Abstract

The global burden of cancer continues to increase largely because of the aging and growth of the world population alongside an increasing adoption of cancer-causing behaviors, particularly smoking, in economically developing countries. Based on the GLOBOCAN 2008 estimates, about 12.7 million cancer cases and 7.6 million cancer deaths are estimated to have occurred in 2008; of these, 56% of the cases and 64% of the deaths occurred in the economically developing world. Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death among females, accounting for 23% of the total cancer cases and 14% of the cancer deaths. Lung cancer is the leading cancer site in males, comprising 17% of the total new cancer cases and 23% of the total cancer deaths. Breast cancer is now also the leading cause of cancer death among females in economically developing countries, a shift from the previous decade during which the most common cause of cancer death was cervical cancer. Further, the mortality burden for lung cancer among females in developing countries is as high as the burden for cervical cancer, with each accounting for 11% of the total female cancer deaths. Although overall cancer incidence rates in the developing world are half those seen in the developed world in both sexes, the overall cancer mortality rates are generally similar. Cancer survival tends to be poorer in developing countries, most likely because of a combination of a late stage at diagnosis and limited access to timely and standard treatment. A substantial proportion of the worldwide burden of cancer could be prevented through the application of existing cancer control knowledge and by implementing programs for tobacco control, vaccination (for liver and cervical cancers), and early detection and treatment, as well as public health campaigns promoting physical activity and a healthier dietary intake. Clinicians, public health professionals, and policy makers can play an active role in accelerating the application of such interventions globally. CA Cancer J Clin 2011;61:69–90. © 2011 American Cancer Society, Inc.

Introduction

Cancer is the leading cause of death in economically developed countries and the second leading cause of death in developing countries.1 The burden of cancer is increasing in economically developing countries as a result of population aging and growth as well as, increasingly, an adoption of cancer-associated lifestyle choices including smoking, physical inactivity, and “westernized” diets. In this article, we provide an overview of the global cancer burden, including the estimated number of new cancer cases and deaths in 2008 and the incidence and mortality rates by region for selected cancer sites. These statistics are based on GLOBOCAN 2008,2 the standard set of worldwide estimates of cancer incidence and mortality produced by the International Agency for Research on Cancer (IARC) for 2008. We comment on the recent incidence and mortality patterns observed for a number of common cancer forms, alongside established preventive measures that can reduce the worldwide cancer burden.

Data Sources and Methods

Incidence data (the number of newly diagnosed cases each year) are derived from population-based cancer registries, which may cover entire national populations but more often cover smaller, subnational areas, and, particularly in developing countries, only urban environments, such as major cities. Although the quality of

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information from most of the developing countries might be considered, in relative terms, of limited quality, it often remains the only source of information available on the profile of cancer and as such provides valuable information. The total number of cancer deaths by country are collected annually and are made available by the World Health Organization (WHO). The advantages of this source of data are its national coverage and long-term availability, although not all datasets are of the same quality or completeness. Provisional estimates of the age- and sex-specific deaths from cancer (of all types) for 2008 have been used in regions of the world with either no death information or where official statistics are deemed unreliable, and corrected for possible incompleteness.

Incidence and mortality rates (number of cases or deaths per 100,000 persons per year) were estimated in GLOBOCAN by country, using the most recently available data collected at the IARC or available in routine reports from the registries themselves. National incidence rates were estimated using one of several methods, dependant on the availability and quality of data, in the following order of priority:
1. National incidence data. When historical data and a sufficient number of recorded cases were available, incidence rates were projected to 2008.
2. National mortality data and local registry data. Estimation of incidence based on regression models, specific for sex, site, and age, derived from subnational or regional cancer registry data.
3. Regional incidence data from one or more cancer registries but no mortality data. National incidence derived from a single set or a weighted average of local rates.
4. Frequency data. Only data on the relative frequency of different cancers (by sex, site, and age groups) available. These proportions are applied to estimates of the all-cancer incidence rate for the country, derived from cancer registry data within the same region.
5. No data available. Country-specific rates equated to those of neighboring countries in the same region.

