, and second, respectively). Conversely, 13 different cancers are the most frequent form of cancer diagnosis or death in 1 or more of the countries studied, and 23 individual cancer sites that explain at least 1% each of the global incidence burden explain 90% when combined. The regional variations in common cancer types signal the extent to which societal, economic, and lifestyle changes interplay to differentially impact on the profile of this most complex group of diseases.

Recent studies in high-income countries have indicated that from one-third to two-fifths of new cancer cases could be avoided by eliminating or reducing exposure to known lifestyle and environmental risk factors.[77,79,80] Although there are several interventions that have proven to be an effective means of cancer prevention, international efforts to promote and implement primary prevention still lack momentum, and policymakers remain unaware of the degree of progress and the benefits that prevention brings.[72]

The recent global assessments of cancers attributable to infection, obesity, and ultraviolet radiation remind us of the sheer variability in their importance for different parts of the world and the need to tailor cancer control actions in accordance with localized patterns of risk factors and cancer burden profiles. With cancer ranking as the first or second cause of premature death in almost 100 countries worldwide, a high-level investment in cancer control alongside other major NCDs was recognized in 2017, with a new cancer resolution unanimously adopted by governments at the World Health Assembly, which noted the potential for cancer prevention in reducing the cancer burden in the future. The resolution builds on the WHO Global Action Plan for the Prevention and Control of NCDs 2013 to 2020 and the United Nations Sustainable Development Goals 2030, which include a specific target of a reduction in premature mortality from NCDs by one-third by 2030.

Equally, the requirements for governments to build population-based systems of data collection to inform cancer control are also unambiguously stated in the resolution. There is a major inequity in the availability of high-quality, local data in many transitioning countries at present that has direct consequences for the corresponding robustness of the estimates presented herein. The fact remains that only 1 in 3 PBCRs report high-quality cancer data to the IARC, and 1 in 5 countries report equivalent mortality data to the WHO. Although the GLOBOCAN estimates provide a valuable global assessment of the magnitude and distribution of cancer, they are not intended as a substitute to the continuous approaches to data recording from high-quality PBCRs and vital registration systems. As part of NCD planning, a cancer surveillance program built around a PBCR provides a means for governments to effectively monitor progress in operationalizing a national cancer control program, as well as a means to evaluate individual cancer control activities.[81,82]

Launched in 2012 and led by the IARC, the Global Initiative for Cancer Registry Development (gicr.iarc.fr) is a partnership of leading cancer organizations seeking to address inequities in the availability of robust cancer incidence data by radically increasing its quality, comparability, and use. Six IARC regional hubs for cancer registration have been established covering Africa, Asia, South and Central America, the Caribbean, and the Pacific Islands that now provide the necessary technical assistance to registries through a broad set of knowledge transfer and capacity-building activities, including a *train the trainer* approach to teaching and the provision of site visits to countries to support local surveillance plans. If the initiative is successful, it then will lead to better global cancer estimates and, just as important, it will provide governments with the local data needed to prioritize and evaluate cancer control efforts to reduce the burden and suffering from cancer in their communities. ■

Acknowledgements: We thank cancer registries worldwide for their collaboration; without their efforts, there would be no global cancer estimates. We also thank Mr. Mathieu Laversanne of the International Agency for Research on Cancer for developing the tables and figures included in this article.

