Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries

Hyuna Sung, PhD [1]; Jacques Ferlay, MSc, ME[2]; Rebecca L. Siegel, MPH [1]; Mathieu Laversanne, MSc[2]; Isabelle Soerjomataram, MD, MSc, PhD[2]; Ahmedin Jemal, DMV, PhD[1]; Freddie Bray, BSc, MSc, PhD[2]

[1]Surveillance and Health Equity Science, American Cancer Society, Atlanta, Georgia; [2]Section of Cancer Surveillance, International Agency for Research on Cancer, Lyon, France.

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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).

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Abstract: This article provides an update on the global cancer burden using the GLOBOCAN 2020 estimates of cancer incidence and mortality produced by the International Agency for Research on Cancer. Worldwide, an estimated 19.3 million new cancer cases (18.1 million excluding nonmelanoma skin cancer) and almost 10.0 million cancer deaths (9.9 million excluding nonmelanoma skin cancer) occurred in 2020. Female breast cancer has surpassed lung cancer as the most commonly diagnosed cancer, with an estimated 2.3 million new cases (11.7%), followed by lung (11.4%), colorectal (10.0 %), prostate (7.3%), and stomach (5.6%) cancers. Lung cancer remained the leading cause of cancer death, with an estimated 1.8 million deaths (18%), followed by colorectal (9.4%), liver (8.3%), stomach (7.7%), and female breast (6.9%) cancers. Overall incidence was from 2-fold to 3-fold higher in transitioned versus transitioning countries for both sexes, whereas mortality varied <2-fold for men and little for women. Death rates for female breast and cervical cancers, however, were considerably higher in transitioning versus transitioned countries (15.0 vs 12.8 per 100,000 and 12.4 vs 5.2 per 100,000, respectively). The global cancer burden is expected to be 28.4 million cases in 2040, a 47% rise from 2020, with a larger increase in transitioning (64% to 95%) versus transitioned (32% to 56%) countries due to demographic changes, although this may be further exacerbated by increasing risk factors associated with globalization and a growing economy. Efforts to build a sustainable infrastructure for the dissemination of cancer prevention measures and provision of cancer care in transitioning countries is critical for global cancer control.
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Keywords: burden, cancer, epidemiology, incidence, mortality

Introduction

Cancer ranks as a leading cause of death and an important barrier to increasing life expectancy in every country of the world.[1] According to estimates from the World Health Organization (WHO) in 2019,[2] cancer is the first or second leading cause of death before the age of 70 years in 112 of 183 countries and ranks third or fourth in a further 23 countries (Fig. 1). Cancer's rising prominence 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.[1]

Overall, the burden of cancer incidence and mortality is rapidly growing worldwide; this reflects 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.[3,4] The extent to which the position of cancer as a cause of premature death reflects national levels of social and economic development can be seen by comparing the maps in Figure 1 and Figure 2A, the latter depicting the 4-tier Human Development Index (HDI) based on the United Nation's 2019 Human Development Report.[5]

In this article, we examine the cancer burden worldwide in 2020 based on the GLOBOCAN estimates of cancer incidence and mortality produced by the International Agency for Research on Cancer.[6] The estimates provided herein do

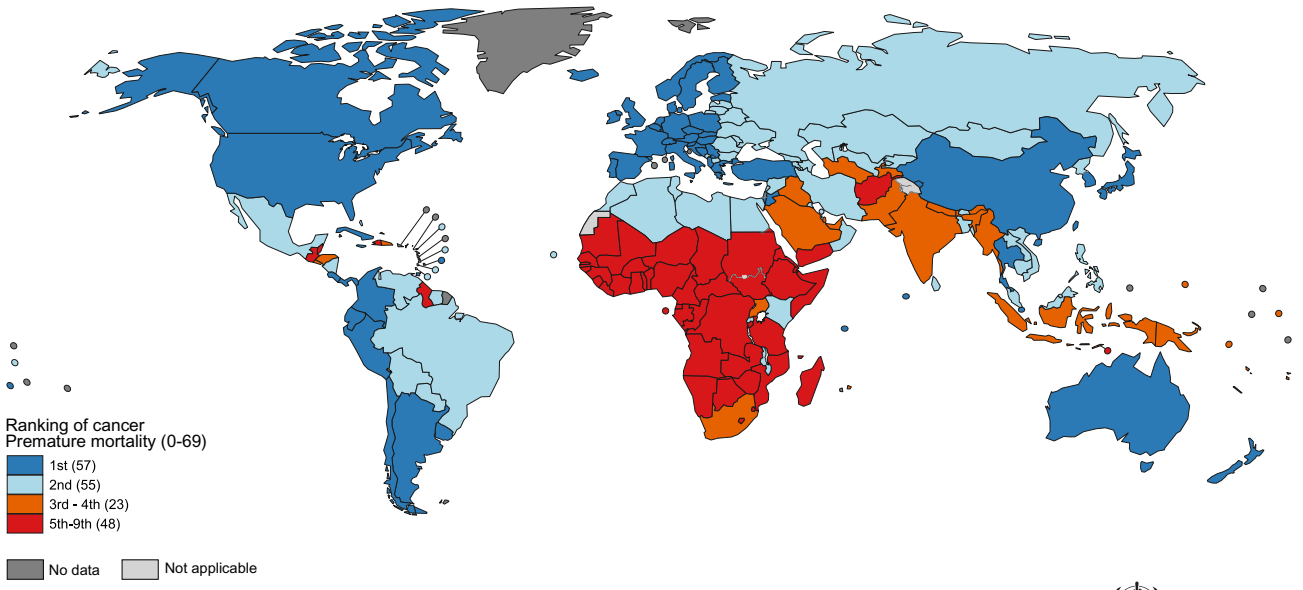

FIGURE 1. National Ranking of Cancer as a Cause of Death at Ages <70 Years in 2019. The numbers of countries represented in each ranking group are included in the legend. Source: World Health Organization.

not reflect the impact of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus responsible for coronavirus disease 2019 (COVID-19),[7,8] as they are based on extrapolations of cancer data collected in earlier years before the pandemic. Although the full extent of the impact of the COVID-19 pandemic in different world regions is currently unknown, delays in diagnosis and treatment associated with the concerns of individuals, health system closures, including suspension of screening programs, and reduced availability of and access to care are expected to cause a short-term decline in cancer incidence followed by increases in advanced-stage diagnoses and cancer mortality in some settings.[9-13]

As with previous reports,[14-17] the primary focus is on a description of the cancer incidence and mortality at the global level and an assessment of the geographic variability observed across 20 predefined world regions (Fig. 2B). We describe the magnitude and distribution of the disease overall and for the major cancer types in 2020, commenting briefly on the associated risk factors and prospects for prevention of the major cancers observed worldwide, and ending with a prediction of the magnitude of the disease in 2040 on the basis of global demographic projections.

Data Sources and Methods

The sources and methods used in compiling the GLOBOCAN estimates for 2020 are described online at the Global Cancer Observatory (GCO) (gco.iarc.fr).[18] The GCO website includes facilities for the tabulation and graphic visualization of the GLOBOCAN database for 185 countries and 36 cancers (as well as all cancers combined), by age and sex. The profile of cancer, globally and by world region, is built up using the best available sources of cancer incidence and mortality data within a given country. Therefore, the validity of the national estimates depends on the degree of representativeness and quality of the source information. The methods used to compile the 2020 estimates are largely based on those developed previously, with an emphasis on the use of short-term predictions and the use of modelled mortality-to-incidence ratios, where applicable.[19] The estimates are available in the GCO for 36 cancer types, based on codes from the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10), including nonmelanoma skin cancer (NMSC) (C44, excluding basal cell carcinomas for incidence).[19] Together with all cancers combined, cancer-specific estimates are provided for 185 countries or territories worldwide by sex and by 18 age groups (ages 0-4, 5-9, …, 80-84, and ≥85 years).

The number of new cancer cases and cancer deaths were extracted from the GLOBOCAN 2020 database for all cancers combined (ICD-10 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), pancreas (C25), larynx (C32), lung (C33-C34, including

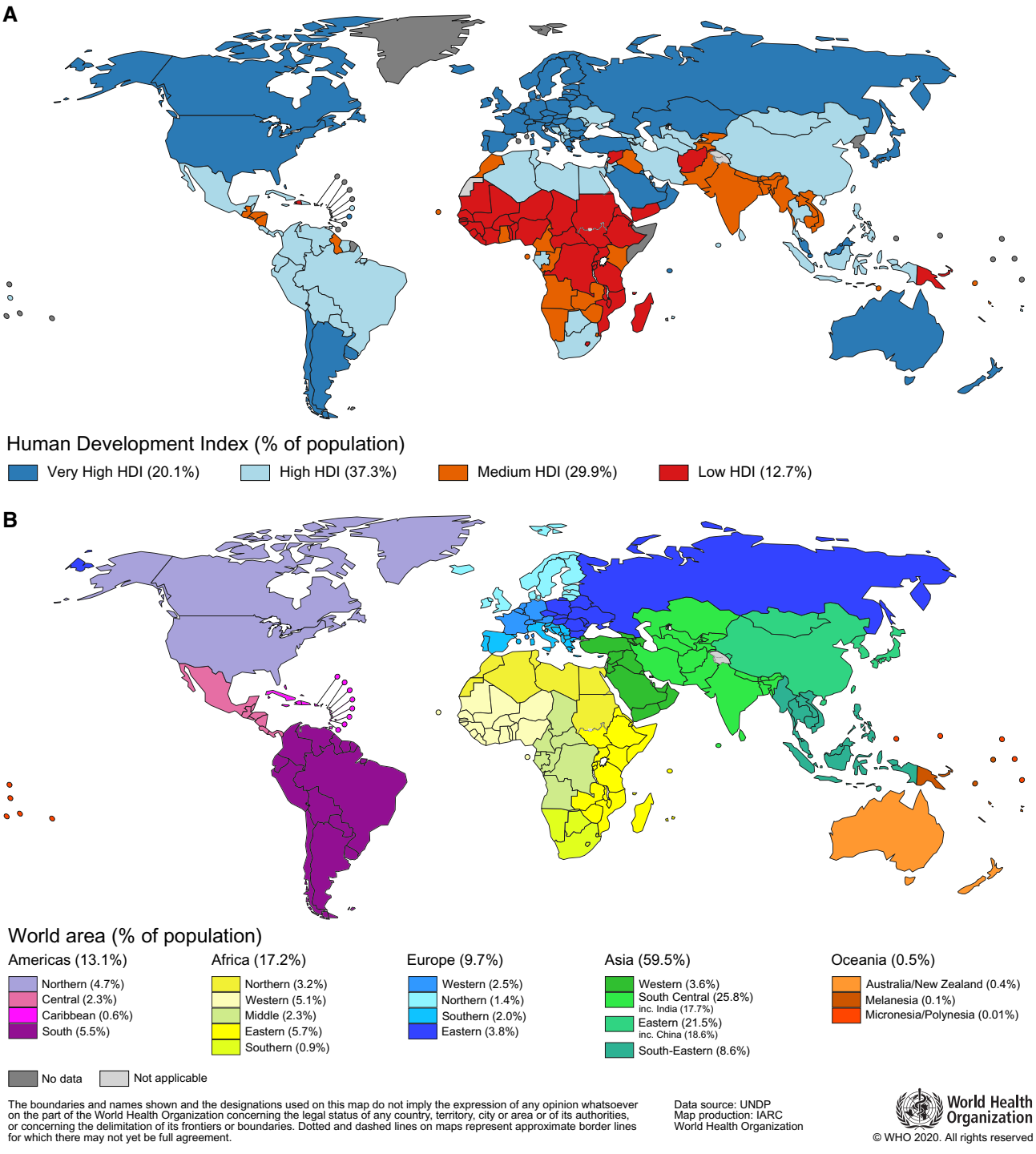

FIGURE 2. (A) The 4-Tier Human Development Index (HDI) and (B) 20 Areas of the World. The sizes of the respective populations are included in the legend. Source: United Nations Procurement Division/United Nations Development Program.

trachea and bronchus), melanoma of 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, C96), multiple myeloma (C88 and C90, including immunoproliferative diseases), and leukemia (C91-C95). For the purposes of consistency with previous exercises,[6] we combine colon, rectum, and anus as colorectal cancer (C18-C21); NMSC (C44, excluding basal cell carcinoma for incidence) is included in the

overall estimation of the total cancer burden, unless otherwise stated, and is included within the *other* category when making comparisons of the relative magnitude of different cancer types.

Further details of definitions and methods are provided in the Supporting Materials. In brief, we present age-standardized incidence or mortality rates (ASR) per 100,000 person-years based on the 1966 Segi-Doll World standard population[20] and the cumulative risk of developing or dying from cancer before age 75 years, assuming the absence of competing causes of death, expressed as a percentage. These indicators allow comparisons between populations that are not influenced by differences in their age structures, and they are presented for the major cancer types globally and across 20 aggregated regions, as defined by the United Nations Population Division (Fig. 2B). We also characterize the burden according to 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). Finally, we also provide a prediction of the future burden of cancer in 2040 based on demographic projections, assuming that national rates estimated in 2020 remain constant. Throughout, we use the terms *transitioning*, *emerging*, and *lower HDI countries/economies* as synonyms for nations classified as low or medium HDI, and we use *transitioned* or *higher HDI countries/economies* for those classified as high or very high HDI.

Results

Distribution of Cases and Deaths by World Region and Cancer Types

There were an estimated 19.3 million new cases (18.1 million excluding NMSC, except basal cell carcinoma) and 10 million cancer deaths (9.9 million excluding NMSC, except basal cell carcinoma) worldwide in 2020 (Table 1). Figure 3 presents the distribution of all-cancer incidence and mortality according to world region for both sexes combined and separately for men and women. For both sexes combined, one-half of all cases and 58.3% of cancer deaths are estimated to occur in Asia in 2020 (Fig. 3A), where 59.5% of the global population resides (Fig. 2B). Europe accounts for 22.8% of the total cancer cases and 19.6% of the cancer deaths, although it represents 9.7% of the global population, followed by the Americas' 20.9% of incidence and 14.2% of mortality worldwide. In contrast to other regions, the share of cancer deaths in Asia (58.3%) and Africa (7.2%) are higher than the share of incidence (49.3% and 5.7%, 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, the top 10 cancer types account for >60% of the newly diagnosed cancer cases and

TABLE 1. New Cases and Deaths for 36 Cancers and All Cancers Combined in 2020

CANCER SITE	NO. OF NEW CASES (% OF ALL SITES)		NO. OF NEW DEATHS (% OF ALL SITES)	
Female breast	2,261,419	(11.7)	684,996	(6.9)
Lung	2,206,771	(11.4)	1,796,144	(18.0)
Prostate	1,414,259	(7.3)	375,304	(3.8)
Nonmelanoma of skin[a]	1,198,073	(6.2)	63,731	(0.6)
Colon	1,148,515	(6.0)	576,858	(5.8)
Stomach	1,089,103	(5.6)	768,793	(7.7)
Liver	905,677	(4.7)	830,180	(8.3)
Rectum	732,210	(3.8)	339,022	(3.4)
Cervix uteri	604,127	(3.1)	341,831	(3.4)
Esophagus	604,100	(3.1)	544,076	(5.5)
Thyroid	586,202	(3.0)	43,646	(0.4)
Bladder	573,278	(3.0)	212,536	(2.1)
Non-Hodgkin lymphoma	544,352	(2.8)	259,793	(2.6)
Pancreas	495,773	(2.6)	466,003	(4.7)
Leukemia	474,519	(2.5)	311,594	(3.1)
Kidney	431,288	(2.2)	179,368	(1.8)
Corpus uteri	417,367	(2.2)	97,370	(1.0)
Lip, oral cavity	377,713	(2.0)	177,757	(1.8)
Melanoma of skin	324,635	(1.7)	57,043	(0.6)
Ovary	313,959	(1.6)	207,252	(2.1)
Brain, nervous system	308,102	(1.6)	251,329	(2.5)
Larynx	184,615	(1.0)	99,840	(1.0)
Multiple myeloma	176,404	(0.9)	117,077	(1.2)
Nasopharynx	133,354	(0.7)	80,008	(0.8)
Gallbladder	115,949	(0.6)	84,695	(0.9)
Oropharynx	98,412	(0.5)	48,143	(0.5)
Hypopharynx	84,254	(0.4)	38,599	(0.4)
Hodgkin lymphoma	83,087	(0.4)	23,376	(0.2)
Testis	74,458	(0.4)	9334	(0.1)
Salivary glands	53,583	(0.3)	22,778	(0.2)
Anus	50,865	(0.3)	19,293	(0.2)
Vulva	45,240	(0.2)	17,427	(0.2)
Penis	36,068	(0.2)	13,211	(0.1)
Kaposi sarcoma	34,270	(0.2)	15,086	(0.2)
Mesothelioma	30,870	(0.2)	26,278	(0.3)
Vagina	17,908	(0.1)	7995	(0.1)
All sites excluding nonmelanoma skin	18,094,716		9,894,402	
All sites	19,292,789		9,958,133	

[a]New cases exclude basal cell carcinoma, whereas deaths include all types of nonmelanoma skin cancer.
Source: GLOBOCAN 2020.

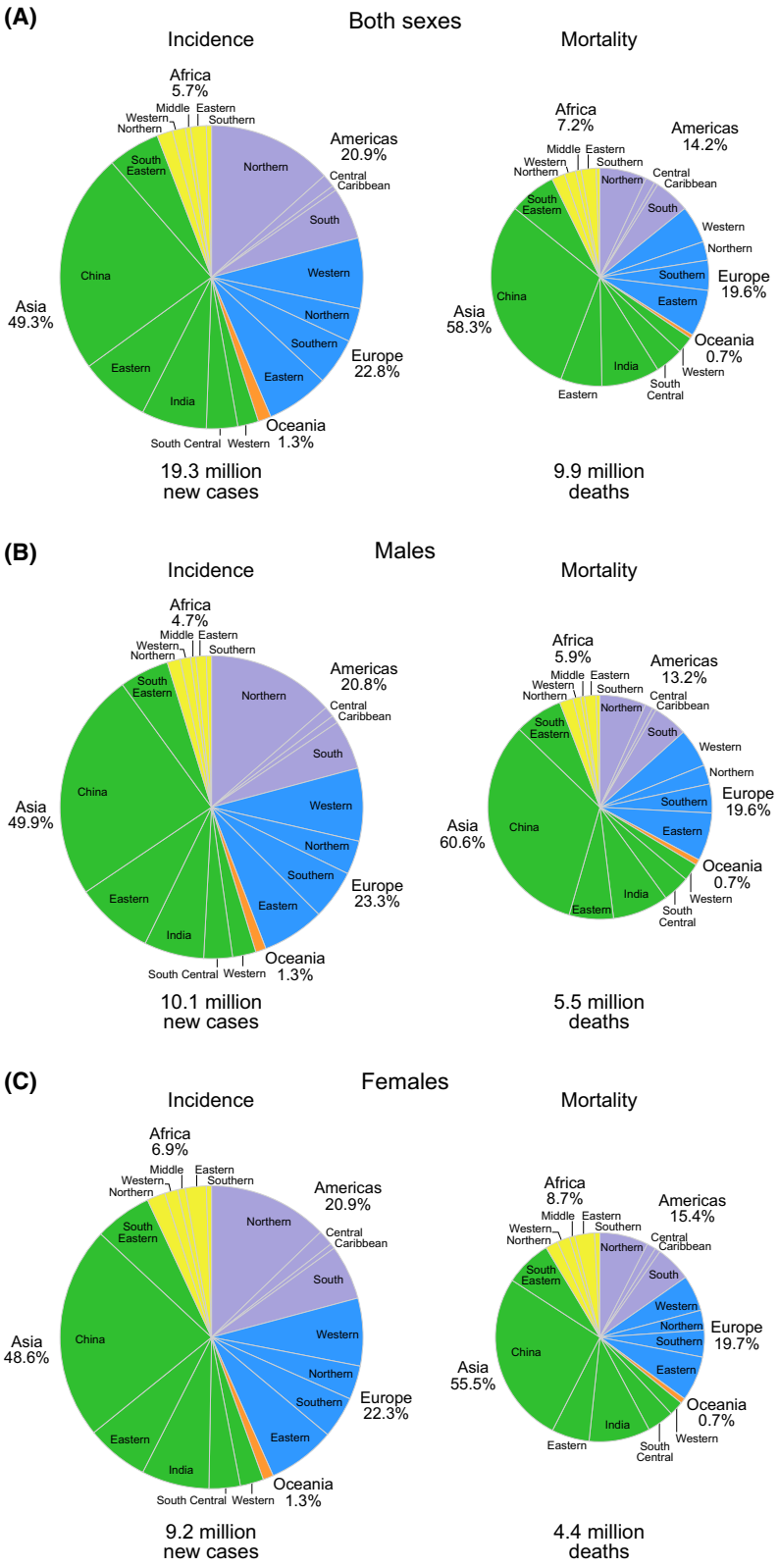

FIGURE 3. Distribution of Cases and Deaths by World Area in 2020 for (A) Both Sexes, (B) Men, and (C) Women. For each sex, the area of the pie chart reflects the proportion of the total number of cases or deaths. Source: GLOBOCAN 2020.

>70% of the cancer deaths. Female breast cancer is the most commonly diagnosed cancer (11.7% of total cases), closely followed by lung (11.4%), colorectal (10.0%), prostate (7.3%), and stomach (5.6%) cancers. Lung cancer is the leading cause of cancer death (18.0% of the total cancer deaths), followed by colorectal (9.4%), liver (8.3%),

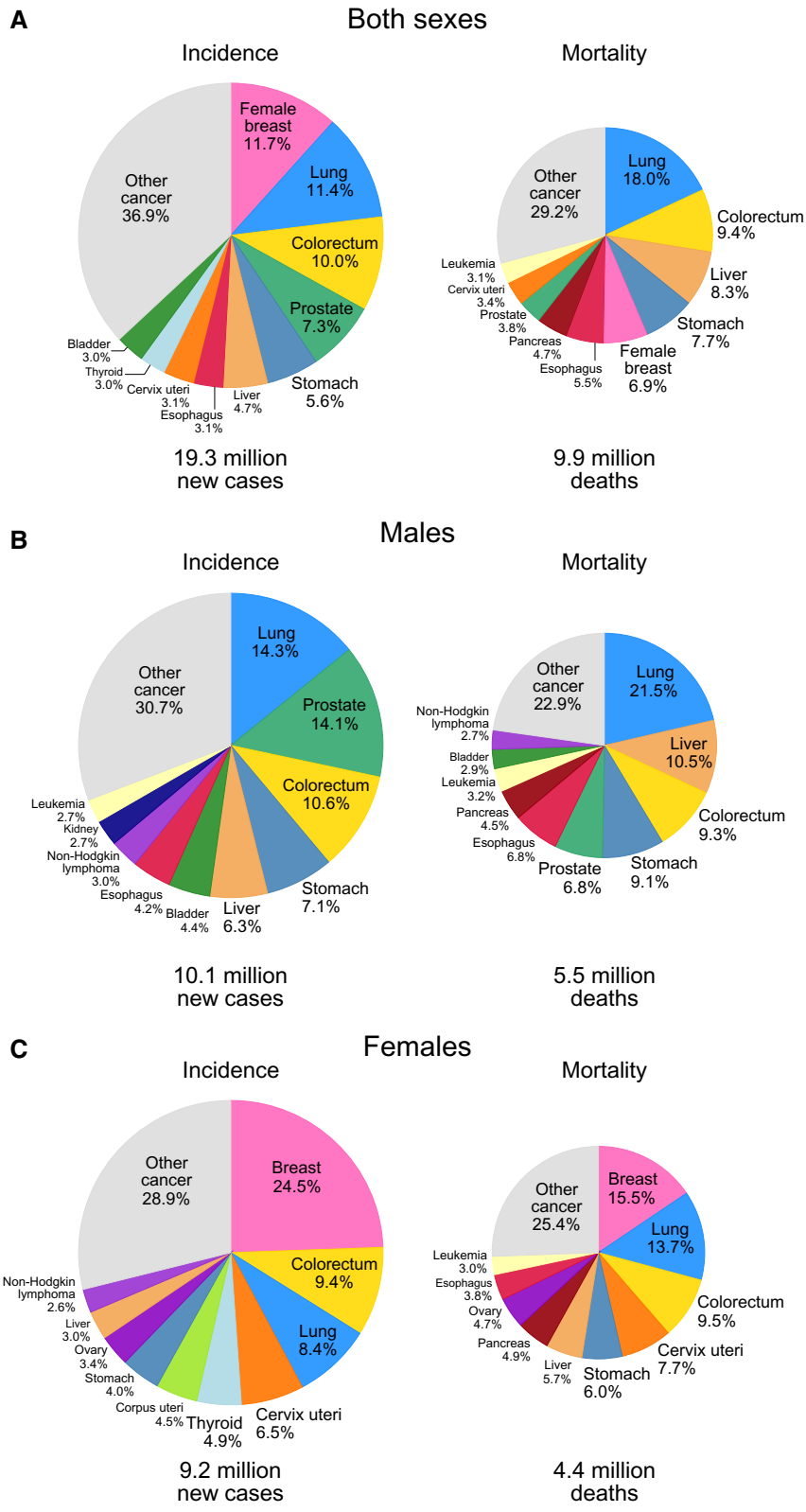

FIGURE 4. Distribution of Cases and Deaths for the Top 10 Most Common Cancers in 2020 for (A) Both Sexes, (B) Men, and (C) Women. For each sex, the area of the pie chart reflects the proportion of the total number of cases or deaths; nonmelanoma skin cancers (excluding basal cell carcinoma for incidence) are included in the "other" category. Source: GLOBOCAN 2020.

stomach (7.7%), and female breast (6.9%) cancers. Lung cancer is the most frequently occurring cancer and the leading cause of cancer death in men, followed by prostate and colorectal cancer for incidence and liver and colorectal cancer for mortality. In women, 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.