Similar procedures were used to estimate country-specific mortality rates, in the following order of priority:
2. Sample mortality data. The age- and sex-specific all-cancer mortality envelopes provided nationally for 2008 by the WHO were partitioned by site using the sample mortality data.
3. No mortality data. National mortality was derived from incidence and country-specific survival probabilities (based on level of gross domestic product), and then scaled to the WHO all-cancer mortality envelope for 2008.

Country-specific incidence and mortality rates were prepared for 27 types of cancer (including Kaposi sarcoma [KS] for sub-Saharan African countries), by sex and for 10 age groups (0-14, 15-39, 40-44, 45-49,...70-74, and 75+ years). A full description of the data and methods used for each country and the corresponding results are available in GLOBOCAN 2008 (available at http://www.globocan.iarc.fr). Estimates for the 20 world regions (Fig. 1) and for more and less developed regions, as defined by the United Nations (UN), were obtained as the population-weighted average of the incidence and mortality rates of the component countries. These rates were age-standardized (ASRs) (per 100,000 person-years) using the World Standard Population as proposed by Segi and modified by Doll et al. The cumulative risk of developing or dying from cancer before the age of 75 years (in the absence of competing causes of death) was also calculated and is expressed as a percentage.

Results and Discussion

Estimated Number of New Cancer Cases and Deaths

About 12.7 million cancer cases and 7.6 million cancer deaths are estimated to have occurred in 2008 worldwide (Fig. 2), with 56% of the cases and 64% of the deaths in the economically developing world. Breast cancer in females and lung cancer in males are the most frequently diagnosed cancers and the leading cause of cancer death for each sex in both economically developed and developing countries, except lung cancer is preceded by prostate cancer as the most frequent cancer among males in economically developed countries. These cancers were followed, without specific rank order, by stomach and liver cancers in males and cervix and lung cancers in females in economically developing countries and by colorectal and lung cancers in females and colorectal and lung or prostate cancers in males in the economically developed world.
Incidence and Mortality Rates for All Cancers Combined and Top 22 Cancer Sites

While incidence rates for all cancers combined in economically developed countries are nearly twice as high as in economically developing countries in both males and females (Table 1), mortality rates for all cancers combined in developed countries are only 21% higher in males and only 2% higher in females. Such disparities in incidence and mortality patterns between developed and developing countries will reflect, for a given cancer, regional differences in the prevalence and distribution of the major risk factors, detection practices, and/or the availability and use of treatment services. Prostate, colorectal, female breast, and lung cancer rates are 2 to 5 times higher in developed countries compared with developing countries, a result of variations in a disparate set of risk factors and diagnostic practices. The converse is true for cancers related to infections such as stomach, liver, and cervical cancers (Table 1). Table 2 shows the overall cancer incidence and mortality rates by sex according to world areas. The incidence rate for both sexes combined is more than 3 times as high in Australia/New Zealand as that in Middle Africa.

It should also be noted that cancer tends to be diagnosed at later stages in many developing countries compared with developed countries and this, combined with reduced access to appropriate therapeutic facilities and drugs (Fig. 3), has an adverse effect on survival. A recent comparative survey of cancer survival rates in Africa, Asia, and Central America based on patients diagnosed in the 1990s indicates substantially lower survival rates in parts of Africa, India, and the Philippines than for those diagnosed in Singapore, South Korea, and parts of China. For example, breast cancer 5-year survival rates were 50% or less in the former populations and over 75% in the latter. Such comparisons were similar to those observed in the CONCORD study for an earlier time period.

Selected Cancers

Female Breast Cancer

Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death in females worldwide, accounting for 23% (1.38 million) of the total new cancer cases and 14% (458,400) of the total cancer deaths in 2008 (Fig. 2). About half the breast cancer cases and 60% of the deaths are estimated to occur in economically developing countries. In general, incidence rates are high in Western and
### TABLE 1. Incidence and Mortality Rates and Cumulative Probability of Developing Cancer by Age 75 by Sex and Cancer Site for More Developed and Less Developed Areas, 2008