References

1. World Health Organization. Global Health Observatory. Geneva: World Health Organization; 2018. who.int/gho/database/en/. Accessed June 21, 2018.
2. Omran AR. The epidemiologic transition. A theory of the epidemiology of population change. *Milbank Mem Fund Q.* 1971;49:509-538.
3. Gersten O, Wilmoth JR. The cancer transition in Japan since 1951. *Demogr Res.* 2002;7:271-306.
4. Bray F. Transitions in human development and the global cancer burden. In: Stewart BW, Wild CP, eds. World Cancer Report 2014. Lyon: IARC Press; 2014:42-55.
5. Maule M, Merletti F. Cancer transition and priorities for cancer control. *Lancet Oncol.* 2012;13:745-746.
6. Ferlay J, Colombet M, Soerjomataram I, et al. Global and Regional Estimates of the Incidence and Mortality for 38 Cancers: GLOBOCAN 2018. Lyon: International Agency for Research on Cancer/World Health Organization; 2018.
7. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. *CA Cancer J Clin.* 2005;55:74-108.
8. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. *CA Cancer J Clin.* 2011;61:69-90.
9. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. *CA Cancer J Clin.* 2015;65:87-108.
10. United Nations Development Programme. Human Development Report 2016: Human Development for Everyone. New York, NY: United Nations Development Programme; 2016.
11. Hankey BF, Feuer EJ, Clegg LX, et al. Cancer surveillance series: interpreting trends in prostate cancer—Part I: evidence of the effects of screening in recent prostate cancer incidence, mortality, and survival rates. *J Natl Cancer Inst.* 1999;91:1017-1024.
12. Vaccarella S, Franceschi S, Bray F, Wild CP, Plummer M, Dal Maso L. Worldwide thyroid-cancer epidemic? The increasing impact of overdiagnosis. *N Engl J Med.* 2016;375:614-617.
13. Bray F, Colombet M, Mery L et al. Cancer Incidence in Five Continents, Vol. XI (electronic version). Lyon: International Agency for Research on Cancer; 2017. ci5.iarc.fr/Default.aspx. Accessed June 21, 2018.
14. Doll R, Payne P, Waterhouse J. Cancer Incidence in Five Continents: A Technical Report. New York: Springer; 1966.
15. Parkin DM, Bray FI, Devesa SS. Cancer burden in the year 2000. The global picture. *Eur J Cancer.* 2001;37(suppl 8):S4-S66.
16. Alonso R, Pineros M, Laversanne M, et al. Lung cancer incidence trends in Uruguay 1990–2014: an age-period-cohort analysis. *Cancer Epidemiol.* 2018;55:17-22.
17. Lortet-Tieulent J, Renteria E, Sharp L, et al. Convergence of decreasing male and increasing female incidence rates in major tobacco-related cancers in Europe in 1988–2010. *Eur J Cancer.* 2015;51:1144-1163.