Global Cancer Patterns

Figures 5 and 6 show the most commonly diagnosed cancers and leading causes of cancer death, respectively, by sex at the national level. The maps reveal substantial global diversity in leading cancer types, particularly for incidence in men (8 different cancer types) and for mortality in both men (8 types) and women (7 types). In men, prostate cancer is the most frequently diagnosed cancer in 112 countries, followed by lung cancer in 36 countries, and colorectal cancer and liver cancer each in 11 countries (Fig. 5A). With regard to mortality (Fig. 6A), lung cancer is the leading cause of cancer death in men in 93 countries, in part because of its high fatality rate,[21] followed by prostate cancer (48 countries) and liver cancer (23 countries). In contrast to men, the most commonly diagnosed cancer in women is dominated by 2 cancer sites: breast cancer (159 countries) and cervical cancer (23 of 26 remaining countries) (Fig. 5B). The mortality profile in women is more heterogeneous (Fig. 6B), with breast and cervical cancer the leading causes of cancer death in 110

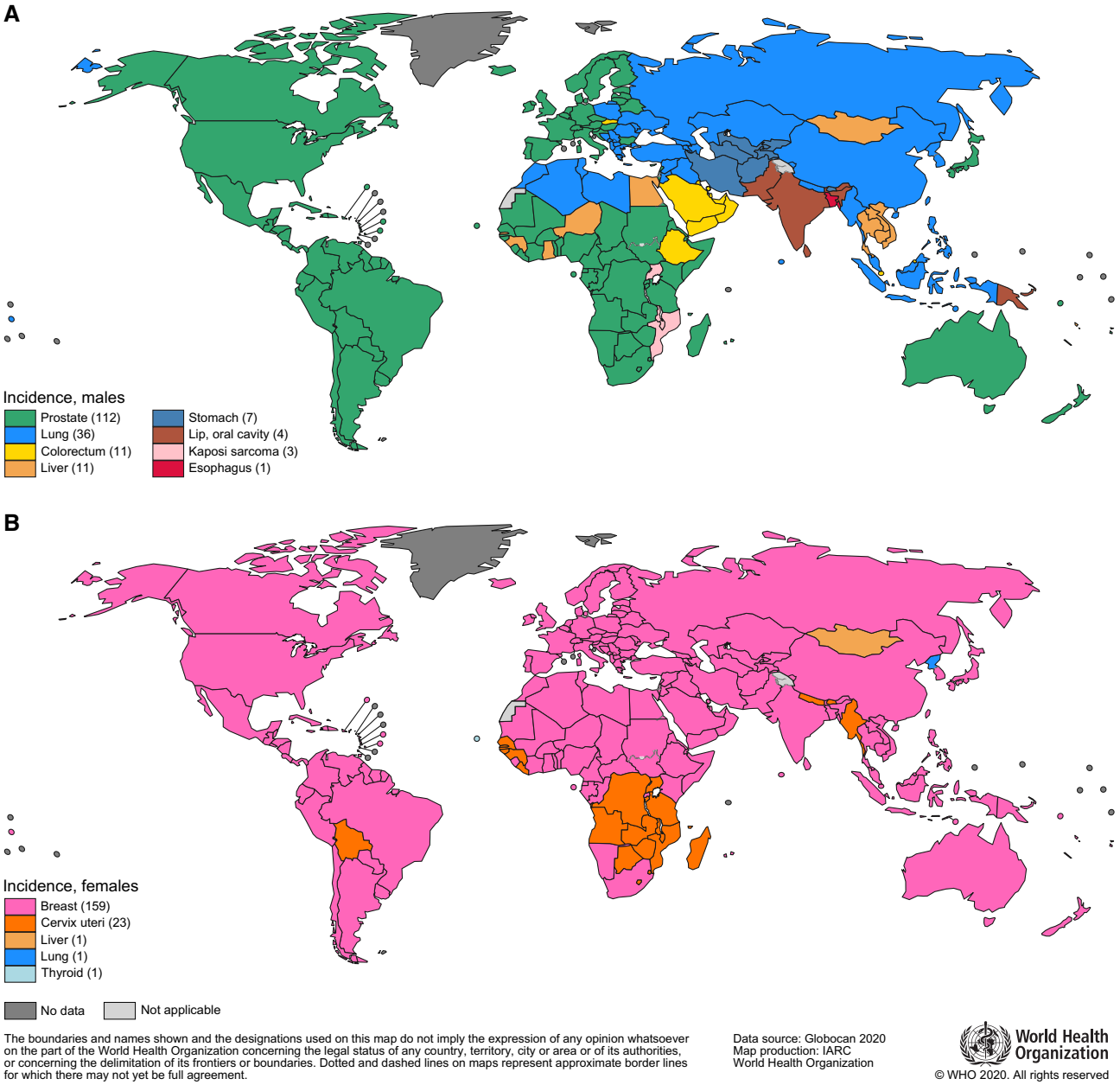

FIGURE 5. Most Common Type of Cancer Incidence in 2020 in Each Country Among (A) Men and (B) Women. The numbers of countries represented in each ranking group are included in the legend. However, nonmelanoma skin cancer (excluding basal cell carcinoma), the most common type of cancer in Australia and New Zealand among men and women and in the United States among men, was excluded when constructing the global maps. Source: GLOBOCAN 2020.

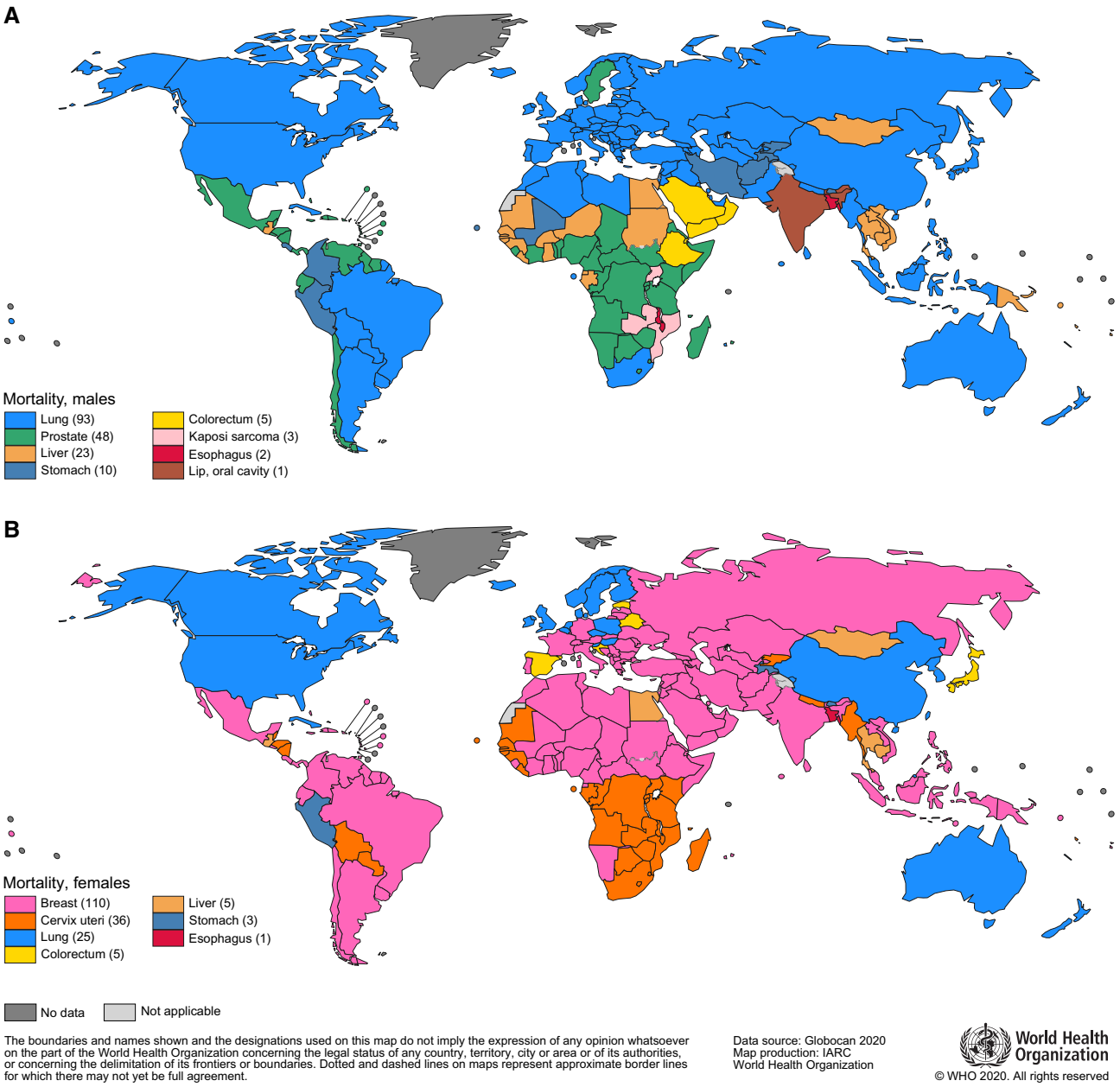

FIGURE 6. Most Common Type of Cancer Mortality by Country in 2020 Among (A) Men and (B) Women. The numbers of countries represented in each ranking group are included in the legend. Source: GLOBOCAN 2020.

and 36 countries, respectively, followed by lung cancer in 25 countries.

Cancer Incidence and Mortality Patterns by the 4-Tier HDI

Incidence rates increased with increasing HDI level, ranging from 104.3 and 128.0 per 100,000 in low HDI countries to 335.3 and 267.6 per 100,000 in very high HDI countries for men and women, respectively (Table 2). Mortality rates are about 2-fold higher in higher HDI countries (122.9-141.1 per 100,000) versus lower HDI countries (76.7-78.0 per 100,000) in men, whereas little variation exists across HDI levels (67.0-88.4 per 100,000) in women (Table 2).

Figures 7A and 7B show cancer incidence and mortality ASRs in higher HDI versus lower HDI countries for men and women, respectively, in 2020. For incidence in men (Fig. 7A), lung cancer ranks first (39 per 100,000) and prostate cancer ranks second (37.5 per 100,000) in higher HDI countries, and vice versa for lower HDI countries (11.3 per 100,000 for prostate cancer and 10.3 per 100,000 for lung cancer). These cancers were followed by colorectal cancer (29 per 100,000) in higher HDI countries, largely reflecting the substantial contribution by the United States,[22] and lip and oral cavity cancer (10.2 per 100,000) in lower HDI countries because of the high burden of the disease in India.[23] In women (Fig. 7B),

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[a]) in 2020

	INCIDENCE				MORTALITY			
	MALES		FEMALES		MALES		FEMALES	
WORLD AREA	AGE-STANDARDIZED RATE (WORLD)	CUMULATIVE RISK, AGES 0-74 YEARS, %	AGE-STANDARDIZED RATE (WORLD)	CUMULATIVE RISK, AGES 0-74 YEARS, %	AGE-STANDARDIZED RATE (WORLD)	CUMULATIVE RISK, AGES 0-74 YEARS, %	AGE-STANDARDIZED RATE (WORLD)	CUMULATIVE RISK, AGES 0-74 YEARS, %
Eastern Africa	112.9	11.91	148.1	15.12	82.5	8.71	102.4	11.02
Middle Africa	109.5	11.70	115.8	11.83	79.2	8.25	79.9	8.54
Northern Africa	145.7	15.14	140.1	14.17	104.6	10.43	77.6	8.06
Southern Africa	232.7	22.74	189.0	18.22	128.8	13.38	98.7	10.22
Western Africa	100.6	10.67	123.2	12.71	74.8	7.89	83.6	8.99
Caribbean	213.9	22.35	174.6	17.44	120.7	11.85	89.2	9.24
Central America	140.9	14.71	141.1	14.01	70.2	7.15	63.1	6.72
South America	217.1	22.09	192.2	18.79	104.9	10.59	82.1	8.51
Northern America	397.9	37.05	332.6	31.10	98.9	10.31	77.7	8.23
Eastern Asia	242.3	24.47	196.4	19.34	157.4	16.34	93.0	9.88
All but China	304.8	30.09	239.2	22.70	112.0	10.76	64.4	6.12
China	225.4	23.25	188.2	18.78	163.9	17.28	98.1	10.59
South-Eastern Asia	159.2	16.46	149.3	15.03	114.1	11.82	80.8	8.55
South Central Asia	103.2	11.13	102.5	10.78	71.2	7.88	63.1	6.95
All but India	122.8	12.97	110.7	11.60	86.2	9.25	68.5	7.49
India	95.7	10.44	99.3	10.47	65.4	7.37	61.0	6.74
Western Asia	198.3	20.77	162.3	16.38	123.5	13.09	79.1	8.38
Eastern Europe	293.8	30.47	220.9	22.18	165.6	18.24	88.7	9.79
Northern Europe	343.7	32.91	296.5	28.19	115.1	11.39	87.9	9.2
Southern Europe	317.8	31.31	249.9	23.85	126.9	13.19	76.3	8.07
Western Europe	365.3	34.90	294.3	27.85	127.1	13.00	83.9	8.84
Australia/New Zealand	494.2	44.37	405.2	36.45	100.7	9.76	73.1	7.38
Melanesia	192.6	20.62	202.5	19.59	125.3	13.21	118.3	12.12
Micronesia/Polynesia	239.5	25.18	206.5	20.62	152.3	16.24	109.4	11.58
Low HDI	104.3	11.04	128.0	13.10	78.0	8.14	88.4	9.46
Medium HDI	109.2	11.75	108.7	11.35	76.7	8.45	67.0	7.32
High HDI	207.7	21.49	178.0	17.79	141.1	14.90	90.3	9.69
Very high HDI	335.3	32.64	267.6	25.75	122.9	12.67	80.0	8.37
World	222.0	22.60	186.0	18.55	120.8	12.59	84.2	8.86

[a]Incidence excludes basal cell carcinoma, whereas mortality includes all types of nonmelanoma skin cancer.
Abbreviation: HDI, Human Development Index.
Source: GLOBOCAN 2020.

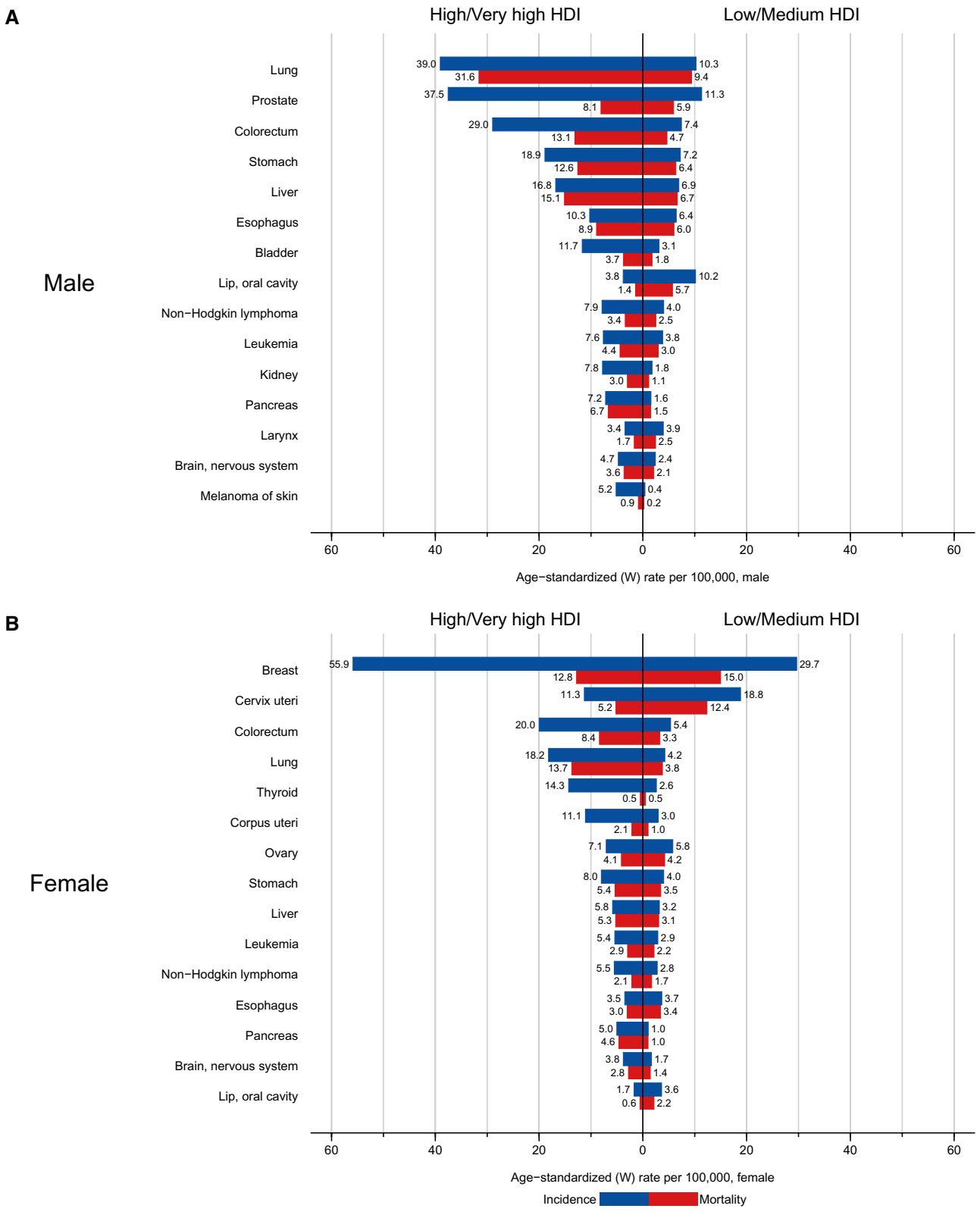

FIGURE 7. Incidence and Mortality Age-Standardized Rates in High/Very High Human Development Index (HDI) Countries Versus Low/Medium HDI Countries Among (A) Men and (B) Women in 2020. The 15 most common cancers in the world (W) are shown in descending order of the overall age-standardized rate for both sexes combined. Source: GLOBOCAN 2020.

incidence rates for breast cancer far exceed those of other cancers in both transitioned (55.9 per 100,000) and transitioning (29.7 per 100,000) countries, followed by colorectal cancer (20 per 100,000) in transitioned countries and cervical cancer (18.8 per 100,000) in transitioning countries.

Cancer Incidence and Death Rates by Sex and World Region

Worldwide, the incidence rate for all cancers combined was 19% higher in men (222.0 per 100,000) than in women (186 per 100,000) in 2020, although rates varied widely across regions. Among men, incidence rates ranged almost 5-fold, from 494.2 per 100,000 in Australia/New Zealand to 100.6 per 100,000 in Western Africa (Table 2); among women, rates varied nearly 4-fold, from 405.2 per 100,000 in Australia/New Zealand to 102.5 per 100,000 in South Central Asia. These variations largely reflect differences in exposure to risk factors and associated cancers (cancer mix) and barriers to high-quality cancer prevention and early detection. For example, the highest overall incidence rates in Australia/New Zealand are caused in part by an elevated risk of NMSC because most of the population is light-skinned, and excessive sun exposure is prevalent, in conjunction with increased detection of the disease.

The gender gap for overall cancer mortality worldwide is twice that for incidence, with death rates 43% higher in men than in women (120.8 and 84.2 per 100,000, respectively) (Table 2), partly because of differences in the distribution of the cancer types. Death rates per 100,000 persons varied from 165.6 per 100,000 in Eastern Europe to 70.2 per 100,000 in Central America among men and from 118.3 per 100,000 in Melanesia to 63.1 per 100,000 in Central America and South Central Asia among women. Notably, the cumulative risk of dying from cancer among women in 2020 was higher in Eastern Africa (11.0%) than in Northern America (8.2%), Western Europe (8.8%), and Australia/New Zealand (7.4%).

Table 3 shows the number of newly diagnosed cancer cases and deaths, the incidence and mortality ASR, and the cumulative risk of developing and dying from cancer overall and for the 36 cancer types separately in men and women. One in 5 men or women develop the disease, and 1 in 8 men and 1 in 11 women die from it. Below, we describe and discuss the variations in sex-specific incidence and mortality rates by world region for 16 of these cancer types.

Female breast cancer

Female breast cancer has now surpassed lung cancer as the leading cause of global cancer incidence in 2020, with an estimated 2.3 million new cases, representing 11.7% of all cancer cases (Table 1, Fig. 4). It is the fifth leading cause of cancer mortality worldwide, with 685,000 deaths. Among women, breast cancer accounts for 1 in 4 cancer cases and for 1 in 6 cancer deaths, ranking first for incidence in the vast majority of countries (159 of 185 countries) (Fig. 5B) and for mortality in 110 countries (Fig. 6B). There are exceptions, most notably in terms of deaths, with the disease preceded by lung cancer in Australia/New Zealand, Northern Europe, Northern America, and China (part of Eastern Asia) and by cervical cancer in many countries in sub-Saharan Africa.

Incidence rates are 88% higher in transitioned countries than in transitioning countries (55.9 and 29.7 per 100,000, respectively) (Fig. 7B), with the highest incidence rates (>80 per 100,000) in Australia/New Zealand, Western Europe (Belgium has the world's highest incidence), Northern America, and Northern Europe and the lowest rates (<40 per 100,000) in Central America, Eastern and Middle Africa, and South Central Asia (Fig. 8). However, women living in transitioning countries have 17% higher mortality rates compared with women in transitioned countries (15.0 and 12.8 per 100,000, respectively) (Fig. 7B) because of high fatality rates, with the highest mortality rates found in Melanesia, Western Africa, Micronesia/Polynesia, and the Caribbean (Barbados has the world's highest mortality) (Fig. 8).

The elevated incidence rates in higher HDI countries reflect a longstanding higher prevalence of reproductive and hormonal risk factors (early age at menarche, later age at menopause, advanced age at first birth, fewer number of children, less breastfeeding, menopausal hormone therapy, oral contraceptives) and lifestyle risk factors (alcohol intake, excess body weight, physical inactivity), as well as increased detection through organized or opportunistic mammographic screening.[24] An exceptionally high prevalence of mutations in high-penetrance genes, such as *BRCA1* and *BRCA2* among women of Ashkenazi Jewish heritage (range, 1%-2.5%), in part accounts for the high incidence in Israel and in certain European subpopulations.[25]

Breast cancer incidence rates uniformly increased rapidly during the 1980s and 1990s in many countries in Northern America, Oceania, and Europe, likely reflecting changes in the prevalence of risk factors coupled with increased detection through widespread uptake of mammographic screening. Then, during the early 2000s, incidence dropped or stabilized,[26] which was largely attributed to a reduction in the use of menopausal hormone therapy and also possibly a plateau in screening participation.[27,28] Since 2007, there has been a slow upturn in incidence rates in the United States of <0.5% annually,[29] and moderate but significant increases have also been reported in many other countries in Europe and Oceania.[30] Findings from studies in the United States,[31,32] Denmark,[33] Ireland,[34] and Scotland[35] using cancer registry data supplemented with tumor maker information have found that increasing incidence is confined to estrogen receptor-positive cancer, and the rates are falling for estrogen receptor-negative cancers. Explanations include the obesity epidemic, given the stronger and more consistent association of excess body weight with estrogen receptor-positive cancer,[36-39] and the impact of mammographic screening, which preferentially detects slow-growing estrogen receptor-positive cancers.[40,41] Countries in historically high-risk regions have benefited most from progress through several

TABLE 3. Incidence (Cases, Age-Standardized Rate, Cumulative Risk) and Mortality (Deaths, Age-Standardized Rate, Cumulative Risk) for 36 Cancers and All Cancers Combined by Sex in 2020

	INCIDENCE						MORTALITY					
	MALES			FEMALES			MALES			FEMALES		
CANCER SITE	CASES	AGE-STANDARDIZED RATE (WORLD)	CUMULATIVE RISK, AGES 0-74 YEARS, %	CASES	AGE-STANDARDIZED RATE (WORLD)	CUMULATIVE RISK, AGES 0-74 YEARS, %	CASES	AGE-STANDARDIZED RATE (WORLD)	CUMULATIVE RISK, AGES 0-74 YEARS, %	CASES	AGE-STANDARDIZED RATE (WORLD)	CUMULATIVE RISK, AGES 0-74 YEARS, %
Lip, oral cavity	264,211	6.0	0.68	113,502	2.3	0.26	125,022	2.8	0.32	52,735	1.0	0.12
Salivary glands	29,694	0.7	0.07	23,889	0.5	0.05	13,353	0.3	0.03	9425	0.2	0.02
Oropharynx	79,045	1.8	0.22	19,367	0.4	0.05	39,590	0.9	0.11	8553	0.2	0.02
Nasopharynx	96,371	2.2	0.24	36,983	0.8	0.09	58,094	1.3	0.16	21,914	0.5	0.05
Hypopharynx	70,254	1.6	0.19	14,000	0.3	0.03	32,303	0.7	0.09	6296	0.1	0.01
Esophagus	418,350	9.3	1.15	185,750	3.6	0.44	374,313	8.3	1.01	169,763	3.2	0.38
Stomach	719,523	15.8	1.87	369,580	7.0	0.79	502,788	11.0	1.29	266,005	4.9	0.55
Colon	600,896	13.1	1.49	547,619	10.0	1.12	302,117	6.4	0.66	274,741	4.6	0.45
Rectum	443,358	9.8	1.18	288,852	5.6	0.65	204,104	4.4	0.50	134,918	2.4	0.26
Anus	21,706	0.5	0.06	29,159	0.6	0.07	9416	0.2	0.02	9877	0.2	0.02
Liver	632,320	14.1	1.65	273,357	5.2	0.60	577,522	12.9	1.49	252,658	4.8	0.55
Gallbladder	41,062	0.9	0.10	74,887	1.4	0.16	30,265	0.7	0.07	54,430	1.0	0.11
Pancreas	262,865	5.7	0.66	232,908	4.1	0.45	246,840	5.3	0.62	219,163	3.8	0.41
Larynx	160,265	3.6	0.45	24,350	0.5	0.06	85,351	1.9	0.23	14,489	0.3	0.03
Lung	1,435,943	31.5	3.78	770,828	14.6	1.77	1,188,679	25.9	3.08	607,465	11.2	1.34
Melanoma of skin	173,844	3.8	0.42	150,791	3.0	0.33	32,385	0.7	0.07	24,658	0.4	0.05
Nonmelanoma of skin[a]	722,348	15.1	1.40	475,725	7.9	0.75	37,596	0.8	0.07	26,135	0.4	0.04
Mesothelioma	21,560	0.5	0.05	9310	0.2	0.02	18,681	0.4	0.04	7597	0.1	0.02
Kaposi sarcoma	23,413	0.5	0.05	10,857	0.3	0.02	9929	0.2	0.02	5157	0.1	0.01
Breast				2,261,419	47.8	5.20				684,996	13.6	1.49
Vulva				45,240	0.9	0.09				17,427	0.3	0.03
Vagina				17,908	0.4	0.04				7995	0.2	0.02
Cervix uteri				604,127	13.3	1.39				341,831	7.3	0.82
Corpus uteri				417,367	8.7	1.05				97,370	1.8	0.22
Ovary				313,959	6.6	0.73				207,252	4.2	0.49
Penis	36,068	0.8	0.09				13,211	0.3	0.03			
Prostate	1,414,259	30.7	3.86				375,304	7.7	0.63			