<table>
<thead>
<tr>
<th></th>
<th><strong>MORE DEVELOPED AREAS</strong></th>
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<th><strong>LESS DEVELOPED AREAS</strong></th>
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<tbody>
<tr>
<td></td>
<td><strong>INCIDENCE</strong></td>
<td><strong>MORTALITY</strong></td>
<td><strong>INCIDENCE</strong></td>
</tr>
<tr>
<td></td>
<td>ASR</td>
<td>CUMULATIVE RISK (%) [AGE 0-74]</td>
<td>ASR</td>
</tr>
<tr>
<td><strong>Males</strong></td>
<td></td>
<td></td>
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<tr>
<td>All cancers* (C00-97, but C44)</td>
<td>300.1</td>
<td>30.1</td>
<td>143.9</td>
</tr>
<tr>
<td>Bladder (C67)</td>
<td>16.6</td>
<td>1.9</td>
<td>4.6</td>
</tr>
<tr>
<td>Brain, nervous system (C70-72)</td>
<td>6.0</td>
<td>0.6</td>
<td>3.9</td>
</tr>
<tr>
<td>Colorectum (C18-21)</td>
<td>37.6</td>
<td>4.4</td>
<td>15.1</td>
</tr>
<tr>
<td>Esophagus (C15)</td>
<td>6.5</td>
<td>0.8</td>
<td>5.3</td>
</tr>
<tr>
<td>Gallbladder (C23-24)</td>
<td>2.4</td>
<td>0.3</td>
<td>1.6</td>
</tr>
<tr>
<td>Hodgkin lymphoma (C81)</td>
<td>2.2</td>
<td>0.2</td>
<td>0.4</td>
</tr>
<tr>
<td>Kidney (C64-66)</td>
<td>11.8</td>
<td>1.4</td>
<td>4.1</td>
</tr>
<tr>
<td>Larynx (C32)</td>
<td>5.5</td>
<td>0.7</td>
<td>3.8</td>
</tr>
<tr>
<td>Leukemia (C91-95)</td>
<td>9.1</td>
<td>0.9</td>
<td>4.8</td>
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<tr>
<td>Liver (C22)</td>
<td>8.1</td>
<td>1.0</td>
<td>7.2</td>
</tr>
<tr>
<td>Lung (C33-34)</td>
<td>47.4</td>
<td>5.7</td>
<td>32.4</td>
</tr>
<tr>
<td>Melanoma of skin (C43)</td>
<td>9.5</td>
<td>1.0</td>
<td>3.8</td>
</tr>
<tr>
<td>Multiple myeloma (C88 + C90)</td>
<td>3.3</td>
<td>0.4</td>
<td>1.9</td>
</tr>
<tr>
<td>Nasopharynx (C11)</td>
<td>0.6</td>
<td>0.1</td>
<td>0.3</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma (C82-85, C96)</td>
<td>10.3</td>
<td>1.1</td>
<td>3.6</td>
</tr>
<tr>
<td>Oral cavity (C00-08)</td>
<td>6.9</td>
<td>0.8</td>
<td>2.3</td>
</tr>
<tr>
<td>Other pharynx (C09-10, C12-14)</td>
<td>4.4</td>
<td>0.5</td>
<td>2.2</td>
</tr>
<tr>
<td>Pancreas (C25)</td>
<td>8.2</td>
<td>1.0</td>
<td>7.9</td>
</tr>
<tr>
<td>Prostate (C61)</td>
<td>62.0</td>
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<td>10.6</td>
</tr>
<tr>
<td>Stomach (C16)</td>
<td>16.7</td>
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<td>10.4</td>
</tr>
<tr>
<td>Testis (C62)</td>
<td>4.6</td>
<td>0.4</td>
<td>0.3</td>
</tr>
<tr>
<td>Thyroid (C73)</td>
<td>2.9</td>
<td>0.3</td>
<td>0.3</td>
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<tr>
<td><strong>Females</strong></td>
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<tr>
<td>All cancers* (C00-97, but C44)</td>
<td>225.5</td>
<td>22.0</td>
<td>87.3</td>
</tr>
<tr>
<td>Bladder (C67)</td>
<td>3.6</td>
<td>0.4</td>
<td>1.0</td>
</tr>
<tr>
<td>Brain, nervous system (C70-72)</td>
<td>4.4</td>
<td>0.4</td>
<td>2.6</td>
</tr>
<tr>
<td>Breast (C50)</td>
<td>66.4</td>
<td>7.1</td>
<td>15.3</td>
</tr>
<tr>
<td>Cervix uteri (C53)</td>
<td>9.0</td>
<td>0.9</td>
<td>3.2</td>
</tr>
<tr>
<td>Colorectum (C18-21)</td>
<td>24.2</td>
<td>2.7</td>
<td>9.7</td>
</tr>
<tr>
<td>Corpus uteri (C54)</td>
<td>12.9</td>
<td>1.6</td>
<td>2.4</td>
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<tr>
<td>Esophagus (C15)</td>
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<td>0.1</td>
<td>1.0</td>
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<td>Liver (C22)</td>
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<td>0.3</td>
<td>2.5</td>
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Northern Europe, Australia/New Zealand, and North America; intermediate in South America, the Caribbean, and Northern Africa; and low in sub-Saharan Africa and Asia (Fig. 4). The factors that contribute to the international variation in incidence rates largely stem from differences in reproductive and hormonal factors and the availability of early detection services. Reproductive factors that increase risk include a long menstrual history, nulliparity, recent use of postmenopausal hormone therapy or oral contraceptives, and late age at first birth. Alcohol consumption also increases the risk of breast cancer. The breast cancer incidence increases observed in many Western countries in the late 1980s and 1990s likely result from changes in reproductive factors (including the increased use of postmenopausal hormone therapy) as well as an increased screening intensity. Reproductive factors that increase risk include a long menstrual history, nulliparity, recent use of postmenopausal hormone therapy or oral contraceptives, and late age at first birth. Alcohol consumption also increases the risk of breast cancer.