18. Thun MJ, Henley SJ, Travis WD. Lung cancer. In: Thun MJ, Linet MS, Cerhan JR, Haiman CA, Schottenfeld D, eds. Cancer Epidemiology and Prevention. 4th ed. New York, NY: Oxford University Press; 2018:519-542.
19. Jemal A, Miller KD, Ma J, et al. Higher lung cancer incidence in young women than young men in the United States. *N Engl J Med.* 2018;378:1999-2009.
20. Jha P. Avoidable global cancer deaths and total deaths from smoking. *Nat Rev Cancer.* 2009;9:655-664.
21. Parkin DM, Bray F, Ferlay J, Jemal A. Cancer in Africa 2012. *Cancer Epidemiol Biomarkers Prev.* 2014;23:953-966.
22. Ferlay J, Bray F, Steliarova-Foucher E, Forman D. Cancer Incidence in Five Continents, CI5plus. IARC CancerBase No. 9. Lyon: International Agency for Research on Cancer; 2018. ci5.iarc.fr/CI5plus/default.aspx. Accessed June 21, 2018.
23. Ziegler RG, Hoover RN, Pike MC, et al. Migration patterns and breast cancer risk in Asian-American women. *J Natl Cancer Inst.* 1993;85:1819-1827.
24. Brinton LA, Gaudet MM, Gierach GL. Breast cancer. In: Thun MJ, Linet MS, Cerhan JR, Haiman CA, Schottenfeld D, eds. Cancer Epidemiology and Prevention. 4th ed. New York: Oxford University Press; 2018:861-888.
25. Bray F, McCarron P, Parkin DM. The changing global patterns of female breast cancer incidence and mortality. *Breast Cancer Res.* 2004;6:229-239.
26. Rossouw JE, Anderson GL, Prentice RL, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. *JAMA* 2002;288:321-333.
27. Ravdin PM, Cronin KA, Howlader N, et al. The decrease in breast-cancer incidence in 2003 in the United States. *N Engl J Med.* 2007;356:1670-1674.
28. Fidler MM, Soerjomataram I, Bray F. A global view on cancer incidence and national levels of the Human Development Index. *Int J Cancer.* 2016;139:2436-2446.
29. Arnold M, Sierra MS, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global patterns and trends in colorectal cancer incidence and mortality. *Gut.* 2017;66:683-691.
30. Schreuders EH, Ruco A, Rabeneck L, et al. Colorectal cancer screening: a global overview of existing programmes. *Gut.* 2015;64:1637-1649.
31. Wu K, Keum N, Nishihara R, Giovannucci EL. Cancers of the colon and rectum. In: Thun MJ, Linet MS, Cerhan JR, Haiman CA, Schottenfeld D, eds. Cancer Epidemiology and Prevention. 4th ed. New York, NY: Oxford University Press; 2018:681-706.
32. World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR). Continuous Update Project Report: Diet, Nutrition, Physical Activity and Colorectal Cancer 2016. Revised 2018. London: World Cancer Research Fund International; 2018. aicr.org/continuous-update-project/reports/colorectal-cancer-2017-report.pdf. Accessed June 21, 2018.
33. Magalhaes B, Peleteiro B, Lunet N. Dietary patterns and colorectal cancer: systematic review and meta-analysis. *Eur J Cancer Prev.* 2012;21:15-23.
34. Rebbeck TR, Devesa SS, Chang BL, et al. Global patterns of prostate cancer incidence, aggressiveness, and mortality in men of African descent [serial online]. *Prostate Cancer.* 2013;2013:560857.
35. Bray F, Kiemeney L. Epidemiology of prostate cancer in Europe: patterns, trends and determinants. In: Bolla M, van Poppel H, eds. Management of Prostate Cancer: A Multidisciplinary Approach. Berlin: Springer-Verlag; 2017:1-11.
36. Kvale R, Auvinen A, Adami HO, et al. Interpreting trends in prostate cancer incidence and mortality in the five Nordic countries. *J Natl Cancer Inst.* 2007;99:1881-1887.