TABLE 3. (Continued)

	INCIDENCE						MORTALITY					
	MALES			FEMALES			MALES			FEMALES		
CANCER SITE	CASES	AGE-STANDARDIZED RATE (WORLD)	CUMULATIVE RISK, AGES 0-74 YEARS, %	CASES	AGE-STANDARDIZED RATE (WORLD)	CUMULATIVE RISK, AGES 0-74 YEARS, %	CASES	AGE-STANDARDIZED RATE (WORLD)	CUMULATIVE RISK, AGES 0-74 YEARS, %	CASES	AGE-STANDARDIZED RATE (WORLD)	CUMULATIVE RISK, AGES 0-74 YEARS, %
Testis	74,458	1.8	0.14				9334	0.2	0.02			
Kidney	271,249	6.1	0.70	160,039	3.2	0.36	115,600	2.5	0.28	63,768	1.2	0.12
Bladder	440,864	9.5	1.05	132,414	2.4	0.26	158,785	3.3	0.30	53,751	0.9	0.08
Brain, nervous system	168,346	3.9	0.40	139,756	3.0	0.31	138,277	3.2	0.34	113,052	2.4	0.26
Thyroid	137,287	3.1	0.33	448,915	10.1	1.02	15,906	0.3	0.04	27,740	0.5	0.05
Hodgkin lymphoma	48,981	1.2	0.10	34,106	0.8	0.07	14,288	0.3	0.03	9088	0.2	0.02
Non-Hodgkin lymphoma	304,151	6.9	0.73	240,201	4.8	0.52	147,217	3.3	0.33	112,576	2.1	0.21
Multiple myeloma	98,613	2.2	0.25	77,791	1.5	0.17	65,197	1.4	0.15	51,880	0.9	0.10
Leukemia	269,503	6.3	0.59	205,016	4.5	0.41	177,818	4.0	0.38	133,776	2.7	0.26
All sites excluding non-melanoma of skin	9,342,957	206.9	21.50	8,751,759	178.1	17.94	5,491,214	120.0	12.53	4,403,188	83.7	8.83
All sites	10,065,305	222.0	22.60	9,227,484	186.0	18.55	5,528,810	120.8	12.59	4,429,323	84.2	8.86

[a]Incidence excludes basal cell carcinoma, whereas mortality includes all types of nonmelanoma skin cancer.
Source: GLOBOCAN 2020

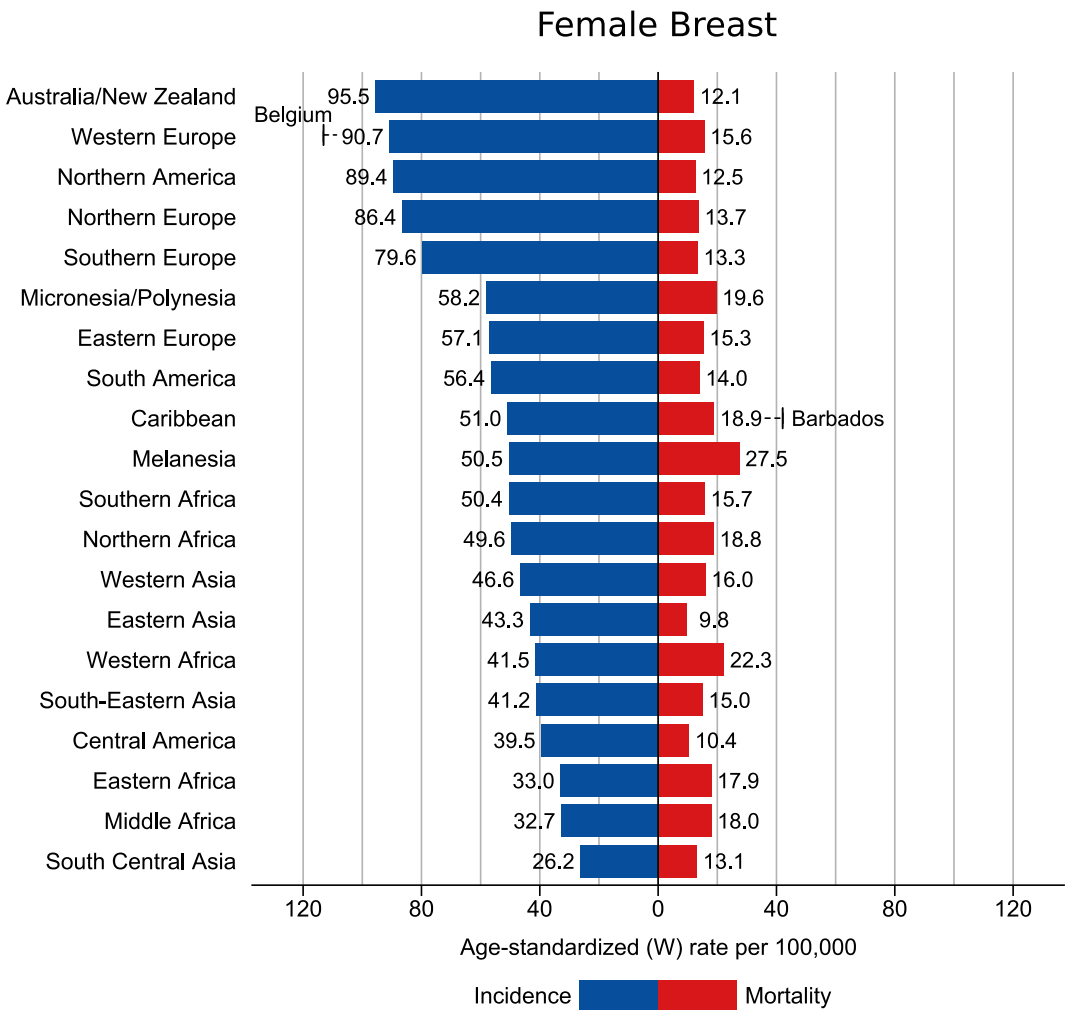

FIGURE 8. Region-Specific Incidence and Mortality Age-Standardized Rates for Female Breast Cancer in 2020. Rates are shown in descending order of the world (W) age-standardized incidence rate, and the highest national age-standardized rates for incidence and mortality are superimposed. Source: GLOBOCAN 2020.

breakthroughs in effective treatment, with mortality rates decreasing since the late 1980s and the early 1990s.[42,43]

Incidence rates of breast cancer are rising fast in transitioning countries in South America, Africa,[44] and Asia[45] as well as in high-income Asian countries (Japan and the Republic of Korea),[30] where rates are historically low. Dramatic changes in lifestyle, sociocultural, and built environments brought about by growing economies and an increase in the proportion of women in the industrial workforce have had an impact on the prevalence of breast cancer risk factors—the postponement of childbearing and having fewer children, greater levels of excess body weight and physical inactivity—and have resulted in a convergence toward the risk factor profile of western countries and narrowing international gaps in breast cancer morbidity.

Some of the most rapid increases are occurring in sub-Saharan Africa. Between the mid-1990s and the mid-2010s, incidence rates increased by >5% per year in Malawi (Blantyre), Nigeria (Ibadan), and the Seychelles and by 3% to 4% per year in South Africa (Eastern Cape) and Zimbabwe (Harare).[44] Mortality rates in sub-Saharan African regions have increased simultaneously and rank now in the world highest (Fig. 8), reflecting weak health infrastructure and subsequently poor survival outcomes. The 5-year age-standardized relative survival in 12 sub-Saharan African countries was 66% for cases diagnosed during 2008 through 2015, sharply contrasting with 85% to 90% for cases diagnosed in high-income countries during 2010 through 2014.[46] The country-specific estimate was as low as 12% in Uganda (Kyadondo) and 20% to 60% in South Africa (Eastern Cape), Kenya (Eldoret), and Zimbabwe (Harare),[47] comparable to 55% in the US state of Connecticut and 57% in Norway during the late 1940s,[48] 3 decades before the introduction of mammography screening and modern therapies.

Low survival rates in sub-Saharan Africa are largely attributable to late-stage presentation. According to a report summarizing 83 studies across 17 sub-Saharan African countries,

77% of all staged cases were stage III/IV at diagnosis.[49] Because organized, population-based mammography screening programs may not be cost effective or feasible in low-resource settings,[50] efforts to promote early detection through improved breast cancer awareness and clinical breast examination by skilled health providers,[51,52] followed by timely and appropriate treatment, are essential components to improving survival.[53] A recent study conducted in 5 sub-Saharan African countries estimated that 28% to 37% of breast cancer deaths in these countries could be prevented through earlier diagnosis of symptomatic disease and adequate treatment, with a fairly equal contribution of each.[54] The Breast Health Global Initiative has established a series of evidence-based, resource-stratified guidelines that supports phased implementation into real-world practice.[55-57]

Establishing primary prevention programs for breast cancer remains a challenge. Nevertheless, efforts to decrease excess body weight and alcohol consumption and to encourage physical activity and breastfeeding may have an impact in stemming the incidence of breast cancer worldwide. Population-wide breast cancer screening programs aim to reduce breast cancer mortality through early detection and effective treatment.[58-61] The WHO recommends organized, population-based mammography screening every 2 years for women at average risk for breast cancer aged 50 to 69 years in well resourced settings.[50] The current guidelines from the American Cancer Society recommend that women aged 45 to 54 years should be screened annually, women aged 40 to 44 years should have the opportunity to begin annual screening, women aged ≥55 years should transition to biennial screening or have the opportunity to continue screening annually, and women should continue screening as long as their overall health is good and they have a life expectancy ≥10 years.[62] Mammographic screening, however, has limitations, such as overdiagnosis and overtreatment.[63-65] There are opportunities to improve the cost effectiveness and benefit-to-harm ratio of screening by adopting a risk-stratified screening strategy using existing and evolving risk prediction models.[66-69] Ongoing screening trials are evaluating the clinical acceptability and utility of risk-stratified screening programs in the general population.[70,71]

Lung cancer

With an estimated 2.2 million new cancer cases and 1.8 million deaths, lung cancer is the second most commonly diagnosed cancer and the leading cause of cancer death in 2020, representing approximately one in 10 (11.4%) cancers diagnosed and one in 5 (18.0%) deaths (Table 1, Fig. 4). Lung cancer is the leading cause of cancer morbidity and mortality in men, whereas, in women, it ranks third for incidence, after breast and colorectal cancer, and second for mortality, after breast cancer. Incidence and mortality rates are roughly 2 times higher in men than in women, although the male-to-female ratio varies widely across regions, ranging from 1.2 in Northern America to 5.6 in Northern Africa (Fig. 9). Lung cancer incidence and mortality rates are 3 to 4 times higher in transitioned countries than in transitioning countries (Fig. 7); this pattern may well change as the tobacco epidemic evolves given that 80% of smokers aged ≥15 years resided in low-income and middle-income countries (LMICs) in 2016.[72]

Among men, lung cancer is the most commonly diagnosed cancer in 36 countries (Fig. 5A), while it is the leading cause of cancer death in 93 countries (Fig. 6A). The highest incidence rates are observed in Micronesia/Polynesia, Eastern and Southern Europe, Eastern Asia, and Western Asia, where Turkey has the highest rate among men globally (Fig. 9). Incidence rates remain generally low in Africa, although they range from intermediate to high in both Southern and Northern regions. Among women, lung cancer is the leading cause of cancer death in 25 countries in Northern America, Oceania, and parts of Europe (Fig. 6B). The highest incidence rates are in Northern America, Northern and Western Europe, Micronesia/Polynesia, and Australia/New Zealand, with Hungary having the highest country-specific rates (Fig. 9). Rates are also high in Eastern Asia, largely reflecting the high burden among Chinese women, which is thought to reflect high outdoor ambient air pollution and exposures to other inhalable agents, such as household burning of solid fuels for heating and cooking given their low smoking prevalence.[73,74] The global proportion of lung cancer deaths attributable to outdoor ambient $PM_{2.5}$ (known as *fine particulate matter*) air pollution was 14% in 2017, ranging from 4.7% in the United States to 20.5% in China.[74]

International variation in lung cancer rates and trends largely reflects the maturity of the tobacco epidemic,[75] with patterns in mortality paralleling those in incidence because of the high fatality rate. Smoking was first established among men in several high-income countries, including the United Kingdom, the United States, Finland, Australia, New Zealand, the Netherlands, Singapore, and, more recently, Germany, Uruguay, and the remaining Nordic countries and was followed by a steep increase in lung cancer.[76,77] Subsequent declines in lung cancer followed peak smoking prevalence by several decades and were first observed in young birth cohorts.[78]

In contrast, among women, the tobacco epidemic is less advanced and defined,[75] and most countries are still observing a rising incidence of lung cancer.[79] Only a relatively few populations, eg, the United States and Switzerland, show signs of a peak and stabilization or decline, albeit at a slower pace compared with those in men.[79,80] As a result of this sex-specific trend, incidence rates among women are approaching or equaling those among men in several countries in Europe and Northern America.[79] From 2006

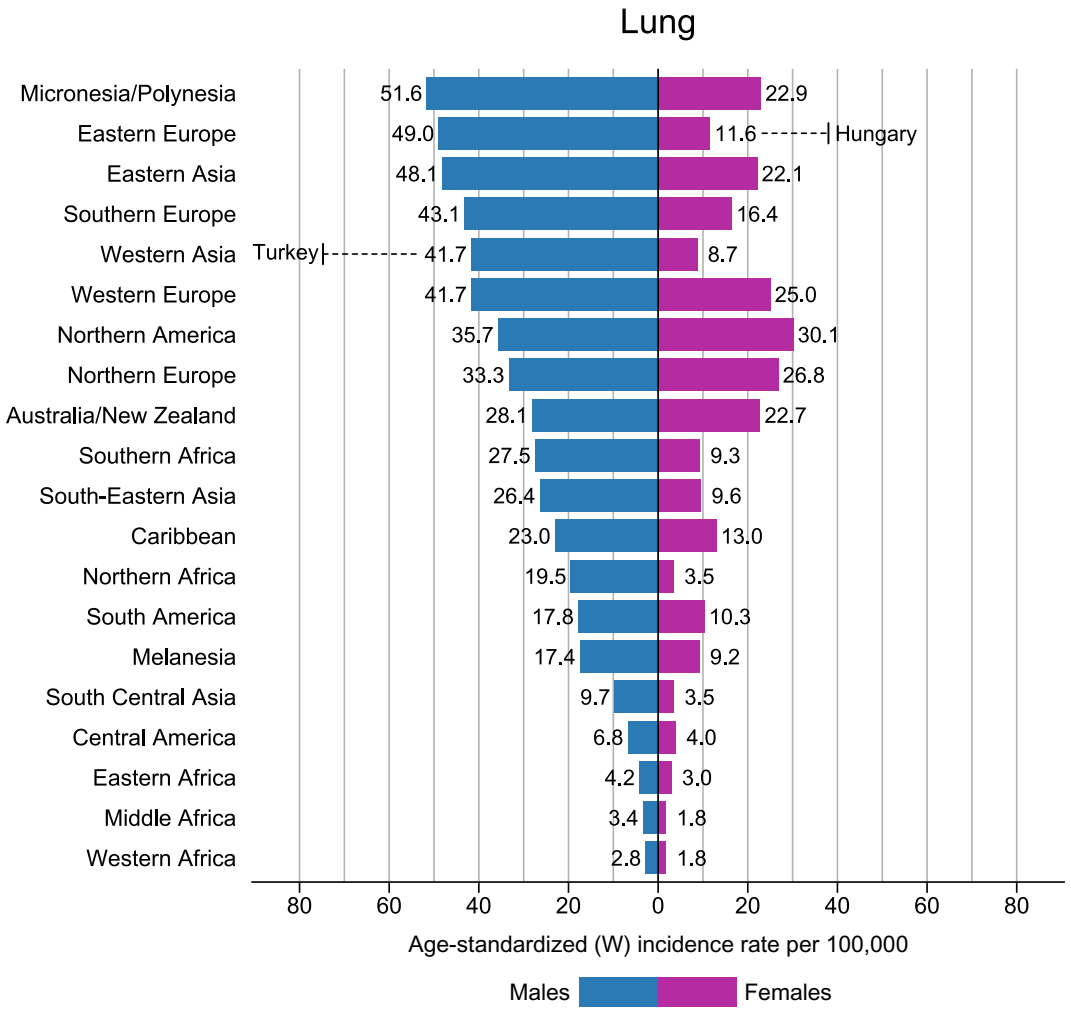

FIGURE 9. Region-Specific Incidence Age-Standardized Rates by Sex for Lung Cancer Among Men and Women in 2020. Rates are shown in descending order of the world (W) age-standardized rate in men, and the highest national rates among men and women are superimposed. Source: GLOBOCAN 2020.

to 2008, female incidence rates were even higher than male incidence (ages 35-64 years) in Denmark, Iceland, and Sweden.[79] More recent studies revealed a higher female-to-male incidence ratio in successively younger birth cohorts in the United States[81] and subsequently in more countries, including Canada, Denmark, Germany, New Zealand, the Netherlands,[82] because of increasing incidence rates among women in contrast to steep declines among men. The increasing female-to-male incidence ratio, however, was not fully explained by sex-specific differences in smoking behaviour.[81,82] In countries where the epidemic is at an earlier stage, including China, Indonesia, and several African countries, smoking has either peaked recently or continues to increase,[83] hence lung cancer rates will likely increase for at least the next few decades barring interventions to accelerate smoking cessation or reduce initiation.[84]

With about two-thirds of lung cancer deaths worldwide attributable to smoking, the disease can be largely prevented through effective tobacco-control policies and regulations. To assist the country-level implementation of effective interventions to reduce the demand of tobacco, the WHO Framework Convention on Tobacco Control introduced the MPOWER package, consisting of 6 policy intervention strategies: *M*onitor tobacco use and prevention policies, *P*rotect people from tobacco smoke, *O*ffer help to quit tobacco use, *W*arn about the dangers of tobacco, *E*nforce bans on tobacco advertising, promotion and sponsorship, and *R*aise taxes on tobacco.[85] Since its introduction by the WHO, progress has been substantial. In 2018, 65% of the world's population in 136 countries was covered by at least one select measure at a comprehensive level compared with 15% of the population in 43 countries in 2007.[86] Furthermore, the prevalence of tobacco use has declined in 116 countries, especially those with stronger implementation measures. In 2018, for the first time, the number of men using tobacco globally began to decline despite population growth, with the decline in the number of female tobacco users continuing since 2000.[87] However, progress is uneven, and there are 59 countries that have yet to adopt a single MPOWER measure, 49 of which are LMICs.[86]

The survival of patients with lung cancer at 5 years after diagnosis is only 10% to 20% in most countries among those diagnosed during 2010 through 2014, although rates are higher in Japan (33%), Israel (27%), and the Republic of Korea (25%).[46] Screening with low-dose computed tomography (CT) for high-risk individuals (current and former heavy smokers) can help diagnose cancer early, when successful treatment is more likely. The efficacy of annual low-dose CT screening in reducing lung cancer mortality has been confirmed in several independent, international, randomized controlled clinical trials.[88-91] Recently, the Dutch-Belgian lung cancer screening trial reported that volume CT screening, with the introduction of growth-rate assessment as an imaging biomarker for indeterminate tests, resulted in a lung cancer mortality reduction at 10 years of follow-up of 24% in men and 33% in women compared with no screening.[91] This outcome was also accompanied by low referral rates for additional assessments, resulting in significant reductions in false-positive tests and unnecessary workup procedures.[91] However, the translation of this benefit to the general population has proven challenging, likely impeding the implementation of lung cancer screening as part of a global strategy to reduce the disease burden, at least in the near term.

Colorectal cancer

More than 1.9 million new colorectal cancer (including anus) cases and 935,000 deaths were estimated to occur in 2020, representing about one in 10 cancer cases and deaths (Table 1). Overall, colorectal ranks third in terms of incidence, but second in terms of mortality (Fig. 4). Incidence rates are approximately 4-fold higher in transitioned countries compared with transitioning countries, but there is less variation in the mortality rates because of higher fatality in transitioning countries (Fig. 7). There is an approximately 9-fold variation in colon cancer incidence rates by world regions, with the highest rates in European regions, Australia/New Zealand, and Northern America, with Hungary and Norway ranking first in men and women, respectively (Fig. 10A). Rectal cancer incidence rates have a similar regional distribution, although rates in Eastern Asia rank among the highest (Fig. 10B). Rates of both colon and rectal cancer incidence tend to be low in most regions of Africa and in South Central Asia.

Colorectal cancer can be considered a marker of socioeconomic development, and, in countries undergoing major transition, incidence rates tend to rise uniformly with increasing HDI.[92,93] Incidence rates have been steadily rising in many countries in Eastern Europe, South Eastern and South Central Asia, and South America.[22,94] The increase in formerly low-risk and lower HDI countries likely reflects changes in lifestyle factors and diet, ie, shifts toward an increased intake of animal-source foods and a more sedentary lifestyle, leading to decreased physical activity and increased prevalence of excess body weight, which are independently associated with colorectal cancer risk.[95] Additional risk factors include heavy alcohol consumption, cigarette smoking, and consumption of red or processed meat, whereas calcium supplements and adequate consumption of whole grains, fiber, and dairy products appear to decrease risk.[96] Primary prevention remains the key strategy to reduce the increasing global burden of colorectal cancer. The expense of mounting a mass screening effort in most LMICs is not currently justified given the significant costs of colonoscopy and inadequate implementation of diagnostic and treatment services. Some evidence, however, suggests that colorectal cancer screening with more affordable and less invasive methods (guaiac testing and fecal immunochemical tests) may be cost-effective, at least in some settings of emerging economies, and offer options for control of the growing burden of the disease.[97,98]

Declines in colorectal cancer incidence in some high-incidence countries have been attributed to population-level changes toward healthier lifestyle choices (eg, declines in smoking) and the uptake of screening,[94,99] although accelerated progress since the early 2000s is chiefly attributed to increased colonoscopy screening and the removal of precursor lesions.[100-102] However, favorable trends for adults aged ≥50 years mask increasing rates of early-onset colorectal cancer (age at diagnosis <50 years) in many countries, including the United States, Canada, Australia, and 6 other high-income countries, with incidence rising by 1% to 4% per year.[103-105] Although rising incidence in young birth cohorts points to the influence of dietary patterns, excess body weight, and lifestyle factors, further research is needed to elucidate specific underlying causal factors because information on risk factors is currently based almost exclusively on data from older cohorts. To mitigate the rising burden of early-onset colorectal cancer, the American Cancer Society lowered the recommended age for screening initiation for individuals at average risk from 50 to 45 years in 2018,[106] and, in October 2020, the US Preventive Services Task Force concurred in a draft recommendation statement.[107]

Prostate cancer

With an estimated almost 1.4 million new cases and 375,000 deaths worldwide (Table 1), prostate cancer is the second most frequent cancer and the fifth leading cause of cancer death among men in 2020 (Fig. 4B). Incidence rates are 3-fold higher in transitioned than in transitioning countries (37.5 and 11.3 per 100,000, respectively), whereas mortality rates are less variable (8.1 and 5.9 per 100,000, respectively) (Fig. 7A). It is the most frequently diagnosed cancer in men in over one-half (112 of 185) of the countries of the world (Fig. 5A). Incidence rates vary from 6.3 to 83.4 per 100,000 men across regions, with the highest rates found in Northern and Western Europe, the Caribbean, Australia/New Zealand, Northern America, and Southern Africa