The breast cancer incidence increases observed in many Western countries in the late 1980s and 1990s likely result from changes in reproductive factors (including the increased use of postmenopausal hormone therapy) as well as an increased screening intensity. Incidence rates in some of these counties, including the United States, United Kingdom, France, and Australia, sharply decreased from the beginning of the millennium, partly due to lower use of combined postmenopausal hormone therapy. In contrast, breast cancer death rates have been decreasing in North America and several European countries over the past 25 years, largely as a result of early detection through mammography and improved treatment.

**Colorectal Cancer**

Colorectal cancer is the third most commonly diagnosed cancer in males and the second in females, with over 1.2 million new cancer cases and 608,700 deaths estimated to have occurred in 2008 (Fig. 2). The highest incidence rates are found in Australia and New Zealand, Europe, and North America, whereas the lowest rates are found in Africa and

<table>
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<th>TABLE 1. (Continued)</th>
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<td>MORE DEVELOPED AREAS</td>
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<tr>
<td>INCIDENCE</td>
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<tr>
<td>ASR</td>
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</tr>
<tr>
<td>Ovary (C56)</td>
</tr>
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<td>Pancreas (C25)</td>
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<tr>
<td>Stomach (C16)</td>
</tr>
<tr>
<td>Thyroid (C73)</td>
</tr>
</tbody>
</table>

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

*Excludes nonmelanoma skin cancer.

Source: GLOBOCAN 2008.
South-Central Asia (Fig. 5). Rates are substantially higher in males than in females.

Colorectal cancer incidence rates are rapidly increasing in several areas historically at low risk, including Spain, and a number of countries within Eastern Asia and Eastern Europe. Notably, rates among males in the Czech Republic and Japan have already exceeded the peak of incidence observed in the United States, Canada, and Australia, where rates are declining or stabilizing. Such unfavorable trends are thought to reflect a combination of factors including changes in dietary patterns, obesity, and an increased prevalence of smoking. The United States is the only country with significantly decreasing incidence rates in both males and females in the most recent time period, which largely reflects detection and removal of precancerous lesions through colorectal cancer screening. While colorectal cancer death rates have been decreasing in several Western countries, largely resulting from improved treatment and increased awareness and early detection, rates continue to increase in many countries with more limited resources and health infrastructure, particularly in Central and South America and Eastern Europe.