37. Zhou CK, Check DP, Lortet-Tieulent J, et al. Prostate cancer incidence in 43 populations worldwide: an analysis of time trends overall and by age group. *Int J Cancer.* 2016;138:1388-1400.
38. Center MM, Jemal A, Lortet-Tieulent J, et al. International variation in prostate cancer incidence and mortality rates. *Eur Urol.* 2012;61:1079-1092.
39. Grossman DC, Curry SJ, Owens DK, et al. Screening for prostate cancer: US Preventive Services Task Force recommendation statement. *JAMA.* 2018;319:1901-1913.
40. Kvale R, Myklebust TA, Engholm G, Heinavaara S, Wist E, Moller B. Prostate and breast cancer in four Nordic countries: a comparison of incidence and mortality trends across countries and age groups 1975–2013. *Int J Cancer.* 2017;141:2228-2242.
41. Bray F, Pineros M. Cancer patterns, trends and projections in Latin America and the Caribbean: a global context. *Salud Publica Mex.* 2016;58:104-117.
42. Wabinga HR, Nambooze S, Amulen PM, Okello C, Mbus L, Parkin DM. Trends in the incidence of cancer in Kampala, Uganda 1991–2010. *Int J Cancer.* 2014;135:432-439.
43. Chokunonga E, Borok MZ, Chirenje ZM, Nyakabau AM, Parkin DM. Trends in the incidence of cancer in the black population of Harare, Zimbabwe 1991–2010. *Int J Cancer.* 2013;133:721-729.
44. Wong MC, Goggins WB, Wang HH, et al. Global incidence and mortality for prostate cancer: analysis of temporal patterns and trends in 36 countries. *Eur Urol.* 2016;70:862-874.
45. Brawley OW. Trends in prostate cancer in the United States. *J Natl Cancer Inst Monogr.* 2012;2012:152-156.
46. Kolonel LN, Hankin JH, Nomura AMY. Multiethnic studies of diet, nutrition, and cancer in Hawaii. In: Hayashi Y, Nagao M, Sugimura T, et al, eds. Diet, Nutrition and Cancer. Proceedings of the 16th International Symposium of the Princess Takamatsu Cancer Research Fund; Tokyo, Japan; 1985. Tokyo: Japan Scientific Societies Press; Utrecht, the Netherlands: VNU Science Press BV; 1986:29-40.
47. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Infection with Helicobacter pylori. *IARC Monogr Eval Carcinog Risks Hum.* 1994;61:177-240.
48. Plummer M, Franceschi S, Vignat J, Forman D, de Martel C. Global burden of gastric cancer attributable to Helicobacter pylori. *Int J Cancer.* 2015;136:487-490.
49. World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR). Continuous Update Project Report: Diet, Nutrition, Physical Activity and Stomach Cancer 2016. Revised 2018. London: World Cancer Research Fund International; 2018. wcrf.org/sites/default/files/Stomach-Cancer-2016-Report.pdf. Accessed June 21, 2018.
50. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Personal habits and indoor combustions. Volume 100 E. A review of human carcinogens. *IARC Monogr Eval Carcinog Risks Hum.* 2012;100(pt E):1-538.
51. Howson CP, Hiyama T, Wynder EL. The decline in gastric cancer: epidemiology of an unplanned triumph. *Epidemiol Rev.* 1986;8:1-27.
52. deMartel C, Parsonnet J. Stomach cancer. In: Thun MJ, Linet MS, Cerhan JR, Haiman CA, Schottenfeld D, eds. Cancer Epidemiology and Prevention. 4th ed. New York: Oxford University Press; 2018:593-610.
53. London WT, Petrick JL, McGlynn KA. Liver cancer. In: Thun MJ, Linet MS, Cerhan JR, Haiman CA, Schottenfeld D, eds. Cancer Epidemiology and Prevention. 4th ed. New York: Oxford University Press; 2018:635-660.
54. Chimed T, Sandagdorj T, Znaor A, et al. Cancer incidence and cancer control in Mongolia: results from the National