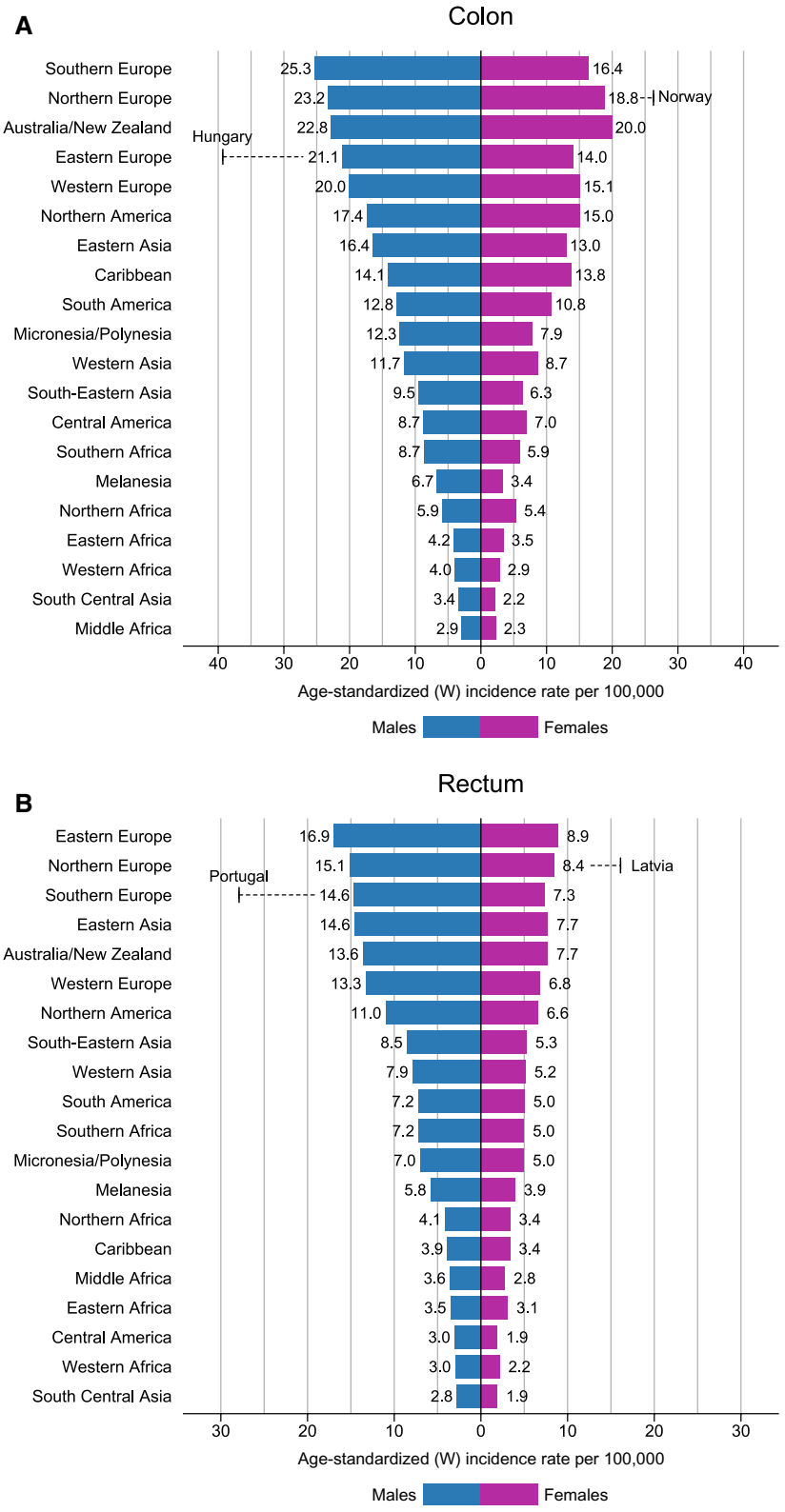

FIGURE 10. Region-Specific Incidence Age-Standardized Rates by Sex for Cancers of the (A) Colon and (B) Rectum (Including Anus) in 2020. Rates are shown in descending order of the world (W) age-standardized rate among men, and the highest national rates among men and women are superimposed. Source: GLOBOCAN 2020.

and the lowest rates in Asia and Northern Africa (Fig. 11). Regional patterns of mortality rates do not follow those of incidence, with the highest mortality rates in the Caribbean, sub-Saharan Africa, and Micronesia/Polynesia. Prostate cancer is the leading cause of cancer death among men in 48 countries, including many countries in sub-Saharan

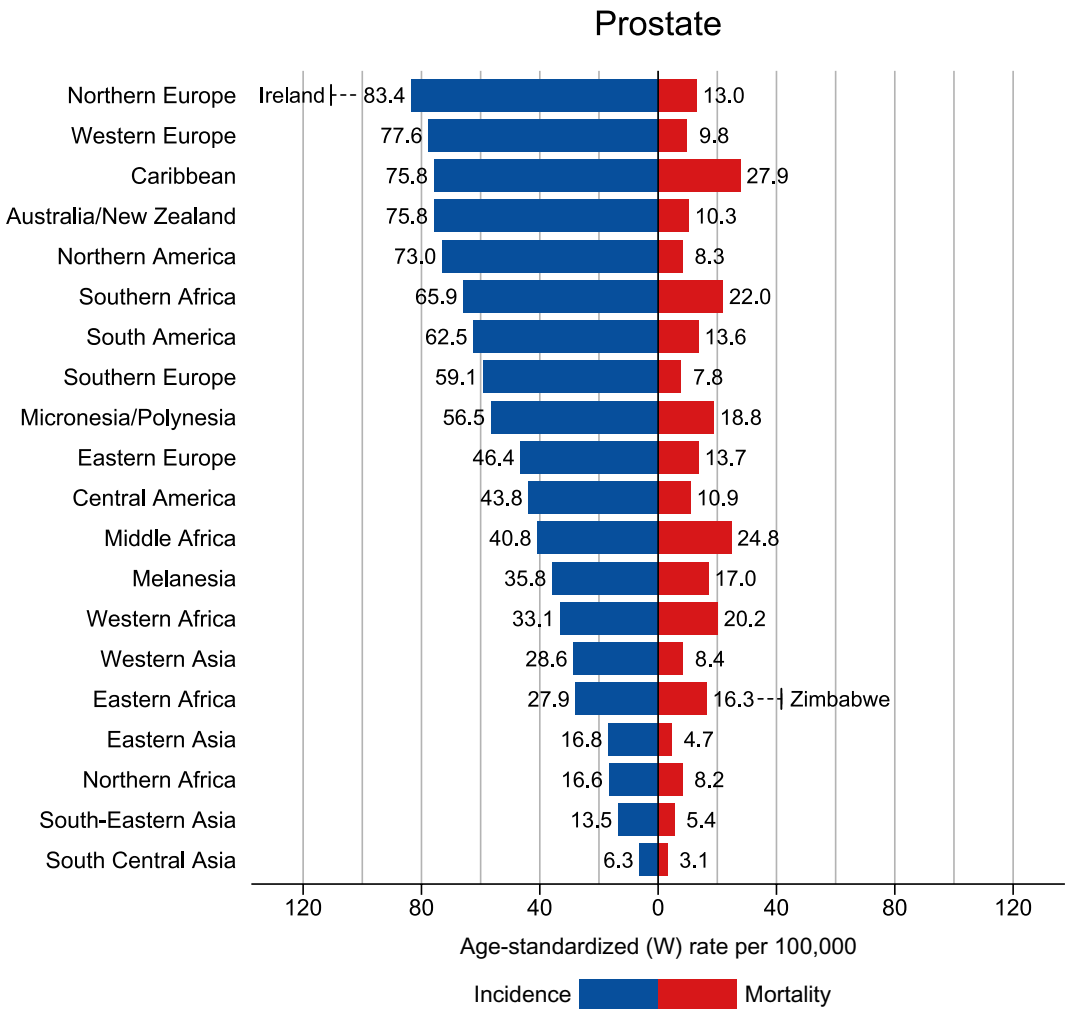

FIGURE 11. Region-Specific Incidence and Mortality Age-Standardized Rates for Prostate Cancer in 2020. Rates are shown in descending order of the world (W) age-standardized incidence rate, and the highest national age-standardized rates for incidence and mortality are superimposed. Source: GLOBOCAN 2020.

Africa, the Caribbean, and Central and South America (eg, Ecuador, Chile, and Venezuela), as well as Sweden (Fig. 6A).

For a disease as common as prostate cancer, relatively little is known about its etiology. Established risk factors are limited to advancing age, family history of this malignancy, and certain genetic mutations (eg, *BRCA1* and *BRCA2*) and conditions (Lynch syndrome). Black men in the United States and the Caribbean have the highest incidence rates globally, supporting the role of Western African ancestry in modulating prostate cancer risk.[108] There have been few lifestyle and environmental factors identified to date for which the evidence is convincing, although this may be accumulating for smoking, excess body weight, and some nutritional factors that may increase the risk of advanced prostate cancer.[109]

International differences in prostate cancer diagnostic practices are likely the greatest contributor to the variation in prostate cancer incidence rates worldwide.[110] In the United States, Canada, and Australia, there were rapid increases in incidence rates in the late 1980s and early 1990s as a result of the widespread introduction of prostate-specific antigen (PSA) testing, allowing the detection of preclinical cancers.[111] The dramatic increases were followed by sharp reductions within a few years, likely reflecting a depletion of prevalent latent cancers in the general population. Further declines in the late 2000s are attributed to a reduction in the use of PSA testing,[110-112] reflecting changes in the recommendations concerning PSA-based screening of asymptomatic men.[113-116] In many countries in Northern and Western European, alongside a few in Southern and Central America and Asia, less marked but similar patterns were observed, reflecting the later and more gradual adoption of PSA testing.[110,111,117,118] In contrast, incidence rates continue to increase in China and countries in Eastern Europe (Belarus, Bulgaria, Slovakia).[118] Rapidly increasing trends have been also found in sub-Saharan Africa, with annual increases ranging from 2% to 10% reported in 9 countries (eg, South Africa, Kenya, Uganda, Mozambique, Zimbabwe) over the time period examined between 1995 and 2018.[119] Reasons for the uniform rise are unclear but

are thought to primarily reflect increased awareness and improvements in the health care system, enabling a broader use of PSA testing and possibly increased use of transurethral resections.[119]

Mortality rates for prostate cancer have decreased in most high-income countries since the mid-1990s, including those in Northern America, Oceania, and Northern and Western Europe,[111,117,120] likely reflecting advancements in treatment and earlier detection through increased screening.[121,122] During the same period, rates increased in many countries in Central and Eastern Europe, Asia, and Africa[111] and continued until recently in some countries (eg, Thailand, Bulgaria, and Ukraine),[118] which may partly reflect an underlying rise in incidence trends combined with limited access to PSA testing and effective treatment. A more contemporary trend (2009-2013) in high-resource countries signals stabilization of mortality declines (eg, the United States, Denmark, Norway, Switzerland, Spain, Argentina, New Zealand, Israel, and Japan), whereas decreasing trends continue in some countries (eg, the United Kingdom, Greece, Italy, Austria, France, Germany, the Netherlands, Brazil, Canada, and Australia).[118] In the United States, there has been an increase in regional and advanced-stage cancer diagnoses since around 2010[123] and a concomitant increase in advanced-stage death rates during 2012 through 2017.[124] The current guideline from the American Cancer Society recommends informed/shared decision-making (ie, an individual choice of men with their health care provider after receiving information about the uncertainties, risks, and potential benefits associated with the screening) for PSA testing in men at average risk, beginning at age 50 years.[125] In 2018, the US Preventive Services Task Force upgraded its recommendation to informed decision for men aged 55 to 69 years[126]; the impact of this change on cancer rates is yet to be determined.

Stomach cancer

Stomach cancer remains an important cancer worldwide and is responsible for over one million new cases in 2020 and an estimated 769,000 deaths (equating to one in every 13 deaths globally), ranking fifth for incidence and fourth for mortality globally (Table 1, Fig. 4A). Rates are 2-fold higher in men than in women. In men, it is the most commonly diagnosed cancer and the leading cause of cancer death in several South Central Asian countries, including Iran, Afghanistan, Turkmenistan, and Kyrgyzstan (Figs. 5A and 6A). Incidence rates are highest in Eastern Asia (Japan and Mongolia, the countries with the highest incidence in men and women, respectively) and Eastern Europe,[18] whereas rates in Northern America and Northern Europe are generally low and equivalent to those seen across the African regions (Fig. 12).

Although stomach cancer is often reported as a single entity, it can generally be classified into two topographical subsites, the cardia (upper stomach) and noncardia (lower stomach). These entities differ in terms of risk factors, carcinogenesis, and epidemiologic patterns. Chronic *Helicobacter pylori* infection is considered the principal cause of noncardia gastric cancer, with almost all cases attributed to this bacterium.[127,128] The prevalence of *H. pylori* infection is extraordinarily high, infecting 50% of the world's population,[129] and its geographic variation correlates reasonably with that of stomach cancer incidence. However, <5% of infected hosts will develop cancer, likely because of differences in bacterial genetics, host genetics, age of infection acquisition, and environmental factors.[130] Established risk factors beyond *H. pylori* for noncardia gastric cancer include alcohol consumption, tobacco smoking, and foods preserved by salting.[96] Low fruit intake and the high consumption of processed meat and of grilled or barbecued meat and fish may increase the risk.[96] Although cancers of the gastric cardia in the presence of *H. pylori* infection show an association with gastric atrophy, cardia cancer is not generally associated with *H. pylori* infection[131] and may even be inversely associated in some populations.[132] Emerging evidence suggests a dual etiology for cardia gastric cancer, with some cancers linked to *H. pylori* infection and some linked to excess body weight and gastroesophageal reflux disease injury, resembling characteristics of esophageal adenocarcinoma (AC).[133]

Incidence and mortality rates of noncardia gastric cancer have been steadily declining over the last one-half century in most populations. The trends are attributed to the *unplanned triumph* of prevention, including a decreased prevalence of *H. pylori* and improvements in the preservation and storage of foods.[134] The historical trends in the incidence of gastric cardia were largely reported in low-risk populations, in which the contribution of cardia versus noncardia gastric cancer to the overall burden tends to be greatest; incidence rates increased from the 1960s to the 1980s in the United Kingdom[135] and the United States[136] and appeared to stabilize during the more recent period in the United States[137] and the Netherlands.[138]

Recent notable findings are the increase in the incidence of stomach cancer (cardia and noncardia gastric cancers combined) among young adults (aged <50 years) in both low-risk and high-risk countries, including the United States, Canada, the United Kingdom, Chile, and Belarus.[139,140] A previous US study focusing on noncardia gastric cancer reported that increases among young individuals was largely confined to non-Hispanic Whites and people living in more affluent counties.[141,142] It has been postulated that the rising prevalence of autoimmune gastritis and dysbiosis of the gastric microbiome, possibly relevant to increased use of antibiotics and

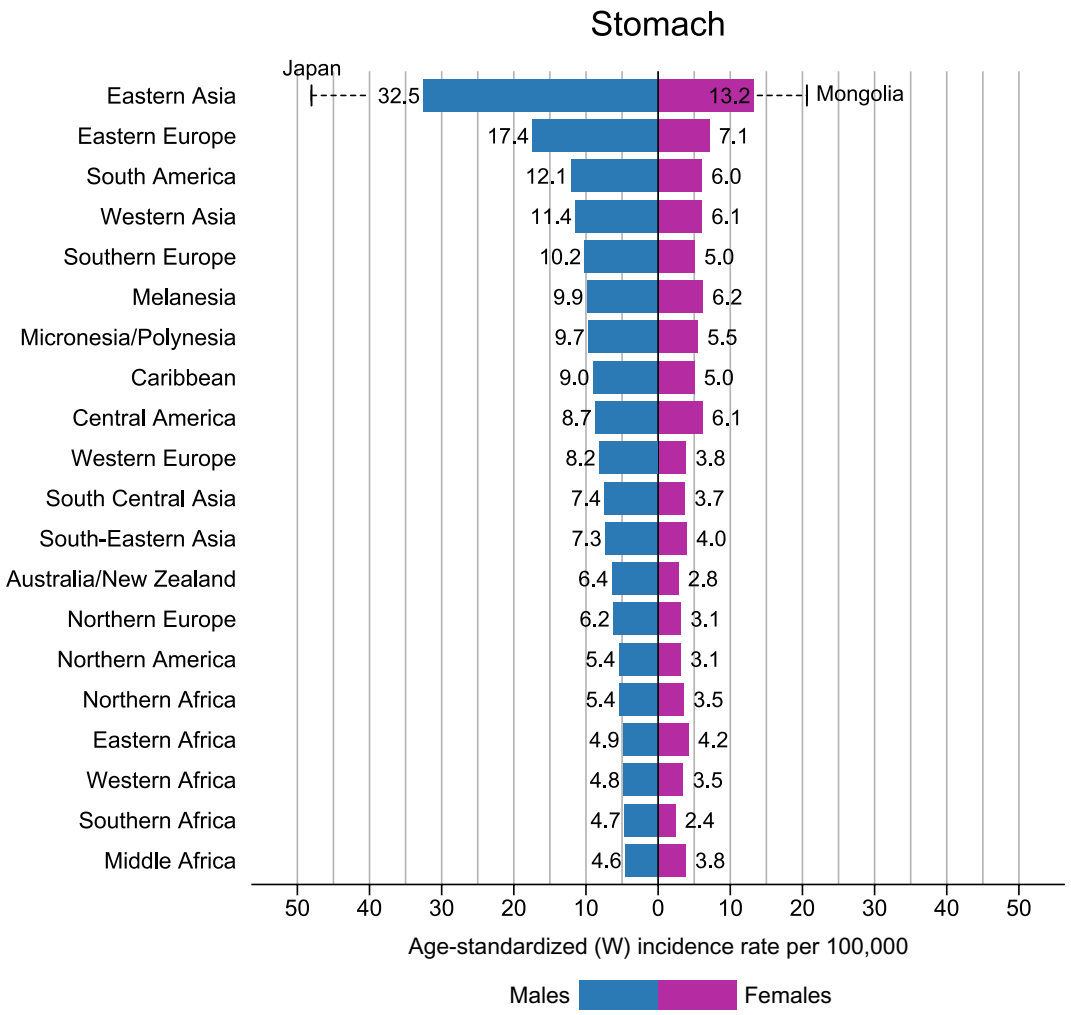

FIGURE 12. Region-Specific Incidence Age-Standardized Rates by Sex for Stomach Cancer in 2020. Rates are shown in descending order of the world (W) age-standardized rate among men, and the highest national rates among men and women are superimposed. Source: GLOBOCAN 2020.

acid suppressants, may have contributed to the paradoxical increase of stomach cancer among younger generations.[141,142]

Liver cancer

Primary liver cancer is the sixth most commonly diagnosed cancer and the third leading cause of cancer death worldwide in 2020, with approximately 906,000 new cases and 830,000 deaths (Table 1, Fig. 4A). Rates of both incidence and mortality are 2 to 3 times higher among men than among women in most regions (Fig. 13), and liver cancer ranks fifth in terms of global incidence and second in terms of mortality for men (Fig. 4B). Incidence rates among men are 2.4-fold greater in transitioned countries (Fig. 7), but the highest rates are observed mainly in transitioning countries, with the disease being the most common cancer in 11 geographically diverse countries in Eastern Asia (Mongolia, which has rates far exceeding any other country), South-Eastern Asia (eg, Thailand, Cambodia, and Viet Nam), and Northern and Western Africa (eg, Egypt and Niger) (Figs. 5A). Liver cancer is the leading cause of cancer death in Mongolia, Thailand, Cambodia, Egypt, Guatemala among both men and women and in an additional 18 countries among men (Fig. 6).

Primary liver cancer includes hepatocellular carcinoma (HCC) (comprising 75%-85% of cases) and intrahepatic cholangiocarcinoma (10%-15%), 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 foods, heavy alcohol intake, excess body weight, type 2 diabetes, and smoking.[143] The major risk factors vary from region to region. In most high-risk HCC areas (China, the Republic of Korea, and sub-Saharan Africa), the key determinants are chronic HBV infection, aflatoxin exposure, or both; whereas, in other countries (Japan, Italy, and Egypt), HCV infection is likely the predominant cause. In Mongolia, HBV and HCV and co-infections of HBV carriers with HCV or hepatitis delta viruses, as well as alcohol consumption, all contribute to the high burden.[144] Although risk factors tend to vary substantially by geographic

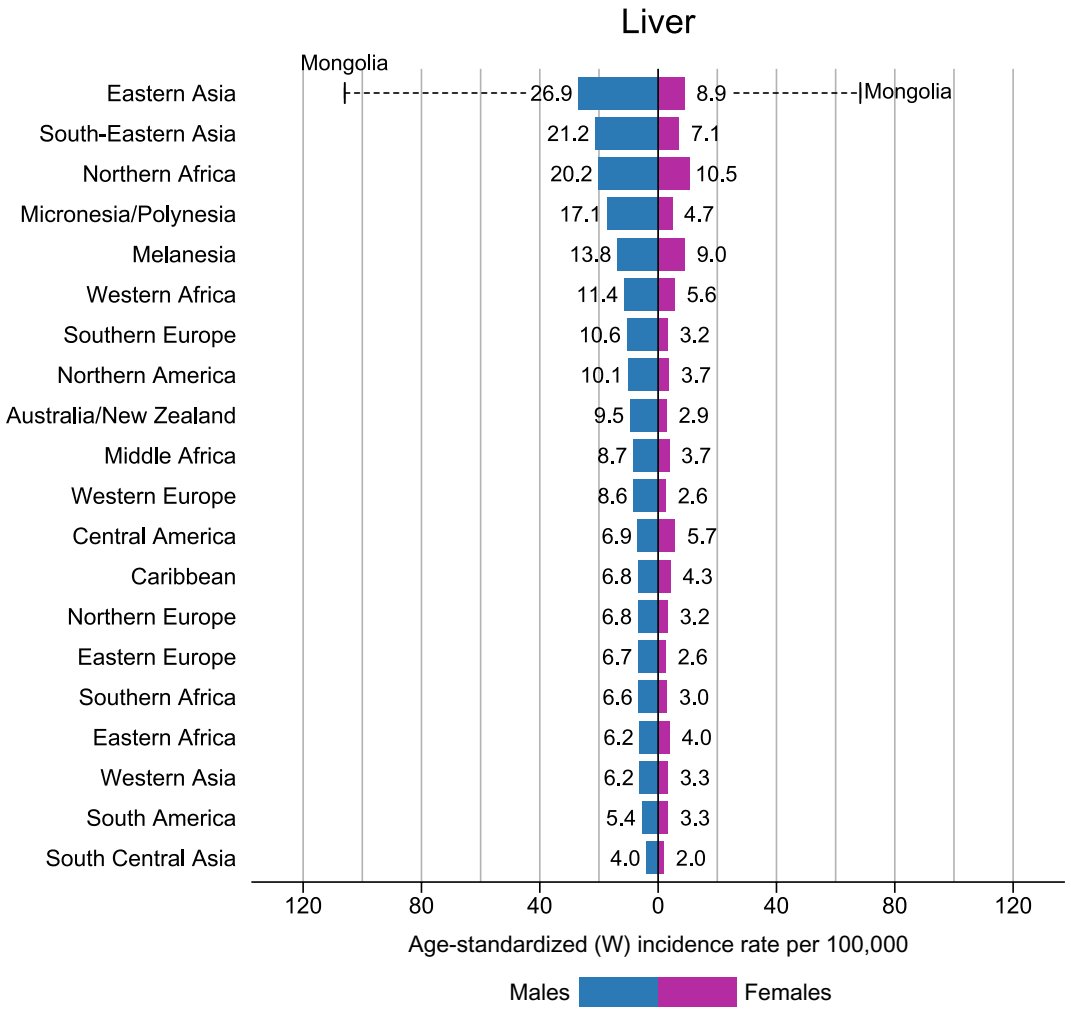

FIGURE 13. Region-Specific Incidence Age-Standardized Rates by Sex for Liver Cancer in 2020. Rates are shown in descending order of the world (W) age-standardized rate among men, and the highest national rates among men and women are superimposed. Source: GLOBOCAN 2020.

region, major risk factors for cholangiocarcinoma include liver flukes (eg, in the Northeast region of Thailand, where *Opisthorchis viverrini* is endemic),[145] metabolic conditions (including obesity, diabetes, and nonalcoholic fatty liver disease), excess alcohol consumption, and HBV or HCV infection.[146-148]

Incidence and mortality rates of liver cancer have decreased in many high-risk countries in Eastern and South-Eastern Asia, including China, Taiwan, the Republic of Korea, the Philippines, since the late 1970s and in Japan since the 1990s.[94,149] Rates in Italy have also declined since 1995.[94,149] These trends likely reflect declines in the population seroprevalence of HBV and HCV as well as a reduction in aflatoxin exposure. Vaccination against HBV, which has been a major public health success, dramatically reduced the prevalence of HBV infection and the incidence of HCC in high-risk countries in Eastern Asia, where it was first introduced in the early 1980s.[150] Although primary liver cancer trends largely reflect those of HCC, there are notable exceptions; in Thailand, where HCC accounts for <30% of liver cancer, HCC incidence rates have sharply decreased since 2000, whereas primary liver cancer continues to rise.[149]

The major risk factors appear to be in transition, with the prevalence of HBV and HCV declining and excess body weight and diabetes increasing in many regions.[151] In China, the rates of liver cancer have begun to plateau in recent birth cohorts, potentially offsetting the gains achieved for the last 3 decades.[149] Furthermore, incidence rates in formerly low-risk countries—most countries across Europe, Northern America, Australia/New Zealand, and South America—have increased or stabilized at a higher level in recent years,[149,152] possibly caused in part by the changing prevalence of excess body weight and diabetes.

Although the relevance of nonviral risk factors is becoming more important on the burden of liver cancer, elimination of viral hepatitis remains the key strategy for primary prevention of liver cancer globally, as HBV infection and HCV infection account for 56% and 20% of liver cancer deaths worldwide, respectively.[153] By the end of 2019, 189 countries had introduced the HBV vaccine into

their national infant immunization programs, and global coverage with 3 doses of hepatitis B vaccine was estimated at 85%.[154] The global coverage of HBV birth-dose, however, was low at 43%, varying up to 84% in the WHO Western Pacific region and falling to only 6% in the WHO African region,[155] where HBV predominates as a cause of liver cancer.[153] Countries with the highest HCV prevalence are mainly LMICs in which a large proportion of infections occur in the health care settings through unsafe injections and other invasive procedures.[156] Enhancing infection control through safety measures, such as screening of transfusions, prevention of mother-to-child transmission, the provision of clean needles, and infection control in health care facilities, is a key aspect of HCV control.[156] Currently, there is no vaccine available to prevent HCV infection, although an 8-week to 12-week course of orally administered, direct-acting antiviral agents appears to cure HCV infection in most instances.[157] Yet chronic infections are usually asymptomatic, and many infected persons remain undiagnosed; as of 2015, an estimated 290 million individuals remained undiagnosed worldwide.[158] A policy shift toward treating all individuals with HCV is expected to have the potential to decrease hepatitis-associated morbidity and mortality.[158] However, challenges to ensuring widespread access to treatment in different settings vary.[156] In most LMICs, affordability of viral testing and treatment is a major barrier,[158,159] underscoring the need for concerted and coordinated efforts by local governments, private and nonprivate public health organizations, and industries to scale up screen-and-treat interventions for viral hepatitis.[160] In high-income countries, those most at risk are often vulnerable populations, including undocumented immigrants, injection drug users, those who have been incarcerated, and homeless and poor people, who experience many barriers to health care access.[158,159]

Esophageal cancer

Esophageal cancer ranks seventh in terms of incidence (604,000 new cases) and sixth in mortality overall (544,000 deaths), the latter signifying that esophageal cancer is responsible for one in every 18 cancer deaths in 2020 (Fig. 4, Table 1). 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 (Table 3). Rates are higher in transitioned versus transitioning countries for men but comparable for women (Fig. 7).[18,94] Eastern Asia exhibits the highest regional incidence rates for both men and women, in part because of the large burden in China, followed by Southern Africa, Eastern Africa, Northern Europe, and South Central Asia (Fig. 14). Cape Verde and Malawi have the highest incidence rates globally in men and women, respectively (Fig. 14). Esophageal cancer is the leading cause of cancer death among Bangladeshi men and women and among Malawian men (Fig. 6).