Modifiable risk factors for colorectal cancer include smoking, physical inactivity, overweight and obesity, red and processed meat consumption, and excessive alcohol consumption. Population-based colorectal screening programs are feasible only in economically developed countries, although future attention should also be focused in those areas of the world with an aging population and increasingly westernized lifestyle (eg, Brazil). According to a recent randomized trial in the United Kingdom, a one-time flexible sigmoidoscopy screening between 55 and 64 years of age reduced colorectal cancer incidence by 33% and mortality by 43%.

**Lung Cancer**

Lung cancer was the most commonly diagnosed cancer as well as the leading cause of cancer death in males in 2008 globally (Fig. 2). Among females, it was the fourth most commonly diagnosed cancer and the second leading cause of cancer death. Lung cancer accounts for 13% (1.6 million) of the total cases and 18% (1.4 million) of the deaths in 2008. In males, the highest lung cancer incidence rates are in Eastern and Southern Europe, North America, Micronesia and Polynesia, and Eastern Asia, while rates are low in sub-Saharan Africa (Fig. 6). In

### TABLE 2. Estimated Age-Standardized Incidence and Mortality Rates Per 100,000 by World Area, 2008*

<table>
<thead>
<tr>
<th>INCIDENCE</th>
<th>MORTALITY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MALE</td>
</tr>
<tr>
<td>Eastern Africa</td>
<td>121.2</td>
</tr>
<tr>
<td>Middle Africa</td>
<td>88.1</td>
</tr>
<tr>
<td>Northern Africa</td>
<td>109.2</td>
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<tr>
<td>Southern Africa</td>
<td>235.9</td>
</tr>
<tr>
<td>Western Africa</td>
<td>92.0</td>
</tr>
<tr>
<td>Eastern Asia</td>
<td>222.1</td>
</tr>
<tr>
<td>South-Central Asia</td>
<td>99.7</td>
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<tr>
<td>South-Eastern Asia</td>
<td>143.9</td>
</tr>
<tr>
<td>Western Asia</td>
<td>152.8</td>
</tr>
<tr>
<td>Caribbean</td>
<td>196.3</td>
</tr>
<tr>
<td>Central America</td>
<td>136.2</td>
</tr>
<tr>
<td>Northern America</td>
<td>334.0</td>
</tr>
<tr>
<td>South America</td>
<td>186.7</td>
</tr>
<tr>
<td>Central and Eastern Europe</td>
<td>259.2</td>
</tr>
<tr>
<td>Northern Europe</td>
<td>292.3</td>
</tr>
<tr>
<td>Southern Europe</td>
<td>289.9</td>
</tr>
<tr>
<td>Western Europe</td>
<td>337.4</td>
</tr>
<tr>
<td>Australia/New Zealand</td>
<td>356.8</td>
</tr>
<tr>
<td>Melanesia</td>
<td>146.0</td>
</tr>
<tr>
<td>Micronesia</td>
<td>153.8</td>
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<tr>
<td>Polynesia</td>
<td>225.0</td>
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</table>

*Excludes nonmelanoma skin cancer.
Source: GLOBOCAN 2008.
females, the highest lung cancer incidence rates are found in North America, Northern Europe, and Australia/New Zealand. Despite their lower prevalence of smoking (less than 4% adult smokers), Chinese females have higher lung cancer rates (21.3 cases per 100,000 females) than those in certain European countries such as Germany (16.4) and Italy (11.4), with an adult smoking prevalence of about 20%. The relatively high burden of lung cancer in women is thought to reflect indoor air pollution from unventilated coal-fueled stoves and from cooking fumes in China. Other known risk factors for lung cancer include exposure to several occupational and environmental carcinogens such as asbestos, arsenic, radon, and polycyclic aromatic hydrocarbons.

The observed variations in lung cancer rates and trends across countries or between males and females within each country largely reflect differences in the stage and degree of the tobacco epidemic. Smoking accounts for 80% of the worldwide lung cancer burden in males and at least 50% of the burden in females. Male lung cancer death rates are decreasing in most Western countries, including many European countries, North America, and Australia, where the tobacco epidemic peaked by the middle of the last century. In contrast, lung cancer rates are increasing in countries such as China and several other countries in Asia and Africa, where the epidemic has been established more recently and smoking prevalence continues to either increase or show signs of stability.