Cancer Registry 2008–12. *Int J Cancer.* 2017;140:302-309.

55. Marengo A, Rosso C, Bugianesi E. Liver cancer: connections with obesity, fatty liver, and cirrhosis. *Annu Rev Med.* 2016;67:103-117.
56. World Health Organization. Global Health Observatory (GHO) data: Hepatitis B 3rd Dose (HepB3) Immunization Coverage. Geneva: World Health Organization; 2017. who.int/gho/immunization/hepatitis/en/. Accessed February 27, 2018.
57. Chang MH, Chen CJ, Lai MS, et al. Universal hepatitis B vaccination in Taiwan and the incidence of hepatocellular carcinoma in children. Taiwan Childhood Hepatoma Study Group. *N Engl J Med* 1997;336:1855-1859.
58. Thursz M, Fontanet A. HCV transmission in industrialized countries and resource-constrained areas. *Nat Rev Gastroenterol Hepatol.* 2014;11:28-35.
59. Blot WJ, Tarone RE. Esophageal cancer. In: Thun MJ, Linet MS, Cerhan JR, Haiman CA, Schottenfeld D, eds. Cancer Epidemiology and Prevention. 4th ed. New York: Oxford University Press; 2017 2018:579-592.
60. McCormack VA, Menya D, Munishi MO, et al. Informing etiologic research priorities for squamous cell esophageal cancer in Africa: a review of setting-specific exposures to known and putative risk factors. *Int J Cancer.* 2017;140:259-271.
61. Arnold M, Laversanne M, Brown LM, Devesa SS, Bray F. Predicting the future burden of esophageal cancer by histological subtype: international trends in incidence up to 2030. *Am J Gastroenterol.* 2017;112:1247-1255.
62. Walboomers JM, Jacobs MV, Manos MM, et al. Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. *J Pathol.* 1999;189:12-19.
63. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Human papillomaviruses. *IARC Monogr Eval Carcinog Risks Hum.* 2007;90:1-636.
64. Herrero R, Murillo R. Cervical cancer. In: Thun MJ, Linet MS, Cerhan JR, Haiman CA, Schottenfeld D, eds. Cancer Epidemiology and Prevention. 4th ed. New York: Oxford University Press; 2018:925-946.
65. International Agency for Research on Cancer (IARC). IARC Handbooks of Cancer Prevention: Volume 10-Cervix Cancer Screening. Lyon: IARC Press; 2005. iarc.fr/en/publications/pdfs-online/prev/handbook10/HANDBOOK10.pdf. Accessed June 21, 2018.
66. Bray F, Carstensen B, Moller H, et al. Incidence trends of adenocarcinoma of the cervix in 13 European countries. *Cancer Epidemiol Biomarkers Prev.* 2005;14:2191-2199.
67. Bray F, Loos AH, McCarron P, et al. Trends in cervical squamous cell carcinoma incidence in 13 European countries: changing risk and the effects of screening. *Cancer Epidemiol Biomarkers Prev.* 2005;14:677-686.
68. Bray F, Lortet-Tieulent J, Znaor A, Brotons M, Poljak M, Arbyn M. Patterns and trends in human papillomavirus-related diseases in central and eastern Europe and central Asia. *Vaccine.* 2013;31(suppl 7):H32-H45.
69. Vaccarella S, Laversanne M, Ferlay J. Cervical cancer in Africa, Latin America and the Caribbean and Asia: regional inequalities and changing trends. *Int J Cancer.* 2017;141:1997-2001.
70. Ronco G, Dillner J, Elfstrom KM, et al. Efficacy of HPV-based screening for prevention of invasive cervical cancer: follow-up of four European randomised controlled trials. *Lancet* 2014;383:524-532.
71. Sankaranarayanan R. HPV vaccination: the most pragmatic cervical cancer primary prevention strategy. *Int J Gynaecol Obstet.* 2015;131(suppl 1):S33-S35.
72. Thun MJ, Wild CP, Colditz G. Framework for understanding cancer prevention. In: Thun MJ, Linet MS, Cerhan JR, Haiman CA, Schottenfeld D, eds. Cancer Epidemiology and Prevention. 4th ed. New York: Oxford University Press; 2018:1193-1204.
73. Bosch FX, Robles C, Diaz M, et al. HPV-FASTER: broadening the scope for prevention of HPV-related cancer. *Nat Rev Clin Oncol.* 2016;13:119-132.
74. Kitahara CM, Schneider AB, Brenner AV. Thyroid cancer. In: Thun MJ, Linet MS, Cerhan JR, Haiman CA, Schottenfeld D, eds. Cancer Epidemiology and Prevention. 4th ed. New York: Oxford University Press; 2018:839-860.
75. Silverman DT, Koutros S, Figueroa JD, Prokunina-Olsson L, Rothman N. Bladder cancer. In: Thun MJ, Linet MS, Cerhan JR, Haiman CA, Schottenfeld D, eds. Cancer Epidemiology and Prevention. 4th ed. New York: Oxford University Press; 2018:977-996.
76. Freedman ND, Silverman DT, Hollenbeck AR, Schatzkin A, Abnet CC. Association between smoking and risk of bladder cancer among men and women. *JAMA.* 2011;306:737-745.
77. Islami F, Goding Sauer A, Miller KD, et al. Proportion and number of cancer cases and deaths attributable to potentially modifiable risk factors in the United States. *CA Cancer J Clin.* 2018;68:31-54.
78. Ferlay J, Partensky C, Bray F. More deaths from pancreatic cancer than breast cancer in the EU by 2017. *Acta Oncol.* 2016;55:1158-1160.
79. Wilson LF, Antonsson A, Green AC, et al. How many cancer cases and deaths are potentially preventable? Estimates for Australia in 2013. *Int J Cancer.* 2018;142:691-701.
80. Brown KF, Rumgay H, Dunlop C, et al. The fraction of cancer attributable to modifiable risk factors in England, Wales, Scotland, Northern Ireland, and the United Kingdom in 2015. *Br J Cancer.* 2018;118:1130-1141.
81. Pineros M, Znaor A, Mery L, Bray F. A global cancer surveillance framework within noncommunicable disease surveillance: making the case for population-based cancer registries. *Epidemiol Rev.* 2017;39:161-169.
82. Parkin DM. The role of cancer registries in cancer control. *Int J Clin Oncol.* 2008;13:102-111.
83. Bray F, Soerjomataram I, Mery L, Ferlay J. Improving the quality and coverage of cancer registries globally. *Lancet* 2015;386:1035-1036.