The geographic variation in esophageal cancer incidence substantially differs between the 2 most common histologic subtypes (squamous cell carcinoma [SCC] and adenocarcinoma [AC]), which have quite different etiologies. The incidence of esophageal SCC in certain high-risk areas in Asia (eg, China) is broadly in decline and may have been preceded by economic gains and dietary improvements, whereas, in several high-income countries (eg, the United States, Australia, France, and the United Kingdom), the reductions are considered primarily due to declines in cigarette smoking.[161] Heavy drinking and smoking and their synergistic effects are the major risk factors for SCC in western settings.[161] However, in lower income countries, including 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, although dietary components (eg, nutritional deficiencies, nitrosamines) have been suspected.[162] Additional suspected risk factors for SCC include betel quid chewing in the Indian subcontinent and consumption of pickled vegetables (eg, in China) and very hot food and beverages (eg, in Uruguay, Iran, and Tanzania).[161]

AC represents roughly two-thirds of esophageal cancer cases in high-income countries, with excess body weight, gastroesophageal reflux disease, and Barrett's esophagus among the key risk factors.[161] Across high-income countries, incidence rates of AC are thus rising rapidly in part because of increased excess body weight and increasing gastroesophageal reflux disease and possibly because of decreasing levels of chronic infection with *H. pylori*, which has been inversely associated with AC.[163] These trends are predicted to continue in the near future, with AC surpassing SCC in many high-income countries; excess body weight is likely to be an increasingly important contributor to the future burden of esophageal cancer.[163]

Cervical cancer

Cervical cancer is the fourth most frequently diagnosed cancer and the fourth leading cause of cancer death in women, with an estimated 604,000 new cases and 342,000 deaths worldwide in 2020 (Table 1, Fig. 4). Cervical cancer is the most commonly diagnosed cancer in 23 countries (Fig. 5B) and is the leading cause of cancer death in 36 countries (Fig. 6B), with the vast majority of these countries found in sub-Saharan Africa, Melanesia, South America, and South-Eastern Asia. The highest regional incidence and mortality is in sub-Saharan Africa (Fig. 15), with rates elevated in Eastern Africa (Malawi has the world's highest incidence and mortality rate), Southern Africa, and Middle Africa. Incidence rates are 7 to 10 times lower in Northern America, Australia/New

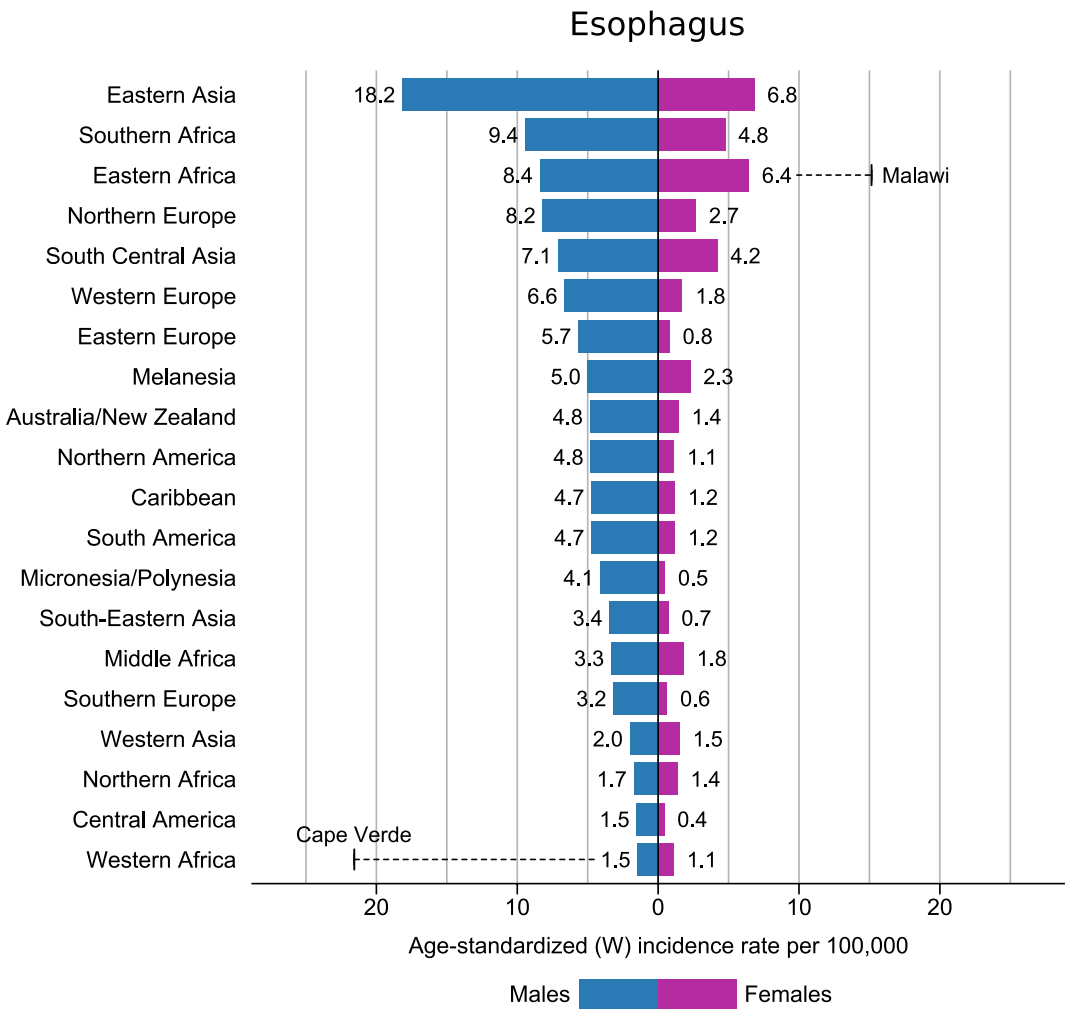

FIGURE 14. Region-Specific Incidence Age-Standardized Rates by Sex for Esophageal Cancer in 2020. Rates are shown in descending order of the world (W) age-standardized rate among men, and the highest national rates among men and women are superimposed. Source: GLOBOCAN 2020.

Zealand, and Western Asia (Saudi Arabia and Iraq), with mortality rates varying up to 18 times.[18]

Human papillomavirus (HPV) is a necessary but not sufficient cause of cervical cancer,[164] with 12 oncogenic types classified as group 1 carcinogens by the International Agency for Research on Cancer Monographs.[165] Other important cofactors include some sexually transmittable infections (HIV and *Chlamydia trachomatis*), smoking, a higher number of childbirths, and long-term use of oral contraceptives.[166] Rates remain disproportionately high in transitioning versus transitioned countries (18.8 vs 11.3 per 100,000 for incidence; 12.4 vs 5.2 per 100,000 for mortality) (Fig. 7B). The HDI and poverty rates have been shown to account for >52% of global variance in mortality.[167] This disparity exists even within high-income countries like the United States, where the cervical cancer death rate is 2-fold higher among women residing in high-poverty versus low-poverty areas.[168]

Incidence and mortality rates have declined in most areas of the world for the past few decades. The declines are ascribed to factors linked to either 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.[169] Cervical cancer screening programs hastened the declines upon their implementation in many countries in Europe, Oceania, and Northern America, despite the observations of increasing risk among younger generations of women in some of these countries[170,171] and also in Japan,[172] which may in part reflect changing sexual behavior and increased transmission of HPV that is insufficiently compensated by cytologic screening.[173,174] Rates have also decreased in countries in the Caribbean and Central and South America (eg, Argentina, Chile, Costa Rica, Brazil, and Colombia) during the 2000s, although incidence rates remain high.[175] In the absence of effective screening, as in Eastern Europe and Central Asia, there have been rapid increases in premature cervical cancer mortality in recent generations.[176] Perhaps most concerning are the uniform rises recently

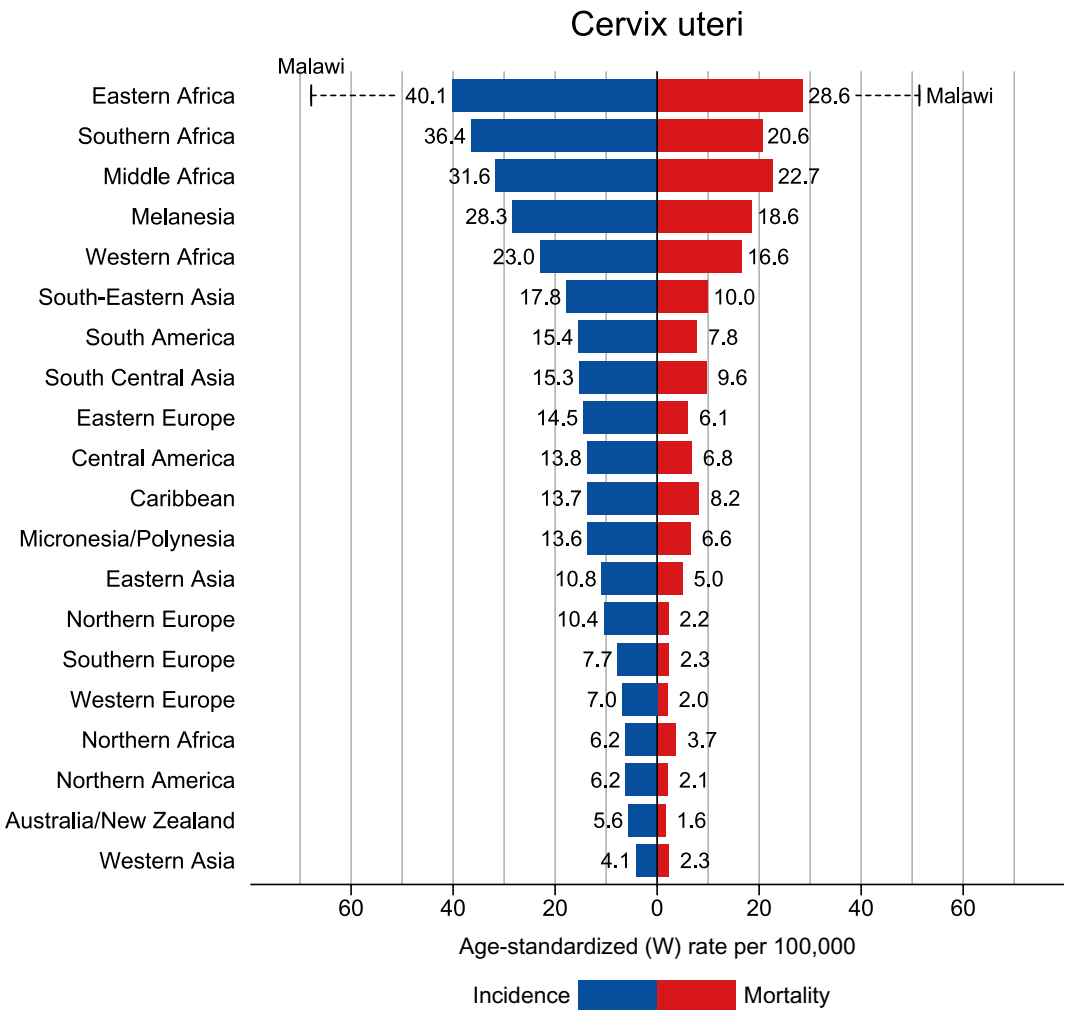

FIGURE 15. Region-Specific Incidence and Mortality Age-Standardized Rates for Cervical Cancer in 2020. Rates are shown in descending order of the world (W) age-standardized incidence rate, and the highest national age-standardized rates for incidence and mortality are superimposed. Source: GLOBOCAN 2020.

reported in 7 of 8 sub-Saharan African countries, including the Gambia, Kenya, Malawi, the Seychelles, South Africa, Uganda, and Zimbabwe.[177]

Cervical cancer is considered nearly completely preventable because of the highly effective primary (HPV vaccine) and secondary (screening) prevention measures. However, these measures have not been equitably implemented across and within countries. As of May 2020, <30% of LMICs had implemented national HPV vaccination programs compared with >80% of high-income countries.[178] Only 44% of women in LMICs have ever been screened for cervical cancer, with the lowest prevalence among women in sub-Saharan Africa (country-level median, 16.9%; range, 0.9%-50.8%),[179] compared with >60% in high-income countries.

In such regions, of critical importance is ensuring that resource-dependent programs of screening and vaccination are implemented to transform the situation.[180] HPV vaccination programs can reduce the long-term future burden of cervical cancer under the assumption of reasonable uptake,[181,182] and the WHO currently recommends 2-dose vaccination of girls aged 9 to 13 years as a *best buy* (ie, efficacious and cost-effective interventions).[183] High-quality screening programs are also important to prevent cervical cancer among unvaccinated women and for oncogenic subtypes not covered by the vaccine. The WHO recommends the screening of women aged 30 to 49 years—either through visual inspection with acetic acid in low-resource settings, a Papanicolaou test (cervical cytology) every 3 to 5 years, or HPV testing every 5 years—coupled with timely and efficacious treatment of precancerous lesions.[183,184] Accumulated evidence supports the use of HPV-based tests for the detection of precancerous lesions as a preferred test for primary screening,[185] which can also offer opportunities of self-sampling to women who live in remote areas or who are reluctant to undergo gynecologic examination.[186] Studies suggested that self-sampled HPV testing can be cost effective, either as an addition to existing screening programs or as a primary screening strategy, by increasing the level of

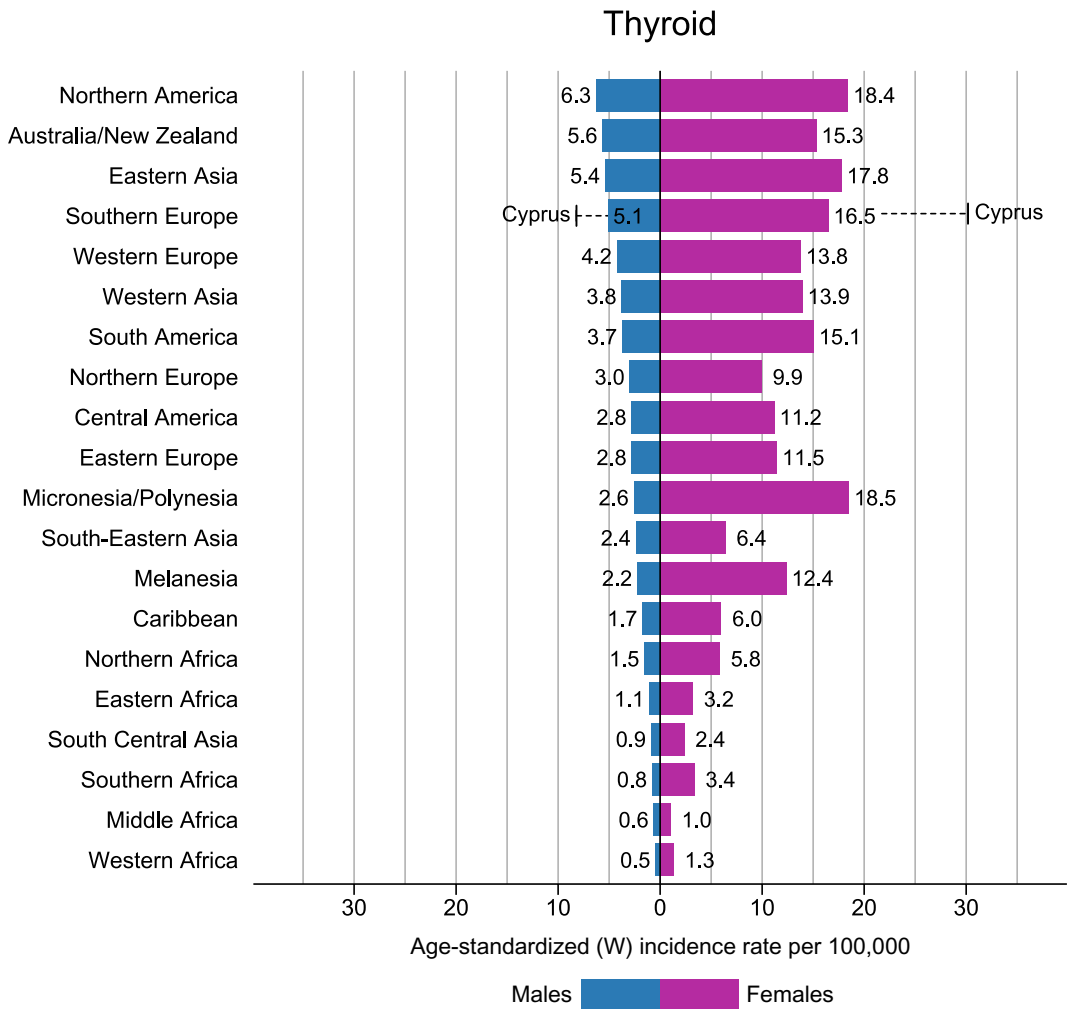

FIGURE 16. Region-Specific Incidence Age-Standardized Rates by Sex for Thyroid Cancer in 2020. Rates are shown in descending order of the world (W) age-standardized rate among men, and the highest national rates among men and women are superimposed. Source: GLOBOCAN 2020.

screening attendance, lowering the cost of testing, and attracting more never-screened or long-term underscreened women.[187,188] Efforts are also needed to increase access to treatment and palliative care among patients with invasive tumors, particularly in transitioning countries.[189,190]

In 2018, given the substantial global burden of cervical cancer and the increasing inequity, the WHO Director-General made a call for global action toward the elimination of cervical cancer (≤4 per 100,000 women worldwide) through the triple-intervention strategy of: 1) vaccinating 90% of all girls by age 15 years, 2) screening 70% of women twice in the age range of 35 to 45 years, and 3) treating at least 90% of all precancerous lesions detected during screening.[191] A modelling exercise predicts that implementing this strategy will result in more than 74 million cases and more than 62 million deaths averted over the course of the next century.[192] This goal is projected to be achieved by 2055 to 2059 in very high HDI countries, whereas, in low HDI countries, it might take until the end of the 21st century,[193] mirroring the glaring gap in underlying incidence rates and resources required to achieve the goal. Findings from recent studies, however, suggest opportunities to prevent cervical cancer in resource-limited settings by adopting the combined vaccination and screening strategy, which has proven to be cost effective across several LMICs[194-196] and is expected to expedite the realization of the goal within 11 to 31 years in low HDI countries.[192,193] The 2020 guideline update from the American Cancer Society recommends that women initiate cervical cancer screening at age 25 years and undergo primary HPV testing every 5 years through age 65 years as a preferred option.[197]

Thyroid cancer

Thyroid cancer is responsible for 586,000 cases worldwide, ranking in 9th place for incidence in 2020. The global incidence rate in women of 10.1 per 100,000 is 3-fold higher than that in men (Table 3), and the disease represents one in every 20 cancers diagnosed among women (Fig. 4C). Mortality rates from the disease are much lower, with rates of 0.5 per 100,000 in women and 0.3 per 100,000 in men

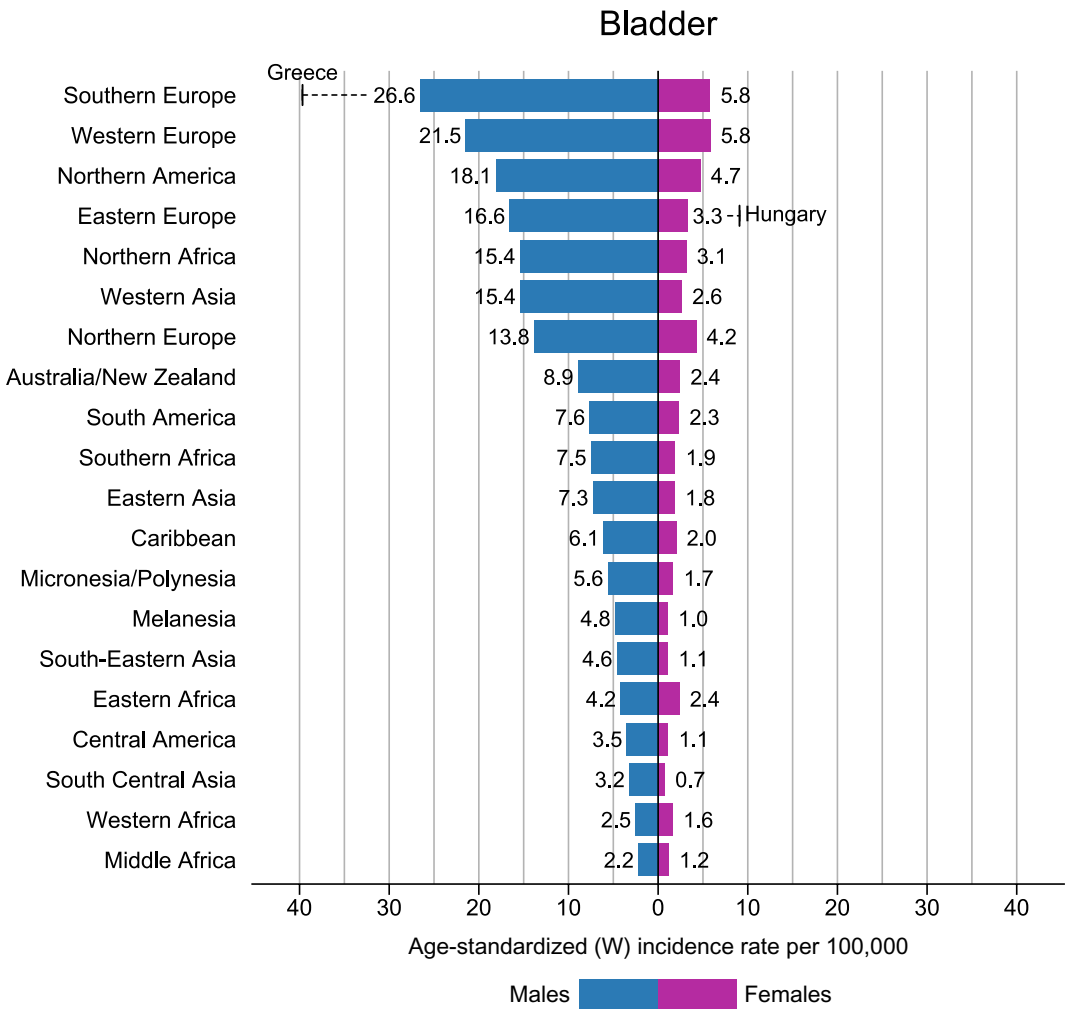

FIGURE 17. Region-Specific Incidence Age-Standardized Rates by Sex for Bladder Cancer in 2020. Rates are shown in descending order of the world (W) age-standardized rate among men, and the highest national rates among men and women are superimposed. Source: GLOBOCAN 2020.

and an estimated 44,000 deaths in both sexes combined. Incidence rates are higher in transitioned countries than in transitioning countries, 4.0 times for men[18] and 5.5 times for women, although mortality rates, in contrast, are rather similar (Fig. 7). The highest incidence rates are found in Northern America, Australia/New Zealand, Eastern Asia, and Southern Europe for both sexes and also in Micronesia/Polynesia, and South America for women (Fig. 16). The highest global rates are estimated in Cyprus for both men and women.

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 (excess body weight, greater height, hormonal exposures, and certain environmental pollutants) may play a role.[198] Since the 1980s, rapid rises in incidence rates and comparatively stable or even declining mortality rates have been observed in much of the world.[198,199] The rapid increase of thyroid cancer, particularly papillary thyroid cancer, has been largely attributed to the progressively available and sensitive use of ultrasonography, along with increased use of other diagnostic imaging modalities,[200,201] which have likely led to a massive detection and diagnosis of a large reservoir of subclinical, indolent lesions of the thyroid that are known to exist in the general population.[202,203] Among women, overdiagnosis was estimated to account for 80% to 95% of newly diagnosed cases from 2008 to 2012 in the Republic of Korea, Belarus, China, Italy, Croatia, Slovakia, and France and from 50% to 70% in Denmark, Norway, Ireland, the United Kingdom, and Japan.[204] Patterns similar to those observed in women, although of a lower magnitude were observed in men (ie, the proportion attributable to overdiagnosis was approximately 10% lower in men than in women in each country).[204]

A growing understanding of the substantial impact of overdiagnosis and the indolent nature of small thyroid cancers has led to modifications of national and international clinical practice guidelines,[205,206] which recommend against screening for thyroid cancer and advocate active surveillance for microcarcinoma.[207,208] The global impact

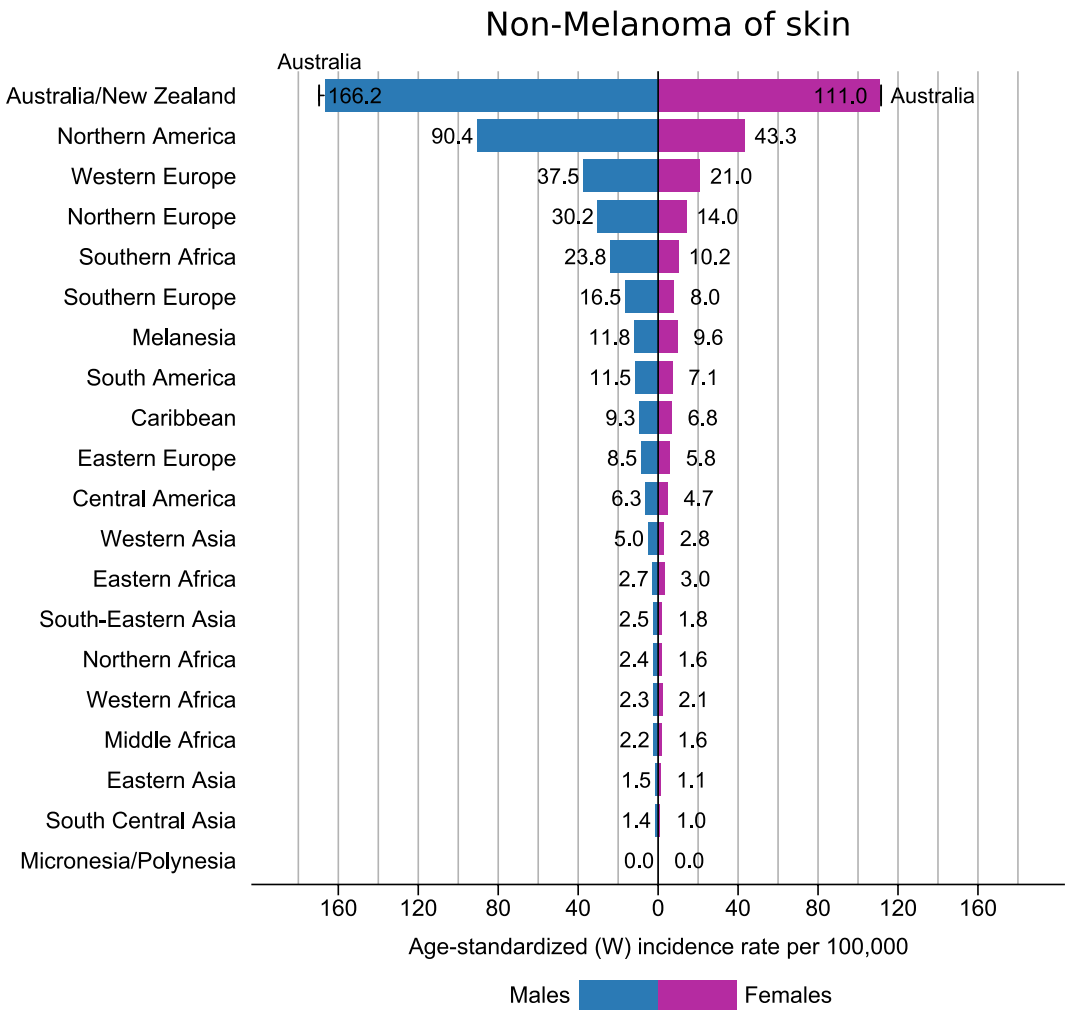

FIGURE 18. Region-Specific Incidence Age-Standardized Rates by Sex for nonmelanoma Skin Cancer (Excluding Basal Cell Carcinoma). Rates are shown in descending order of the world (W) age-standardized rate among men, and the highest national rates among men and women are superimposed. Source: GLOBOCAN 2020.

of changing guidelines needs to be determined, although the significant decline in thyroid cancer incidence rates observed in the Republic of Korea since 2010[203,209] and in the United States since 2015[210,211] suggest that greater acceptance of guidelines and adoption of active surveillance may already be mitigating some of the harms related to overdiagnosis.

In addition, the change in the prevalence of risk factors may also have partly contributed to the observed trend.[212] A study from the United States showed an increase in distant-stage thyroid cancer diagnoses during 1993 through 2013, coinciding with a slow increase in overall mortality.[213] A study linking secular trends of thyroid cancer incidence in the United States to those of the prevalence of obesity estimated that 16% of overall cancers and 63% of large-size tumors diagnosed from 2013 to 2015 were attributable to obesity,[214] suggesting that controlling obesity might help to prevent the development of thyroid cancer.

Bladder cancer

Bladder cancer is the 10th most commonly diagnosed cancer worldwide, with approximately 573,000 new cases and 213,000 deaths (Table 1). It is more common in men than in women, with respective incidence and mortality rates of 9.5 and 3.3 per 100,000 among men, which are approximately 4 times those among women globally (Table 3). Thus the disease ranks higher among men, for whom it is the 6th most common cancer and the 9th leading cause of cancer death (Fig. 4B). Incidence rates in both sexes are highest in Southern Europe (Greece [with the highest incidence rate among men globally], Spain, and Italy), Western Europe (Belgium and the Netherlands), and Northern America, although the highest global rates are in Hungary among women (Fig. 17).[18]

The observed geographic and temporal patterns of bladder cancer incidence worldwide appear to reflect the prevalence of tobacco smoking, although infection with *Schistosoma haematobium* (parts of Northern and sub-Saharan

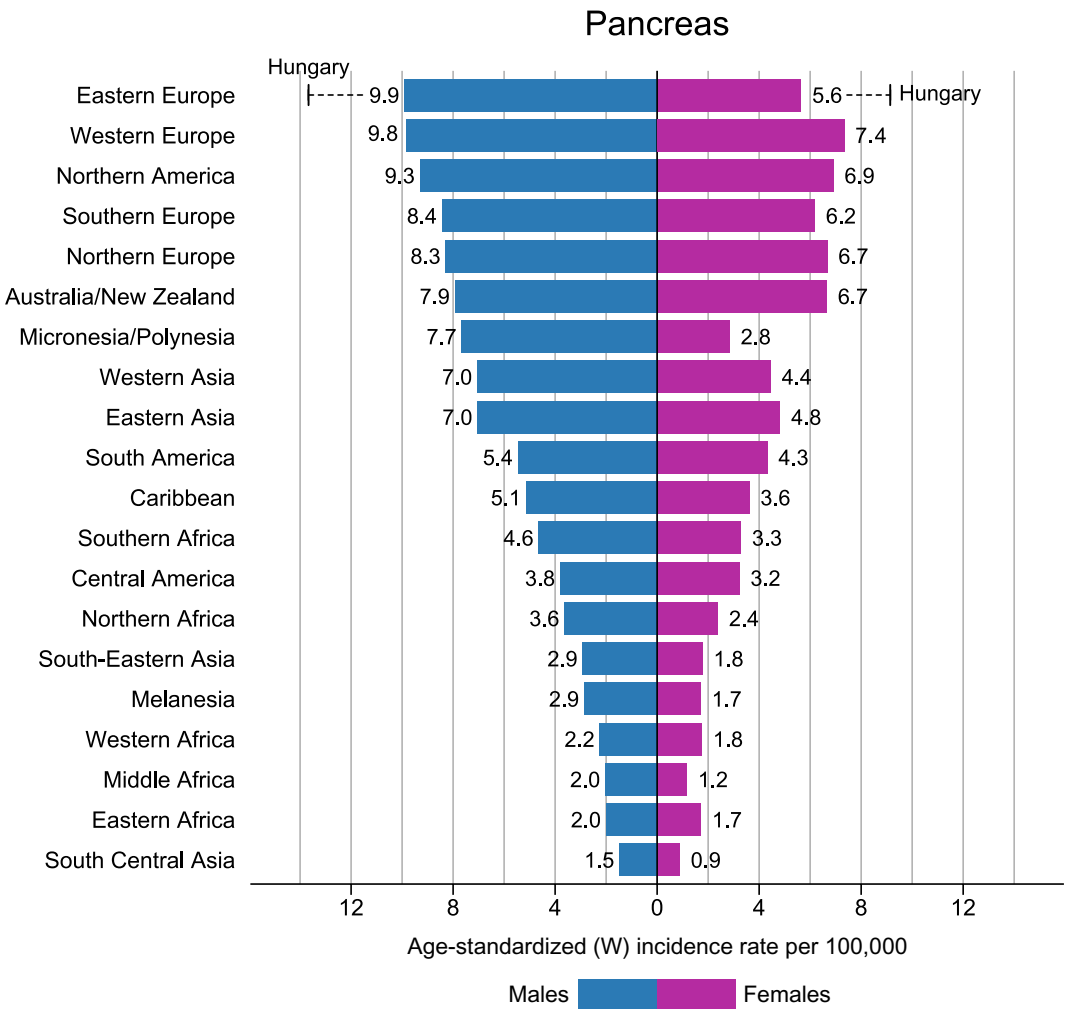

FIGURE 19. Region-Specific Incidence Age-Standardized Rates by Sex for Pancreatic Cancer in 2020. Rates are shown in descending order of the world (W) age-standardized rate among men, and the highest national rates among men and women are superimposed. Source: GLOBOCAN 2020.

Africa) and other risk factors (occupational exposures to aromatic amines and other chemicals affecting workers in the painting, rubber, or aluminum industries and arsenic contamination in drinking water) may be major causes in some populations.[215,216]

Diverging incidence trends were observed by sex in many countries from the 1990s and the early 2010s, with stabilizing or declining rates in men but some increasing trends seen for women (eg, Spain, the Netherlands, Germany, and Belarus).[216,217] With the rising smoking prevalence among women, 39% of bladder cancer cases among women were estimated to be attributable to smoking in 2014 in the United States, compared with 49% among men.[218] Mortality rates have been in decline mainly in the most developed settings due in part to improvements in treatment (eg, endoscopic resection, adjuvant instillation of chemotherapy, and intravesical immunotherapy)[219]; the exceptions are countries undergoing rapid economic transition, including in Central and South America; some Central, Southern, and Eastern European countries; and the Baltic countries.[216] Of note, differences in coding and registration practices need to be considered in terms of inclusion or otherwise of noninvasive cancers.[216,220,221] Because noninvasive cancers reflect a large proportion of all bladder cancers[222] and are commonly associated with a good prognosis, mortality rates may be of greater utility when comparing international and temporal variations and assessing overall progress in controlling the disease.[216,220]

Other cancers common in certain regions

Nonmelanoma skin cancer is responsible for over one million new cases (excluding basal cell carcinoma) and 64,000 deaths globally (Table 1), with incidence rates approximately 2 times higher among men than among women (Table 3). It is the most frequently diagnosed cancer in Australia/New Zealand where the rates are the world highest in both men and women (Fig. 18). The overall melanoma incidence in Australia has been decreasing since 2005 (−0.7% per year),[223] in part reflecting some successes in mass media campaigns,[224] accompanied by policies, supportive environments

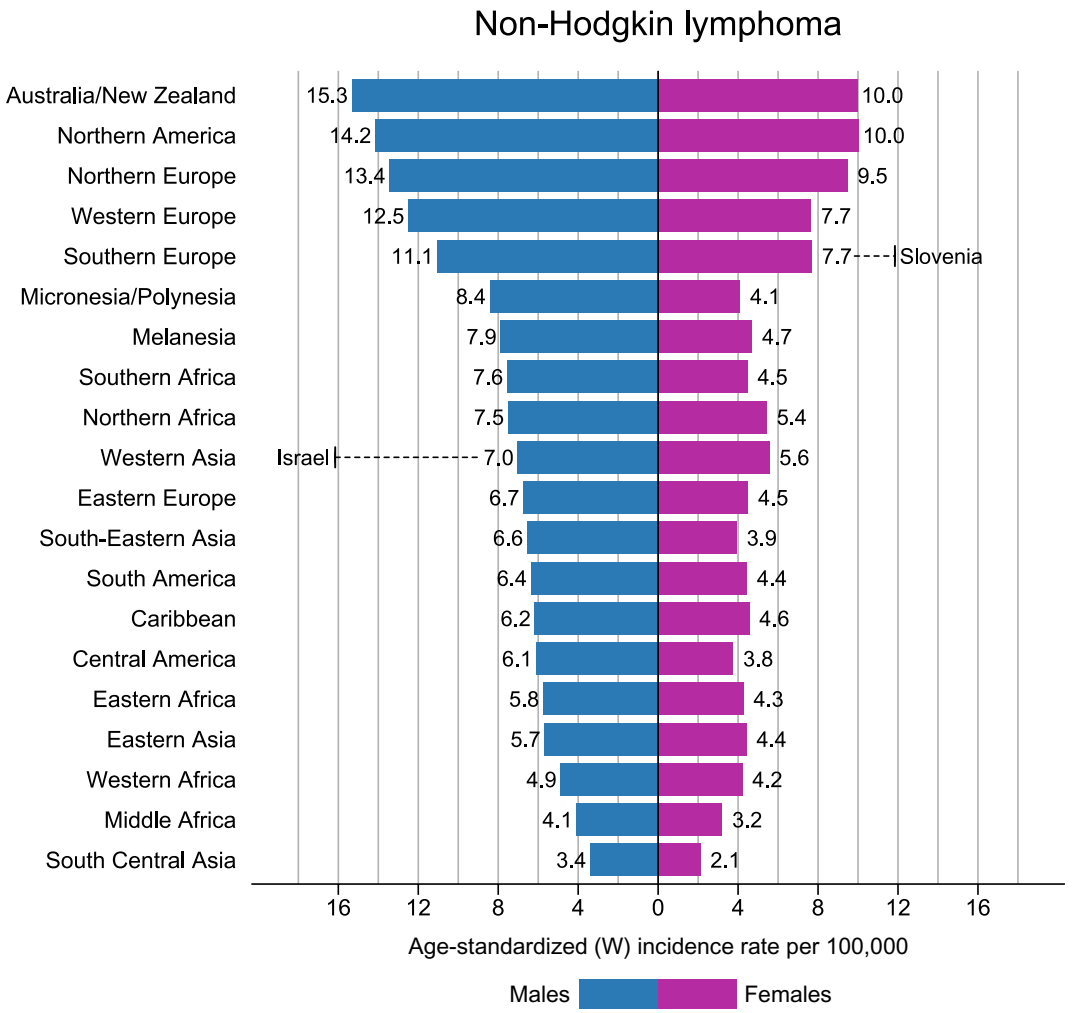

FIGURE 20. Region-Specific Incidence Age-Standardized Rates by sex for Non-Hodgkin Lymphoma in 2020. Rates are shown in descending order of the world (W) age-standardized rate among men, and the highest national rates among men and women are superimposed. Source: GLOBOCAN 2020.

such as shade, and access to quality sun-protection products governed by national standards.[225] Although incidence rates in New Zealand increased until the early 2010s, they are projected to decline in the future,[223] reflecting birth cohort effects in younger generations.[226] A rapid decline in death rates for melanoma has been reported in the United States by 6.4% per year since 2013 through 2017 after the introduction of new therapies, including immune checkpoint inhibitors and targeted therapies for metastatic melanoma.[227,228]

Pancreatic cancer accounts for almost as many deaths (466,000) as cases (496,000) because of its poor prognosis and is the seventh leading cause of cancer death in both sexes (Fig. 4). Rates are from 4-fold to 5-fold higher in higher HDI countries (Fig. 7), with the highest incidence rates in Europe, Northern America, and Australia/New Zealand (Fig. 19). Both incidence and mortality rates either have been stable or have slightly increased in many countries, likely reflecting the increasing prevalence of obesity, diabetes, and alcohol consumption, although improvements in diagnostic and cancer registration practices may also be in play in some countries.[94] Given that the rates of this disease are rather stable relative to the declining rates of breast cancer, it has been projected that pancreatic cancer will surpass breast cancer as the third leading cause of cancer death by 2025 in a study of 28 European countries.[229]

Non-Hodgkin lymphoma is responsible for 544,000 new cases and 260,000 deaths in 2020 (Table 1). Incidence rates are approximately 2-fold higher in transitioned countries than in transitioning countries (Fig. 7). The highest incidence rates are found in Australia/New Zealand, Northern America, and Europe, with Israel and Slovenia ranking first for men and women, respectively (Fig. 20). In many countries in the high-risk regions, increasing incidence rates during the 1980s and 1990s have plateaued in recent years.[230] In the United States, this trend appeared in a similar fashion for both HIV-infected and HIV-uninfected individuals, and reasons for the long-term increase in non-Hodgkin lymphoma incidence in the general population remain unknown.[231]

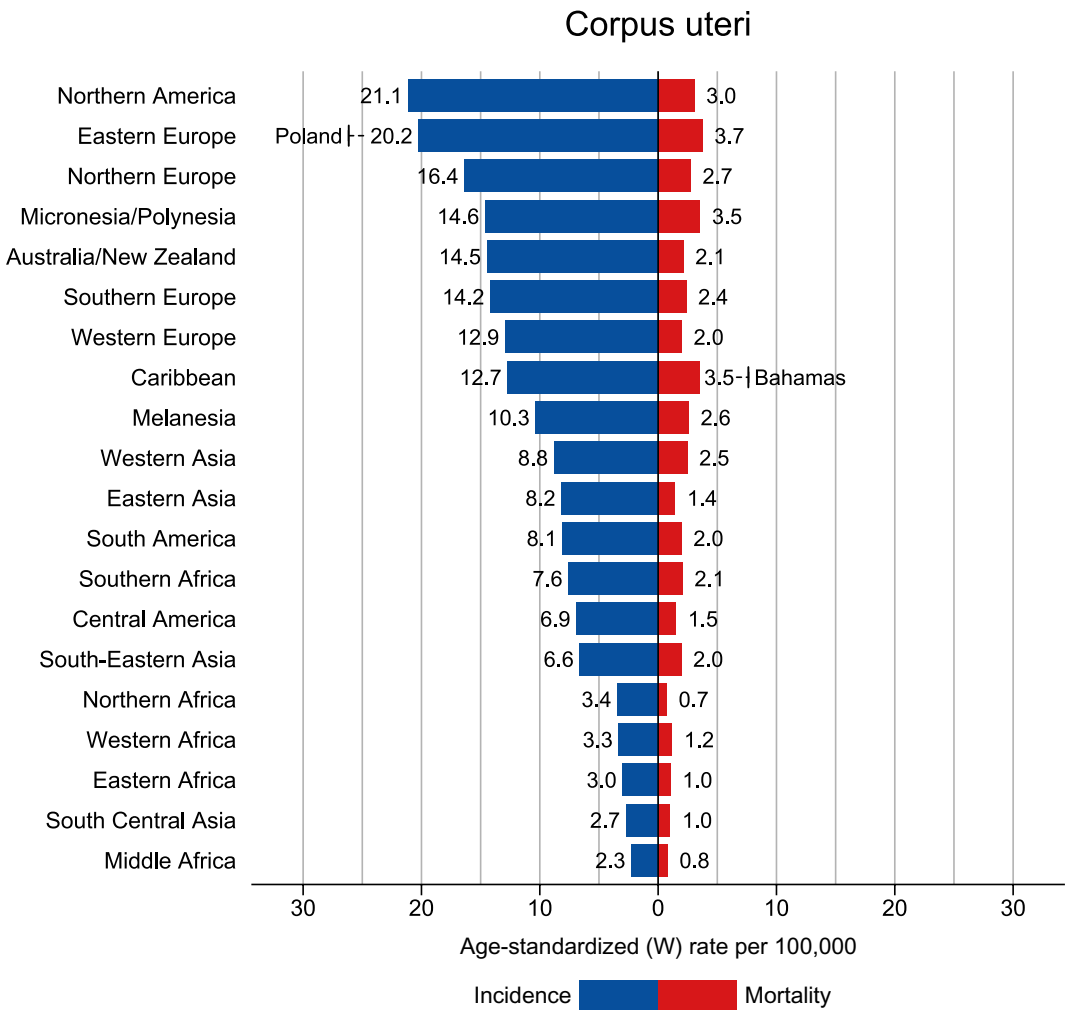

FIGURE 21. Region-Specific Incidence and Mortality Age-Standardized Rates for Uterine Corpus Cancer in 2020. Rates are shown in descending order of the world (W) age-standardized incidence rate, and the highest national age-standardized rates for incidence and mortality are superimposed. Source: GLOBOCAN 2020.

Uterine corpus cancer is the sixth most commonly diagnosed cancer in women, with 417,000 new cases and 97,000 deaths in 2020 (Table 1). Incidence rates vary 10-fold across world regions with the highest rates seen in Northern America, Europe, Micronesia/Polynesia, and Australia/New Zealand and the lowest incidence rates in most African regions and South Central Asia (Fig. 21). Less regional variation was seen for mortality rates, with the highest in Eastern Europe, Micronesia/Polynesia, the Caribbean, and Northern America. Incidence rates have increased or stabilized since the late 1990s in many countries across regions, with South Africa and several countries in Asia showing the fastest increase.[232] Birth cohort effects were most evident in Japan, the Philippines, Belarus, Singapore, India, Belarus, Lithuania, Costa Rica, and New Zealand,[232] possibly in part reflecting increases in the prevalence of risk factors (eg, excess body weight, physical inactivity) in subsequently younger generations.

There are several cancers that, although not featured among the top 10 cancers, are major cancers within certain regions or specific countries. With approximately 34,000 new cases and 15,000 deaths (Table 1), Kaposi sarcoma is a relatively rare cancer worldwide but is endemic in several countries in Southern and Eastern Africa (Fig. 22) and is the leading cause of both cancer incidence and mortality among men in 2020 in Mozambique and Uganda (Figs. 5A and 6A); rates are the highest worldwide in Mozambique for men and in Zambia for women (Fig. 22). Cancers of the lip and oral cavity cancers are highly frequent in South Central Asia (eg, India, Sri Lanka, and Pakistan)[18] as well as Melanesia (Papua New Guinea, with the highest incidence rate worldwide in both sexes) (Fig. 23), reflecting the popularity of betel nut chewing.[233] It is also the leading cause of cancer death in India among men (Fig. 6A). Incidence rates are also high in Eastern and Western Europe and in Australia/New Zealand and have

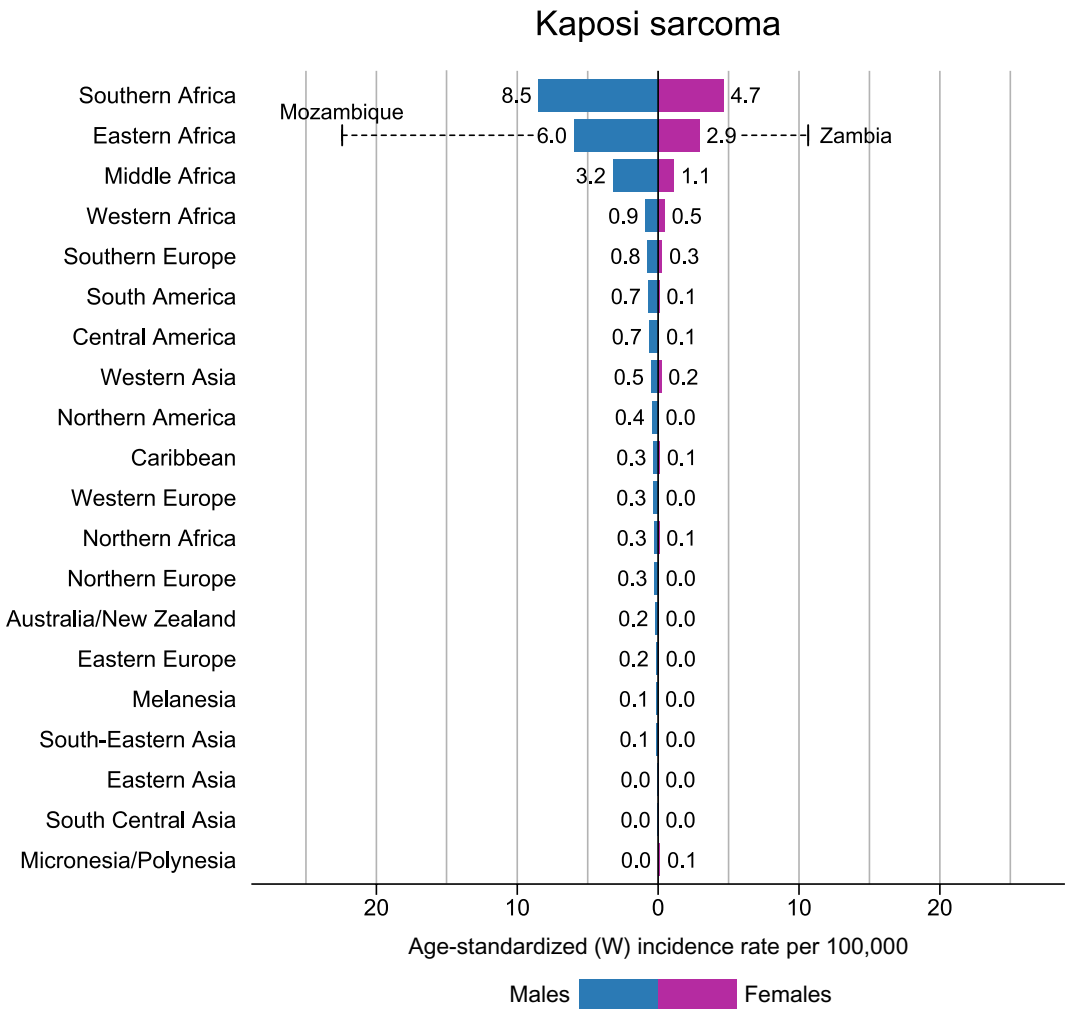

FIGURE 22. Region-Specific Incidence Age-Standardized Rates by Sex for Kaposi Sarcoma in 2020. Rates are shown in descending order of the world (W) age-standardized rate among men, and the highest national rates in men and women are superimposed. Source: GLOBOCAN 2020.

been linked to alcohol consumption, tobacco smoking, HPV infection for cancers of the oropharyngeal region, and to ultraviolet radiation from sunlight exposure for lip cancer.[233-236]

Future Burden of Cancer in 2040

Worldwide, an estimated 28.4 million new cancer cases (including NMSC, except basal cell carcinoma) are projected to occur in 2040, a 47% increase from the corresponding 19.3 million cases in 2020, assuming that national rates estimated in 2020 remain constant (Fig. 24). The relative magnitude of increase is most striking in low HDI countries (95%) and in medium HDI countries (64%). In terms of the absolute burden, the high HDI countries are expected to experience the greatest increase in incidence, with 4.1 million new cases more in 2040 compared with 2020. This projection is solely due to the growth and aging of the population and may be further exacerbated by an increasing prevalence of risk factors in many parts of the world.

Although the burden of cancer increases substantially at all HDI levels, the epidemiologic transition of cancer in emerging HDI countries will likely to be most affected, in which an increasing magnitude of the disease is paralleled by a changing profile of common cancer types. Many countries classified with low and medium HDI levels are experiencing a marked increase in the prevalence of known cancer risk factors that prevail in high-income western countries (eg, smoking, unhealthy diet, excess body weight, and physical inactivity).[4,92,237] A recurring observation is the ongoing displacement of infection-related and poverty-related cancers (eg, cervix, liver, stomach) with cancers that are uniformly common in the most developed countries (eg, breast, lung, colorectum, prostate), requiring changes in the priorities in national cancer control strategies.[93]

Increases in the incidence of these cancers will likely be paralleled by increases in mortality rates, which have been observed for breast and colorectal cancer, unless resources are placed within health services to appropriately treat and

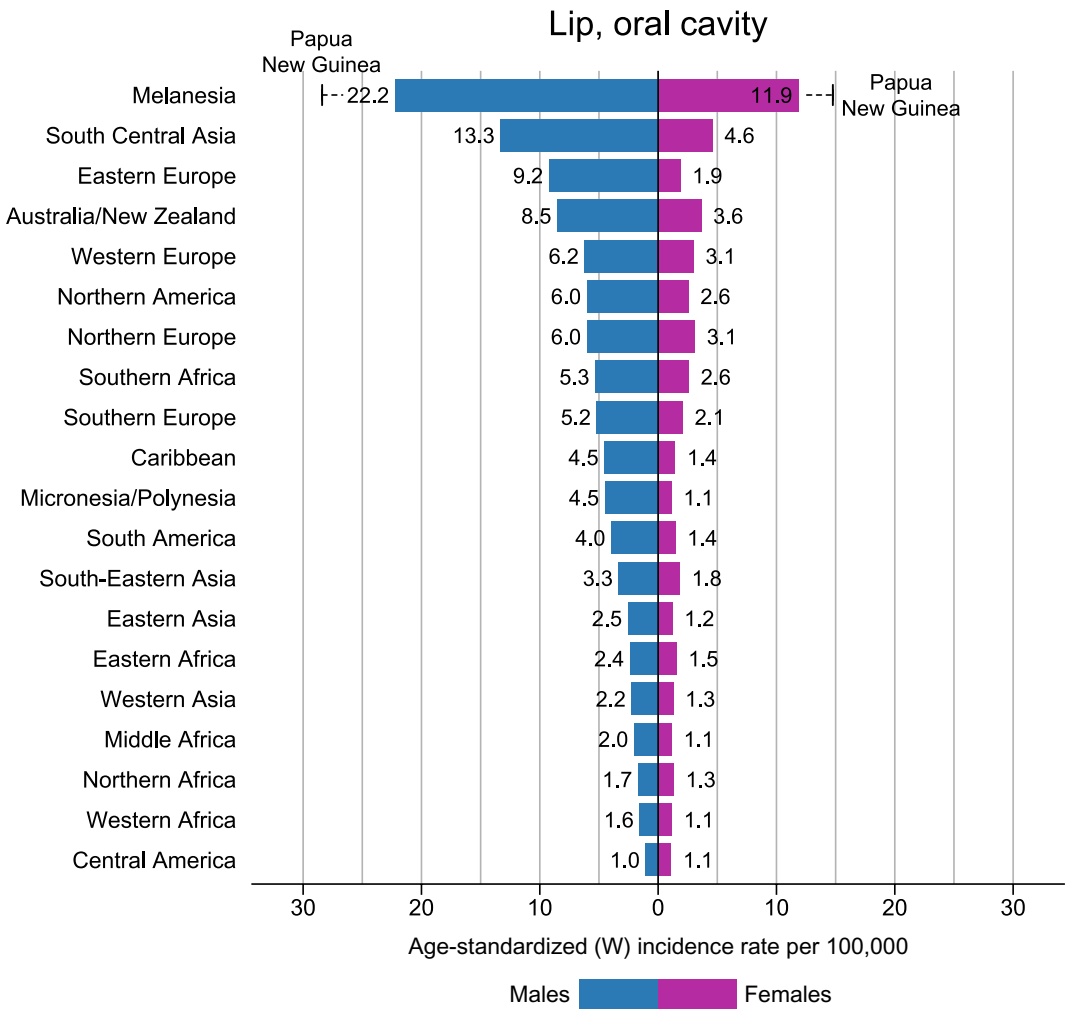

FIGURE 23. Region-Specific Incidence Age-Standardized Rates by Sex for Cancers of the Lip and Oral Cavity in 2020. Rates are shown in descending order of the world (W) age-standardized rate among men, and the highest national rates among men and women are superimposed. Source: GLOBOCAN 2020.

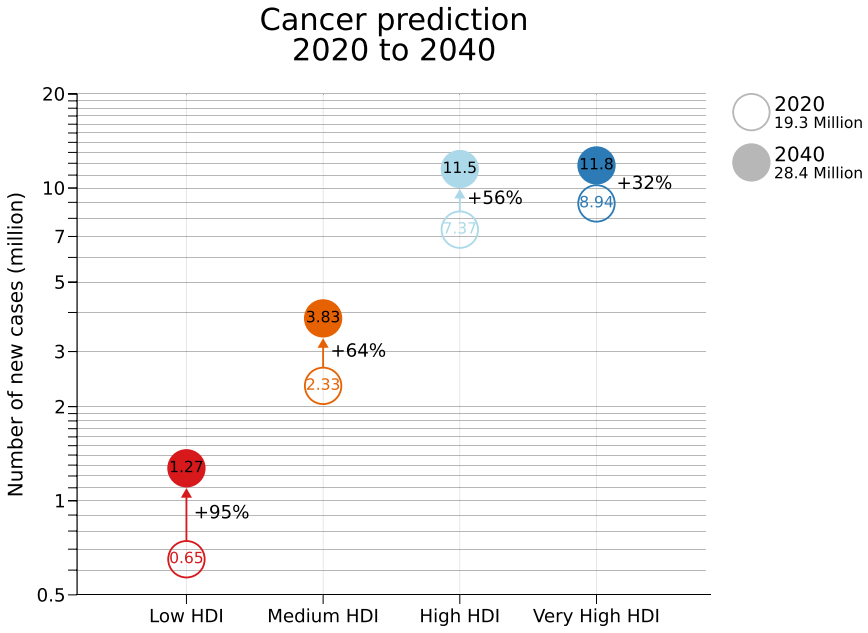

FIGURE 24. Projected Number of New Cases for All Cancers Combined (Both Sexes Combined) in 2040 According to the 4-Tier Human Development Index (HDI). Source: GLOBOCAN 2020.

manage the growing number of cancers.[238] In addition to a residual burden of cancers associated with infections,[84] the increasing burden of cancers associated with social and economic transition may overwhelm health care systems in many lower income countries if left unchecked.[239] Primary prevention is a particularly effective way to control cancer, up to half of all cancers are preventable.[240] However, much needs to be done to integrate current effective interventions into existing health plans, while cultivating new interventions that either tackle exposures that are increasing globally or cancers for which prevention options remain limited.[241]

Summary and Conclusions

The GLOBOCAN 2020 estimates presented in this study indicate that there were 19.3 million new cases of cancer and almost 10 million deaths from cancer in 2020. The disease is an important cause of morbidity and mortality worldwide, in every world region, and irrespective of the level of human development. It is worth reiterating that, in Africa, the cumulative risk of death from cancer among women in 2020 is broadly comparable to the risks observed among women in Northern America and in the highest income countries of Europe. Therefore, efforts to build a sustainable infrastructure for the dissemination of proven cancer prevention measures and the provision of cancer care in transitioning countries are critical for global cancer control.

The extraordinary diversity of cancer continues to offer clues to the underlying causes but also reenforces the need for a global escalation of efforts to control the disease. Packages of effective and resource-sensitive preventative and curative interventions are available for cancer,[183,242] and their tailored integration into health planning nationally can serve to reduce the future burden and suffering from cancer worldwide, while narrowing the evident cancer inequities between transitioning and transitioned countries observed today. ■

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References

1. Bray F, Laversanne M, Weiderpass E, Soerjomataram I. The ever-increasing importance of cancer as a leading cause of premature death worldwide. *Cancer*. In press.
2. World Health Organization (WHO). Global Health Estimates 2020: Deaths by Cause, Age, Sex, by Country and by Region, 2000-2019. WHO; 2020. Accessed December 11, 2020. who.int/data/gho/data/themes/mortality-and-global-health-estimates/ghe-leading-causes-of-death
3. Omran AR. The epidemiologic transition. A theory of the epidemiology of population change. *Milbank Mem Fund Q*. 1971;49:509-538.
4. Gersten O, Wilmoth JR. The cancer transition in Japan since 1951. *Demogr Res*. 2002;7:271-306.
5. United Nations Development Programme (UNDP). Human Development Report 2019. Beyond Income, Beyond Averages, Beyond Today: Inequalities in Human Development in the 21st Century. UNDP; 2019. Accessed November 25, 2020. hdr.undp.org/en/content/human-development-report-2019
6. Ferlay J, Colombet M, Soerjomataram I, et al. Global and Regional Estimates of the Incidence and Mortality for 38 Cancers: GLOBOCAN 2018. International Agency for Research on Cancer/World Health Organization; 2018.
7. Valencia DN. Brief review on COVID-19: the 2020 pandemic caused by SARS-CoV-2. *Cureus*. 2020;12:e7386.
8. World Health Organization (WHO). Coronavirus disease (COVID-19) pandemic. WHO; 2020. Accessed November 11, 2020. who.int/emergencies/diseases/novel-coronavirus-2019
9. Corley DA, Sedki M, Ritzwoller DP, et al. Cancer screening during COVID-19: a perspective from NCI's PROSPR consortium. *Gastroenterology*. Published online October 21, 2020. doi:10.1053/j.gastro.2020.10.030
10. Kutikov A, Weinberg DS, Edelman MJ, Horwitz EM, Uzzo RG, Fisher RI. A war on two fronts: cancer care in the time of COVID-19. *Ann Intern Med*. 2020;172:756-758.
11. Dinmohamed AG, Visser O, Verhoeven RHA, et al. Fewer cancer diagnoses during the COVID-19 epidemic in the Netherlands. *Lancet Oncol*. 2020;21:750-751.
12. Maringe C, Spicer J, Morris M, et al. The impact of the COVID-19 pandemic on cancer deaths due to delays in diagnosis in England, UK: a national, population-based, modelling study. *Lancet Oncol*. 2020;21:1023-1034.
13. Sharpless NE. COVID-19 and cancer. *Science*. 2020;368:1290.
14. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. *CA Cancer J Clin*. 2005;55:74-108.
15. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. *CA Cancer J Clin*. 2011;61:69-90.
16. 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.
17. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2018;68:394-424.
18. Ferlay J, Ervik M, Lam F, et al, eds. Global Cancer Observatory: Cancer Today. International Agency for Research on Cancer; 2020. Accessed November 25, 2020. gco.iarc.fr/today
19. Ferlay J, Colombet M, Soerjomataram I, et al. Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. *Int J Cancer*. 2019;144:1941-1953.
20. Doll R, Payne P, Waterhouse J, eds. Cancer Incidence in Five Continents: A Technical Report. Springer-Verlag (for UICC); 1966.
21. Arnold M, Rutherford MJ, Bardot A, et al. Progress in cancer survival, mortality, and incidence in seven high-income countries 1995-2014 (ICBP SURVMARK-2): a population-based study. *Lancet Oncol*. 2019;20:1493-1505.
22. 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.

23. Miranda-Filho A, Bray F. Global patterns and trends in cancers of the lip, tongue and mouth. *Oral Oncol.* 2020;102:104551.
24. Brinton LA, Gaudet MM, Gierach GL. Breast cancer. In: Thun M, Linet MS, Cerhan JR, Haiman CA, Schottenfeld D, eds. Cancer Epidemiology and Prevention. 4th ed. Oxford University Press; 2018:861-888.
25. Metcalfe KA, Poll A, Royer R, et al. Screening for founder mutations in BRCA1 and BRCA2 in unselected Jewish women. *J Clin Oncol.* 2010;28:387-391.
26. Torre LA, Islami F, Siegel RL, Ward EM, Jemal A. Global cancer in women: burden and trends. *Cancer Epidemiol Biomarkers Prev.* 2017;26:444-457.
27. 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.
28. Breen N, Gentleman JF, Schiller JS. Update on mammography trends: comparisons of rates in 2000, 2005, and 2008. *Cancer.* 2011;117:2209-2218.
29. DeSantis CE, Ma J, Gaudet MM, et al. Breast cancer statistics, 2019. *CA Cancer J Clin.* 2019;69:438-451.
30. Heer E, Harper A, Escandor N, Sung H, McCormack V, Fidler-Benaoudia MM. Global burden and trends in premenopausal and postmenopausal breast cancer: a population-based study. *Lancet Glob Health.* 2020;8:e1027-e1037.
31. Glass AG, Lacey JV, Carreon D, Hoover RN. Breast cancer incidence, 1980-2006: combined roles of menopausal hormone therapy, screening mammography, and estrogen receptor status. *J Natl Cancer Inst.* 2007;99:1152-1161.
32. Anderson WF, Katki HA, Rosenberg PS. Incidence of breast cancer in the United States: current and future trends. *J Natl Cancer Inst.* 2011;103:1397-1402.
33. Anderson WF, Rosenberg PS, Petito L, et al. Divergent estrogen receptor-positive and -negative breast cancer trends and etiologic heterogeneity in Denmark. *Int J Cancer.* 2013;133:2201-2206.
34. Mullooly M, Murphy J, Gierach GL, et al. Divergent oestrogen receptor-specific breast cancer trends in Ireland (2004-2013): amassing data from independent Western populations provide etiologic clues. *Eur J Cancer.* 2017;86:326-333.
35. Mesa-Eguiagaray I, Wild SH, Rosenberg PS, et al. Distinct temporal trends in breast cancer incidence from 1997 to 2016 by molecular subtypes: a population-based study of Scottish cancer registry data. *Br J Cancer.* 2020;123:852-859.
36. Reeves GK, Pirie K, Beral V, Green J, Spencer E, Bull D. Cancer incidence and mortality in relation to body mass index in the Million Women Study: cohort study. *BMJ.* 2007;335:1134-1139.
37. Renehan AG, Tyson M, Egger M, Heller RF, Zwahlen M. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. *Lancet.* 2008;371:569-578.
38. Munsell MF, Sprague BL, Berry DA, Chisholm G, Trentham-Dietz A. Body mass index and breast cancer risk according to postmenopausal estrogen-progestin use and hormone receptor status. *Epidemiol Rev.* 2014;36:114-136.
39. Suzuki R, Orsini N, Saji S, Key TJ, Wolk A. Body weight and incidence of breast cancer defined by estrogen and progesterone receptor status—a meta-analysis. *Int J Cancer.* 2009;124:698-712.
40. Gilliland FD, Joste N, Stauber PM, et al. Biologic characteristics of interval and screen-detected breast cancers. *J Natl Cancer Inst.* 2000;92:743-749.
41. Porter PL, El-Bastawissi AY, Mandelson MT, et al. Breast tumor characteristics as predictors of mammographic detection: comparison of interval- and screen-detected cancers. *J Natl Cancer Inst.* 1999;91:2020-2028.
42. Malvezzi M, Carioli G, Bertuccio P, et al. European cancer mortality predictions for the year 2019 with focus on breast cancer. *Ann Oncol.* 2019;30:781-787.
43. Althuis MD, Dozier JM, Anderson WF, Devesa SS, Brinton LA. Global trends in breast cancer incidence and mortality 1973-1997. *Int J Epidemiol.* 2005;34:405-412.
44. Joko-Fru WY, Jedy-Agba E, Korir A, et al. The evolving epidemic of breast cancer in sub-Saharan Africa: results from the African Cancer Registry Network. *Int J Cancer.* 2020;147:2131-2141.
45. Bray F, McCarron P, Parkin DM. The changing global patterns of female breast cancer incidence and mortality. *Breast Cancer Res.* 2004;6:229-239.
46. Allemani C, Matsuda T, Di Carlo V, et al. Global surveillance of trends in cancer survival 2000-14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. *Lancet.* 2018;391:1023-1075.
47. Joko-Fru WY, Miranda-Filho A, Soerjomataram I, et al. Breast cancer survival in sub-Saharan Africa by age, stage at diagnosis and Human Development Index (HDI): a population-based registry study. *Int J Cancer.* 2020;146:1208-1218.
48. Cutler SJ. International Symposium on End Results of Cancer Therapy. Computation of survival rates. *Natl Cancer Inst Monogr.* 1964;15:381-385.
49. Jedy-Agba E, McCormack V, Adebamowo C, Dos-Santos-Silva I. Stage at diagnosis of breast cancer in sub-Saharan Africa: a systematic review and meta-analysis. *Lancet Glob Health.* 2016;4:e923-e935.
50. World Health Organization (WHO). WHO Position Paper on Mammography Screening. WHO; 2014. Accessed December 14, 2020. paho.org/hq/dmdocuments/2015/WHO-ENG-Mammography-Factsheet.pdf
51. Ngan TT, Nguyen NTQ, Van Minh H, Donnelly M, O'Neill C. Effectiveness of clinical breast examination as a 'stand-alone' screening modality: an overview of systematic reviews. *BMC Cancer.* 2020;20:1070.
52. Birnbaum JK, Duggan C, Anderson BO, Etzioni R. Early detection and treatment strategies for breast cancer in low-income and upper middle-income countries: a modelling study. *Lancet Glob Health.* 2018;6:e885-e893.
53. Anderson BO, Lipscomb J, Murillo RH, Thomas DB. Chapter 3. Breast cancer. In: Gelband H, Jha P, Sankaranarayanan R, Horton S, eds. Cancer: Disease Control Priorities. 3rd ed. Volume 3. The International Bank for Reconstruction and Development/The World Bank; 2015:45-68.
54. McCormack V, McKenzie F, Foerster M, et al. Breast cancer survival and survival gap apportionment in sub-Saharan Africa (ABC-DO): a prospective cohort study. *Lancet Glob Health.* 2020;8:e1203-e1212.
55. Anderson BO, Cazap E, El Saghir NS, et al. Optimisation of breast cancer management in low-resource and middle-resource countries: executive summary of the Breast Health Global Initiative consensus, 2010. *Lancet Oncol.* 2011;12:387-398.
56. Dvaladze A, Duggan C, Anderson BO. Phased implementation for breast cancer management in low-income and middle-income countries: a proposal for the strategic application of resource-stratified guidelines by the Breast Health

Global Initiative. *Cancer.* 2020;126(suppl 10):2337-2338.

57. Duggan C, Dvaladze A, Rositch AF, et al. The Breast Health Global Initiative 2018 Global Summit on Improving Breast Healthcare Through Resource-Stratified Phased Implementation: methods and overview. *Cancer.* 2020;126(suppl 10):2339-2352.
58. Independent UK Panel on Breast Cancer Screening. The benefits and harms of breast cancer screening: an independent review. *Lancet.* 2012;380:1778-1786.
59. Coldman A, Phillips N, Wilson C, et al. Pan-Canadian study of mammography screening and mortality from breast cancer. *J Natl Cancer Inst.* 2014;106:dju261.
60. Tabar L, Dean PB, Chen TH, et al. The incidence of fatal breast cancer measures the increased effectiveness of therapy in women participating in mammography screening. *Cancer.* 2019;125:515-523.
61. International Agency for Research on Cancer (IARC) Working Group on the Evaluation of Cancer-Preventive Strategies. Breast Cancer Screening. IARC Handbooks of Cancer Prevention. Volume 15. IARC Press; 2016.
62. Oeffinger KC, Fontham ET, Etzioni R, et al. Breast cancer screening for women at average risk: 2015 guideline update from the American Cancer Society. *JAMA.* 2015;314:1599-1614.
63. Prasad V, Lenzer J, Newman DH. Why cancer screening has never been shown to "save lives"—and what we can do about it. *BMJ.* 2016;352:h6080.
64. Puliti D, Duffy SW, Miccinesi G, et al. Overdiagnosis in mammographic screening for breast cancer in Europe: a literature review. *J Med Screen.* 2012;19(suppl 1):42-56.
65. Michalopoulos D, Duffy SW. Estimation of overdiagnosis using short-term trends and lead time estimates uncontaminated by overdiagnosed cases: results from the Norwegian breast screening programme. *J Med Screen.* 2016;23:192-202.
66. Narod SA. Personalised medicine and population health: breast and ovarian cancer. *Hum Genet.* 2018;137:769-778.
67. Pashayan N, Morris S, Gilbert FJ, Pharoah PDP. Cost-effectiveness and benefit-to-harm ratio of risk-stratified screening for breast cancer: a life-table model. *JAMA Oncol.* 2018;4:1504-1510.
68. Mukama T, Kharazmi E, Xing X, et al. Risk-adapted starting age of screening for relatives of patients with breast cancer. *JAMA Oncol.* 2019;6:68-74.
69. Pal Choudhury P, Wilcox AN, Brook MN, et al. Comparative validation of breast cancer risk prediction models and projections for future risk stratification. *J Natl Cancer Inst.* 2020;112:278-285.
70. Antoniou A, Anton-Culver H, Borowsky A, et al. A response to "Personalised medicine and population health: breast and ovarian cancer." *Hum Genet.* 2019;138:287-289.
71. Gierach GL, Choudhury PP, Garcia-Closas M. Toward risk-stratified breast cancer screening: considerations for changes in screening guidelines. *JAMA Oncol.* 2020;6:31-33.
72. World Health Organization (WHO). WHO global report on trends in prevalence of tobacco smoking 2000-2025. 2nd ed. WHO; 2018. Accessed December 2, 2020. apps.who.int/iris/handle/10665/272694
73. Mu L, Liu L, Niu R, et al. Indoor air pollution and risk of lung cancer among Chinese female non-smokers. *Cancer Causes Control.* 2013;24:439-450.
74. Turner MC, Andersen ZJ, Baccarelli A, et al. Outdoor air pollution and cancer: an overview of the current evidence and public health recommendations. *CA Cancer J Clin.* 2020;70:460-479.
75. Thun M, Peto R, Boreham J, Lopez AD. Stages of the cigarette epidemic on entering its second century. *Tob Control.* 2012;21:96-101.
76. Parkin DM, Bray FI, Devesa SS. Cancer burden in the year 2000. The global picture. *Eur J Cancer.* 2001;37(suppl 8):S4-S66.
77. 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.
78. Devesa SS, Blot WJ, Fraumeni JF Jr. Declining lung cancer rates among young men and women in the United States: a cohort analysis. *J Natl Cancer Inst.* 1989;81:1568-1571.
79. 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.
80. Thun MJ, Henley SJ, Travis WD. Lung cancer. In: Thun M, Linet MS, Cerhan JR, Haiman CA, Schottenfeld D, eds. Cancer Epidemiology and Prevention. 4th ed. Oxford University Press; 2018: 519-578.
81. 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.
82. Fidler-Benaoudia MM, Torre LA, Bray F, Ferlay J, Jemal A. Lung cancer incidence in young women vs. young men: a systematic analysis in 40 countries. *Int J Cancer.* 2020;147:811-819.
83. Jha P. Avoidable global cancer deaths and total deaths from smoking. *Nat Rev Cancer.* 2009;9:655-664.
84. Parkin DM, Bray F, Ferlay J, Jemal A. Cancer in Africa 2012. *Cancer Epidemiol Biomarkers Prev.* 2014;23:953-966.
85. World Health Organization (WHO). WHO Report on the Global Tobacco Epidemic, 2008—The MPOWER Package. WHO; 2008. Accessed November 25, 2020. who.int/tobacco/mpower/2008/en/
86. World Health Organization (WHO). WHO report on the global tobacco epidemic 2019: offer help to quit tobacco use. WHO; 2020. Accessed November 21, 2020. who.int/tobacco/global_report/en/
87. World Health Organization (WHO). WHO global report on trends in prevalence of tobacco use 2000-2025. 3rd ed. WHO; 2019. Accessed November 2, 2020. who.int/publications/i/item/who-global-report-on-trends-in-prevalence-of-tobacco-use-2000-2025-third-edition
88. National Lung Screening Trial Research Team; Aberle DR, Adams AM, et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. *N Engl J Med.* 2011;365:395-409.
89. National Lung Screening Trial Research Team. Lung cancer incidence and mortality with extended follow-up in the National Lung Screening Trial. *J Thorac Oncol.* 2019;14:1732-1742.
90. Pastorino U, Silva M, Sestini S, et al. Prolonged lung cancer screening reduced 10-year mortality in the MILD trial: new confirmation of lung cancer screening efficacy. *Ann Oncol.* 2019;30:1162-1169.
91. de Koning HJ, van der Aalst CM, de Jong PA, et al. Reduced lung-cancer mortality with volume CT screening in a randomized trial. *N Engl J Med.* 2020;382:503-513.
92. Bray F. Transitions in human development and the global cancer burden. In: Stewart BW, Wild CP, eds. World Cancer Report 2014. WHO Press; 2014:42-55.
93. 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.
94. Arnold M, Abnet CC, Neale RE, et al. Global burden of 5 major types of gastrointestinal cancer. *Gastroenterology.* 2020;159:335-349.e15.

95. Siegel RL, Miller KD, Goding Sauer A, et al. Colorectal cancer statistics, 2020. *CA Cancer J Clin.* 2020;70:145-164.

96. World Cancer Research Fund/American Institute for Cancer Research. The Continuous Update Project Expert Report 2018. Diet, Nutrition, Physical Activity and Cancer: Colorectal Cancer. Accessed October 23, 2020. wcrf.org/sites/default/files/Colorectal-cancer-report.pdf

97. Sullivan T, Sullivan R, Ginsburg OM. Chapter 12. Screening for cancer: considerations for low- and middle-income countries. In: Gelband H, Jha P, Sankaranarayanan R, Horton S, eds. Cancer: Disease Control Priorities. 3rd ed. Volume 3. The International Bank for Reconstruction and Development/The World Bank; 2015:211-222.

98. Navarro M, Nicolas A, Ferrandez A, Lanas A. Colorectal cancer population screening programs worldwide in 2016: an update. *World J Gastroenterol.* 2017;23:3632-3642.

99. Edwards BK, Ward E, Kohler BA, et al. Annual report to the nation on the status of cancer, 1975-2006, featuring colorectal cancer trends and impact of interventions (risk factors, screening, and treatment) to reduce future rates. *Cancer.* 2010;116:544-573.

100. Schreuders EH, Ruco A, Rabeneck L, et al. Colorectal cancer screening: a global overview of existing programmes. *Gut.* 2015;64:1637-1649.

101. Siegel RL, Ward EM, Jemal A. Trends in colorectal cancer incidence rates in the United States by tumor location and stage, 1992-2008. *Cancer Epidemiol Biomarkers Prev.* 2012;21:411-416.

102. Keum N, Giovannucci E. Global burden of colorectal cancer: emerging trends, risk factors and prevention strategies. *Nat Rev Gastroenterol Hepatol.* 2019;16:713-732.

103. Siegel RL, Torre LA, Soerjomataram I, et al. Global patterns and trends in colorectal cancer incidence in young adults. *Gut.* 2019;68:2179-2185.

104. Araghi M, Soerjomataram I, Bardot A, et al. Changes in colorectal cancer incidence in seven high-income countries: a population-based study. *Lancet Gastroenterol Hepatol.* 2019;4:511-518.

105. Vuik FE, Nieuwenburg SA, Bardou M, et al. Increasing incidence of colorectal cancer in young adults in Europe over the last 25 years. *Gut.* 2019;68:1820-1826.

106. Wolf AMD, Fontham ETH, Church TR, et al. Colorectal cancer screening for average-risk adults: 2018 guideline update from the American Cancer Society. *CA Cancer J Clin.* 2018;68:250-281.

107. U.S. Preventive Services Task Force. Draft Recommendation Statement. Colorectal Cancer: Screening. October 27, 2020. Accessed November 2, 2020. uspreventiveservicestaskforce.org/uspstf/draft-recommendation/colorectal-cancer-screening3

108. Rebbeck TR, Devesa SS, Chang BL, et al. Global patterns of prostate cancer incidence, aggressiveness, and mortality in men of African descent. *Prostate Cancer.* 2013;2013:560857.

109. World Cancer Research Fund/American Institute for Cancer Research. Continuous Update Project Expert Report 2018. Body fatness and weight gain and the risk of cancer. Accessed October 27, 2020. dietandcancerreport.org

110. 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.

111. Center MM, Jemal A, Lortet-Tieulent J, et al. International variation in prostate cancer incidence and mortality rates. *Eur Urol.* 2012;61:1079-1092.

112. 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.

113. US Preventive Services Task Force. Screening for prostate cancer: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med.* 2008;149:185-191.

114. Moyer VA; U.S. Preventive Services Task, Force. Screening for prostate cancer: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med.* 2012;157:120-134.

115. Tikkinen KAO, Dahm P, Lytvyn L, et al. Prostate cancer screening with prostate-specific antigen (PSA) test: a clinical practice guideline. *BMJ.* 2018;362:k3581.

116. Zargar H, van den Bergh R, Moon D, Lawrentschuk N, Costello A, Murphy D. The impact of the United States Preventive Services Task Force (USPTSTF) recommendations against prostate-specific antigen (PSA) testing on PSA testing in Australia. *BJU Int.* 2017;119:110-115.

117. 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.

118. Culp MB, Soerjomataram I, Efstathiou JA, Bray F, Jemal A. Recent global patterns in prostate cancer incidence and mortality rates. *Eur Urol.* 2020;77:38-52.

119. Seraphin TP, Joko-Fru WY, Kamate B, et al. Rising prostate cancer incidence in sub-Saharan Africa: a trend analysis of data from the African Cancer Registry Network. *Cancer Epidemiol Biomarkers Prev*. Published online October 8, 2020. doi:10.1158/1055-9965.EPI-20-1005

120. 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.

121. Tsodikov A, Gulati R, Heijnsdijk EAM, et al. Reconciling the effects of screening on prostate cancer mortality in the ERSPC and PLCO trials. *Ann Intern Med.* 2017;167:449-455.

122. Etzioni R, Tsodikov A, Mariotto A, et al. Quantifying the role of PSA screening in the US prostate cancer mortality decline. *Cancer Causes Control.* 2008;19:175-181.

123. Jemal A, Culp MB, Ma J, Islami F, Fedewa SA. Prostate cancer incidence 5 years after US Preventive Services Task Force recommendations against screening. *J Natl Cancer Inst*. Published online May 20, 2020. doi:10.1093/jnci/djaa068

124. Fedewa SA, Ma J, Jemal A. Response to Lehrer and Rheinstein. *J Natl Cancer Inst.* 2020;112:1069-1070.

125. Wolf AM, Wender RC, Etzioni RB, et al. American Cancer Society guideline for the early detection of prostate cancer: update 2010. *CA Cancer J Clin.* 2010;60:70-98.

126. US Preventive Services Task Force, Grossman DC, Curry SJ, et al. Screening for prostate cancer: US Preventive Services Task Force recommendation statement. *JAMA*. 2018;319:1901-1913.

127. Infection with Helicobacter pylori. *IARC Monogr Eval Carcinog Risks Hum.* 1994;61:177-240.

128. 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.

129. Hooi JKY, Lai WY, Ng WK, et al. Global prevalence of Helicobacter pylori infection: systematic review and meta-analysis. *Gastroenterology.* 2017;153:420-429.

130. Kidd M, Lastovica AJ, Atherton JC, Louw JA. Heterogeneity in the Helicobacter pylori vacA and cagA genes: association with gastroduodenal disease in South Africa? *Gut.* 1999;45:499-502.

131. Koshiol J, Wei WQ, Kreimer AR, et al. The gastric cardia is not a target for human papillomavirus-induced carcinogenesis. *Cancer Epidemiol Biomarkers Prev.* 2010;19:1137-1139.

132. Kamangar F, Dawsey SM, Blaser MJ, et al. Opposing risks of gastric cardia and noncardia gastric adenocarcinomas associated with Helicobacter pylori seropositivity. *J Natl Cancer Inst.* 2006;98:1445-1452.

133. de Martel C, Parsonnet J. Stomach cancer. In: Thun M, Linet MS, Cerhan JR, Haiman CA, Schottenfeld D, eds. Cancer Epidemiology and Prevention. 4th ed. Oxford University Press; 2018:593-610.

134. Howson CP, Hiyama T, Wynder EL. The decline in gastric cancer: epidemiology of an unplanned triumph. *Epidemiol Rev.* 1986;8:1-27.

135. Powell J, McConkey CC. Increasing incidence of adenocarcinoma of the gastric cardia and adjacent sites. *Br J Cancer.* 1990;62:440-443.

136. Devesa SS, Blot WJ, Fraumeni JF Jr. Changing patterns in the incidence of esophageal and gastric carcinoma in the United States. *Cancer.* 1998;83:2049-2053.

137. Sung H, Siegel RL, Rosenberg PS, Jemal A. Emerging cancer trends among young adults in the USA: analysis of a population-based cancer registry. *Lancet Public Health.* 2019;4:e137-e147.

138. Dikken JL, Lemmens VE, Wouters MW, et al. Increased incidence and survival for oesophageal cancer but not for gastric cardia cancer in the Netherlands. *Eur J Cancer.* 2012;48:1624-1632.

139. Arnold M, Park JY, Camargo MC, Lunet N, Forman D, Soerjomataram I. Is gastric cancer becoming a rare disease? A global assessment of predicted incidence trends to 2035. *Gut.* 2020;69:823-829.

140. Heer EV, Harper AS, Sung H, Jemal A, Fidler-Benaoudia MM. Emerging cancer incidence trends in Canada: the growing burden of young adult cancers. *Cancer.* 2020;126:4553-4562.

141. Anderson WF, Rabkin CS, Turner N, Fraumeni JF Jr, Rosenberg PS, Camargo MC. The changing face of noncardia gastric cancer incidence among US non-Hispanic whites. *J Natl Cancer Inst.* 2018;110:608-615.

142. Camargo MC, Anderson WF, King JB, et al. Divergent trends for gastric cancer incidence by anatomical subsite in US adults. *Gut.* 2011;60:1644-1649.

143. Thomas London W, Petrick JL, McGlynn KA. Liver cancer. In: Thun M, Linet MS, Cerhan JR, Haiman CA, Schottenfeld D, eds. Cancer Epidemiology and Prevention. 4th ed. Oxford University Press; 2018:635-660.

144. 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.

145. Prueksapanich P, Piyachaturawat P, Aumpansub P, Ridtitid W, Chaiteerakij R, Rerknimitr R. Liver fluke-associated biliary tract cancer. *Gut Liver.* 2018;12:236-245.

146. Petrick JL, Yang B, Altekruse SF, et al. Risk factors for intrahepatic and extrahepatic cholangiocarcinoma in the United States: a population-based study in SEER-Medicare. *PLoS One.* 2017;12:e0186643.

147. Welzel TM, Mellemkjaer L, Gloria G, et al. Risk factors for intrahepatic cholangiocarcinoma in a low-risk population: a nationwide case-control study. *Int J Cancer.* 2007;120:638-641.

148. Donato F, Gelatti U, Tagger A, et al. Intrahepatic cholangiocarcinoma and hepatitis C and B virus infection, alcohol intake, and hepatolithiasis: a case-control study in Italy. *Cancer Causes Control.* 2001;12:959-964.

149. Petrick JL, Florio AA, Znaor A, et al. International trends in hepatocellular carcinoma incidence, 1978-2012. *Int J Cancer.* 2020;147:317-330.

150. 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 [see comments]. *N Engl J Med.* 1997;336:1855-1859.

151. Marengo A, Rosso C, Bugianesi E. Liver cancer: connections with obesity, fatty liver, and cirrhosis. *Annu Rev Med.* 2016;67:103-117.

152. Florio AA, Ferlay J, Znaor A, et al. Global trends in intrahepatic and extrahepatic cholangiocarcinoma incidence from 1993 to 2012. *Cancer.* 2020;126:2666-2678.

153. Plummer M, de Martel C, Vignat J, Ferlay J, Bray F, Franceschi S. Global burden of cancers attributable to infections in 2012: a synthetic analysis. *Lancet Glob Health.* 2016;4:e609-e616.

154. World Health Organization (WHO). Hepatitis B 3rd dose (HepB3) immunization coverage. Accessed October 28, 2020. who.int/gho/immunization/hepatitis/en/

155. World Health Organization (WHO). Immunization coverage. WHO; 2020. Accessed October 20, 2020. who.int/news-room/fact-sheets/detail/immunization-coverage

156. Lanini S, Easterbrook PJ, Zumla A, Ippolito G. Hepatitis C: global epidemiology and strategies for control. *Clin Microbiol Infect.* 2016;22:833-838.

157. Sulkowski MS, Gardiner DF, Rodriguez-Torres M, et al. Daclatasvir plus sofosbuvir for previously treated or untreated chronic HCV infection. *N Engl J Med.* 2014;370:211-221.

158. Cooke GS, Andrieux-Meyer I, Applegate TL, et al. Accelerating the elimination of viral hepatitis: a Lancet Gastroenterology & Hepatology Commission. *Lancet Gastroenterol Hepatol.* 2019;4:135-184.

159. Cox AL, El-Sayed MH, Kao JH, et al. Progress towards elimination goals for viral hepatitis. *Nat Rev Gastroenterol Hepatol.* 2020;17:533-542.

160. Lemoine M, Shimakawa Y, Njie R, et al. Acceptability and feasibility of a screen-and-treat programme for hepatitis B virus infection in The Gambia: the Prevention of Liver Fibrosis and Cancer in Africa (PROLIFICA) study. *Lancet Glob Health.* 2016;4:e559-e567.

161. Blot WJ, Tarone RE. Esophageal cancer. In: Thun M, Linet MS, Cerhan JR, Haiman CA, Schottenfeld D, eds. Cancer Epidemiology and Prevention. 4th ed. Oxford University Press; 2018:579-593.

162. 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.

163. 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.

164. Walboomers JMM, Jacobs MV, Manos MM, et al. Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. *J Pathol.* 1999;189:12-19.

165. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Human papillomaviruses. *IARC Monogr Eval Carcinog Risks Hum.* 2007;90:1-636.

166. Herrero R, Murillo R. Cervical cancer. In: Thun M, Linet MS, Cerhan JR, Haiman CA, Schottenfeld D, eds. Cancer Epidemiology and Prevention. 4th ed. Oxford University Press; 2018:925-946.

167. Singh GK, Azuine RE, Siahpush M. Global inequalities in cervical cancer incidence and mortality are linked to deprivation, low socioeconomic status, and human development. *Int J MCH AIDS.* 2012;1:17-30.

168. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. *CA Cancer J Clin.* 2019;69:7-34.

169. International Agency for Research on Cancer (IARC). IARC Handbooks of

Cancer Prevention. Volume 10. Cervix Cancer Screening. IARC Press; 2005. Accessed November 23, 2020. publications.iarc.fr/Book-And-Report-Series/Iarc-Handbooks-Of-Cancer-Prevention/Cervix-Cancer-Screening-2005

170. 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.

171. 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.

172. Utada M, Chernyavskiy P, Lee WJ, et al. Increasing risk of uterine cervical cancer among young Japanese women: comparison of incidence trends in Japan, South Korea and Japanese-Americans between 1985 and 2012. *Int J Cancer.* 2019;144:2144-2152.

173. Castanon A, Sasieni P. Is the recent increase in cervical cancer in women aged 20-24 years in England a cause for concern? *Prev Med.* 2018;107:21-28.

174. McDonald SA, Qendri V, Berkhof J, de Melker HE, Bogaards JA. Disease burden of human papillomavirus infection in the Netherlands, 1989-2014: the gap between females and males is diminishing. *Cancer Causes Control.* 2017;28:203-214.

175. Pilleron S, Cabasag CJ, Ferlay J, et al. Cervical cancer burden in Latin America and the Caribbean: where are we? *Int J Cancer.* 2020;147:1638-1648.

176. 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.

177. Jedy-Agba E, Joko WY, Liu B, et al. Trends in cervical cancer incidence in sub-Saharan Africa. *Br J Cancer.* 2020;123:148-154.

178. PATH. Global HPV Vaccine Introduction Overview: projected and current national introductions, demonstration/pilot projects, gender-neutral vaccination programs, and global HPV vaccine introduction maps (2006-2023). PATH; 2020. Accessed November 23, 2020. path.org/resources/global-hpv-vaccine-introduction-overview/

179. Lemp JM, De Neve JW, Bussmann H, et al. Lifetime prevalence of cervical cancer screening in 55 low- and middle-income countries. *JAMA.* 2020;324:1532-1542.

180. Vaccarella S, Laversanne M, Ferlay J, Bray F. Cervical cancer in Africa, Latin America and the Caribbean and Asia: regional inequalities and changing trends. *Int J Cancer.* 2017;141:1997-2001.

181. Palmer T, Wallace L, Pollock KG, et al. Prevalence of cervical disease at age 20 after immunisation with bivalent HPV vaccine at age 12-13 in Scotland: retrospective population study. *BMJ.* 2019;365:l1161.

182. Lei J, Ploner A, Elfstrom KM, et al. HPV vaccination and the risk of invasive cervical cancer. *N Engl J Med.* 2020;383:1340-1348.

183. World Health Organization (WHO). 'Best buys' and other recommended interventions for the prevention and control of noncommunicable diseases: updated Appendix 3 of the Global Action Plan for the Prevention and Control of Noncommunicable Diseases 2013-2020. WHO; 2017. Accessed November 25, 2020. who.int/ncds/governance/appendix3-update/en/

184. World Health Organization (WHO). WHO guidelines for the use of thermal ablation for cervical pre-cancer lesions. WHO; 2019. Accessed November 23, 2020. who.int/reproductivehealth/publications/thermal-ablation-for-cervical-pre-cancer-lesions/en/

185. 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.

186. Arbyn M, Smith SB, Temin S, et al. Detecting cervical precancer and reaching underscreened women by using HPV testing on self samples: updated meta-analyses. *BMJ.* 2018;363:k4823.

187. Mezei AK, Armstrong HL, Pedersen HN, et al. Cost-effectiveness of cervical cancer screening methods in low- and middle-income countries: a systematic review. *Int J Cancer.* 2017;141:437-446.

188. Malone C, Barnabas RV, Buist DSM, Tiro JA, Winer RL. Cost-effectiveness studies of HPV self-sampling: a systematic review. *Prev Med.* 2020;132:105953.

189. Holme F, Kapambwe S, Nessa A, Basu P, Murillo R, Jeronimo J. Scaling up proven innovative cervical cancer screening strategies: challenges and opportunities in implementation at the population level in low- and lower-middle-income countries. *Int J Gynaecol Obstet.* 2017;138(suppl 1):63-68.

190. Knaul FM, Farmer PE, Krakauer EL, et al. Alleviating the access abyss in palliative care and pain relief-an imperative of universal health coverage: the Lancet Commission report. *Lancet.* 2018;391:1391-1454.

191. World Health Organization (WHO). WHO Director-General calls for all countries to take action to help end the suffering caused by cervical cancer. WHO; 2018. Accessed October 26, 2020. who.int/reproductivehealth/call-to-action-elimination-cervical-cancer/en/

192. Canfell K, Kim JJ, Brisson M, et al. Mortality impact of achieving WHO cervical cancer elimination targets: a comparative modelling analysis in 78 low-income and lower-middle-income countries. *Lancet.* 2020;395:591-603.

193. Brisson M, Kim JJ, Canfell K, et al. Impact of HPV vaccination and cervical screening on cervical cancer elimination: a comparative modelling analysis in 78 low-income and lower-middle-income countries. *Lancet.* 2020;395:575-590.

194. Canfell K, Shi JF, Lew JB, et al. Prevention of cervical cancer in rural China: evaluation of HPV vaccination and primary HPV screening strategies. *Vaccine.* 2011;29:2487-2494.

195. Campos NG, Sharma M, Clark A, et al. The health and economic impact of scaling cervical cancer prevention in 50 low- and lower-middle-income countries. *Int J Gynaecol Obstet.* 2017;138(suppl 1):47-56.

196. 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.

197. Fontham ETH, Wolf AMD, Church TR, et al. Cervical cancer screening for individuals at average risk: 2020 guideline update from the American Cancer Society. *CA Cancer J Clin.* 2020;70:321-346.

198. Kitahara CM, Schneider AB, Brenner AV. Thyroid cancer. In: Thun M, Linet MS, Cerhan JR, Haiman CA, Schottenfeld D, eds. Cancer Epidemiology and Prevention. 4th ed. Oxford University Press; 2018:839-860.

199. Lortet-Tieulent J, Franceschi S, Dal Maso L, Vaccarella S. Thyroid cancer "epidemic" also occurs in low- and middle-income countries. *Int J Cancer.* 2019;144:2082-2087.

200. Udelsman R, Zhang Y. The epidemic of thyroid cancer in the United States: the role of endocrinologists and ultrasounds. *Thyroid.* 2014;24:472-479.

201. Brito JP, Morris JC, Montori VM. Thyroid cancer: zealous imaging has increased detection and treatment of low risk tumours. *BMJ.* 2013;347:f4706.

202. Furuya-Kanamori L, Bell KJL, Clark J, Glasziou P, Doi SAR. Prevalence of differentiated thyroid cancer in autopsy

studies over six decades: a meta-analysis. *J Clin Oncol.* 2016;34:3672-3679.

203. Ahn HS, Welch HG. South Korea's thyroid cancer "epidemic"—turning the tide. *N Engl J Med.* 2015;373:2389-2390.
204. Li M, Dal Maso L, Vaccarella S. Global trends in thyroid cancer incidence and the impact of overdiagnosis. *Lancet Diabetes Endocrinol.* 2020;8:468-470.
205. Panato C, Vaccarella S, Dal Maso L, et al. Thyroid cancer incidence in India between 2006 and 2014 and impact of overdiagnosis. *J Clin Endocrinol Metab.* 2020;105:dgaa192.
206. Togawa K, Ahn HS, Auvinen A, et al. Long-term strategies for thyroid health monitoring after nuclear accidents: recommendations from an expert group convened by IARC. *Lancet Oncol.* 2018;19:1280-1283.
207. US Preventive Services Task Force, Bibbins-Domingo K, Grossman DC, et al. Screening for thyroid cancer: US Preventive Services Task Force recommendation statement. *JAMA.* 2017;317:1882-1887.
208. Haugen BR, Alexander EK, Bible KC, et al. 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. *Thyroid.* 2016;26:1-133.
209. Jung KW, Won YJ, Kong HJ, Lee ES. Cancer statistics in Korea: incidence, mortality, survival, and prevalence in 2016. *Cancer Res Treat.* 2019;51:417-430.
210. Shi LL, DeSantis C, Jemal A, Chen AY. Changes in thyroid cancer incidence, post-2009 American Thyroid Association guidelines. *Laryngoscope.* 2017;127:2437-2441.
211. Kitahara CM, Sosa JA, Shiels MS. Influence of nomenclature changes on trends in papillary thyroid cancer incidence in the United States, 2000 to 2017. *J Clin Endocrinol Metab.* 2020;105:e4823-e4830.
212. Kitahara CM, Sosa JA. Understanding the ever-changing incidence of thyroid cancer. *Nat Rev Endocrinol.* 2020;16:617-618.
213. Lim H, Devesa SS, Sosa JA, Check D, Kitahara CM. Trends in thyroid cancer incidence and mortality in the United States, 1974-2013. *JAMA.* 2017;317:1338-1348.
214. Kitahara CM, Pfeiffer RM, Sosa JA, Shiels MS. Impact of overweight and obesity on US papillary thyroid cancer incidence trends (1995-2015). *J Natl Cancer Inst.* 2020;112:810-817.
215. Silverman DT, Koutros S, Figueroa JD, Prokunina-Olsson L, Rothman N. Bladder cancer. In: Thun M, Linet MS, Cerhan JR, Haiman CA, Schottenfeld D, eds. Cancer Epidemiology and Prevention. 4th ed. Oxford University Press; 2018:977-996.
216. Antoni S, Ferlay J, Soerjomataram I, Znaor A, Jemal A, Bray F. Bladder cancer incidence and mortality: a global overview and recent trends. *Eur Urol.* 2017;71:96-108.
217. Teoh JYC, Huang J, Ko WYK, et al. Global trends of bladder cancer incidence and mortality, and their associations with tobacco use and gross domestic product per capita. *Eur Urol.* 2020;78:893-906.
218. 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.
219. Babjuk M, Burger M, Zigeuner R, et al. EAU guidelines on non-muscle-invasive urothelial carcinoma of the bladder: update 2013. *Eur Urol.* 2013;64:639-653.
220. Parkin DM. The global burden of urinary bladder cancer. *Scand J Urol Nephrol Suppl.* 2008;218:12-20.
221. Public Health Scotland. Scottish Cancer Registry. Accessed December 9, 2020. isdscotland.org/Health-Topics/Cancer/Scottish-Cancer-Registry.asp
222. Nielsen ME, Smith AB, Meyer AM, et al. Trends in stage-specific incidence rates for urothelial carcinoma of the bladder in the United States: 1988 to 2006. *Cancer.* 2014;120:86-95.
223. Whiteman DC, Green AC, Olsen CM. The growing burden of invasive melanoma: projections of incidence rates and numbers of new cases in six susceptible populations through 2031. *J Invest Dermatol.* 2016;136:1161-1171.
224. Cancer Council Australia.Slip, Slop, Slap, Seek, Slide. Accessed December 3, 2020. cancer.org.au/cancer-information/causes-and-prevention/sun-safety/campaigns-and-events/slip-slop-slap-seek-slide
225. Iannacone MR, Green AC. Towards skin cancer prevention and early detection: evolution of skin cancer awareness campaigns in Australia. *Melanoma Manag.* 2014;1:75-84.
226. Erdmann F, Lortet-Tieulent J, Schuz J, et al. International trends in the incidence of malignant melanoma 1953-2008—are recent generations at higher or lower risk? *Int J Cancer.* 2013;132:385-400.
227. Berk-Krauss J, Stein JA, Weber J, Polsky D, Geller AC. new systematic therapies and trends in cutaneous melanoma deaths among US whites, 1986-2016. *Am J Public Health.* 2020;110:731-733.
228. Mason R, Au L, Ingles Garces A, Larkin J. Current and emerging systemic therapies for cutaneous metastatic melanoma. *Expert Opin Pharmacother.* 2019;20:1135-1152.
229. 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.
230. Miranda-Filho A, Pineros M, Znaor A, Marcos-Gragera R, Steliarova-Foucher E, Bray F. Global patterns and trends in the incidence of non-Hodgkin lymphoma. *Cancer Causes Control.* 2019;30:489-499.
231. Shiels MS, Engels EA, Linet MS, et al. The epidemic of non-Hodgkin lymphoma in the United States: disentangling the effect of HIV, 1992-2009. *Cancer Epidemiol Biomarkers Prev.* 2013;22:1069-1078.
232. Lortet-Tieulent J, Ferlay J, Bray F, Jemal A. International patterns and trends in endometrial cancer incidence, 1978-2013. *J Natl Cancer Inst.* 2018;110:354-361.
233. Gupta S, Gupta R, Sinha DN, Mehrotra R. Relationship between type of smokeless tobacco and risk of cancer: a systematic review. *Indian J Med Res.* 2018;148:56-76.
234. Bagnardi V, Rota M, Botteri E, et al. Alcohol consumption and site-specific cancer risk: a comprehensive dose-response meta-analysis. *Br J Cancer.* 2015;112:580-593.
235. Han AY, Kuan EC, Mallen-St Clair J, Alonso JE, Arshi A, St John MA. Epidemiology of squamous cell carcinoma of the lip in the United States: a population-based cohort analysis. *JAMA Otolaryngol Head Neck Surg.* 2016;142:1216-1223.
236. Rigel DS. Cutaneous ultraviolet exposure and its relationship to the development of skin cancer. *J Am Acad Dermatol.* 2008;58(5 suppl 2):S129-S132.
237. Maule M, Merletti F. Cancer transition and priorities for cancer control. *Lancet Oncol.* 2012;13:745-746.
238. Lortet-Tieulent J, Georges D, Bray F, Vaccarella S. Profiling global cancer incidence and mortality by socioeconomic development. *Int J Cancer.* 2020;147:3029-3036.
239. Bray F, Jemal A, Torre LA, Forman D, Vineis P. Long-term realism and

cost-effectiveness: primary prevention in combatting cancer and associated inequalities worldwide. *J Natl Cancer Inst.* 2015;107:djv273.

240. Vineis P, Wild CP. Global cancer patterns: causes and prevention. *Lancet.* 2014;383:549-557.

241. Thun MJ, Wild CP, Colditz G. Framework for understanding cancer prevention. In: Thun M, Linet MS, Cerhan JR, Haiman CA, Schottenfeld D, eds. Cancer Epidemiology and Prevention. 4th ed. Oxford University Press; 2018: 1193-1204.

242. Gelband H, Sankaranarayanan R, Gauvreau CL, et al. Costs, affordability, and feasibility of an essential package of cancer control interventions in low-income and middle-income countries: key messages from Disease Control Priorities, 3rd edition. *Lancet.* 2016;387:2133-2144.