Generally, lung cancer trends among females lag behind males because females started smoking in large numbers several decades later than males. Therefore, lung cancer rates in females are increasing in many countries except the United States, Canada, the United Kingdom, and Australia, where they are plateauing. Notably, in Spain, France, Belgium, and the Netherlands rates are increasing in more recent female birth cohorts, suggesting that the lung cancer burden in females in these countries will likely continue to increase for several decades barring any major interventions.

Most of the worldwide burden of lung cancer could be avoided by applying proven tobacco control interventions that include raising the price of cigarettes and other tobacco products, banning smoking in public places, the restriction of advertising of tobacco products, counter advertising, and treating tobacco dependence. To illustrate, a 10% increase in cigarette prices has been shown to reduce cigarette consumption by 3% to 5%. In 2003, the WHO established the Framework Convention on Tobacco Control to enable international coordinated efforts to curb the tobacco
The United States is among the few countries that have yet to ratify the treaty.

Prostate Cancer

Prostate cancer is the second most frequently diagnosed cancer and the sixth leading cause of cancer death in males, accounting for 14% (903,500) of the total new cancer cases and 6% (258,400) of the total cancer deaths in males in 2008 (Fig. 2). Incidence rates vary by more than 25-fold worldwide, with the highest rates recorded primarily in the developed countries of Oceania, Europe, and North America (Fig. 7), largely because of the wide utilization of prostate-specific antigen (PSA) testing that detects clinically important tumors as well as other slow-growing cancers that might otherwise escape diagnosis. In contrast, males of African descent in the Caribbean region have the highest prostate cancer mortality rates in the world, which is thought to reflect partly difference in genetic susceptibility.61,62

Temporal trends in incidence rates in countries with higher uptake of PSA testing such as the United States, Australia, Canada, and the Nordic countries followed similar patterns.63,64 Rates rose rapidly in the early 1990s, soon after the introduction of PSA testing, followed by a sharp decline due to a smaller pool of prevalent cases. In other high-income countries with a low and gradual increase in the prevalence of PSA testing, such as Japan and the United Kingdom, rates continue to increase slightly.63

Death rates for prostate cancer have been decreasing in many developed countries, including...
Australia, Canada, the United Kingdom, the United States, Italy, and Norway in part because of the improved treatment with curative intent.63,65,66 The role of PSA testing in the reduction of the prostate cancer mortality rates at the population level has been difficult to quantify. A large US-based randomized trial on the efficacy of PSA testing in reducing mortality from prostate cancer found no benefit,67 while another similar European-based trial found a modest benefit.68 Differences in study design, sample size (statistical power), follow up, and possible contamination of controls may have contributed to the different findings between these 2 studies. In contrast to the trends in Western countries, incidence and mortality rates are rising in several Asian and Central and Eastern European countries, such as Japan.63,65 Older age, race (black), and family history remain the only well-established risk factors and there are no established preventable risk factors for prostate cancer.69

**Stomach Cancer**

A total of 989,600 new stomach cancer cases and 738,000 deaths are estimated to have occurred in 2008, accounting for 8% of the total cases and 10% of total deaths (Fig. 2). Over 70% of new cases and deaths occur in developing countries. Generally, stomach cancer rates are about twice as high in males as in females (Table 1). The highest incidence rates are in Eastern Asia, Eastern Europe, and South America and the lowest rates are in North America and most parts of Africa (Fig. 8). Regional variations in part reflect differences in dietary patterns, particularly in European countries, and the prevalence of *Helicobacter pylori* infection.70

Stomach cancer rates have decreased substantially in most parts of the world,71 in part due to factors related to the increased use and availability of refrigeration including the increased availability of fresh fruits and vegetables, and a decreased reliance on salted and preserved foods. Other major determinants for the favorable trends are reductions in chronic *H. pylori* infection in most parts of the world72-74 and smoking in some parts of the developed world.71 In Japan, mortality rates may have declined via the introduction of screening using photofluorography,75 which may have also contributed to the persistently high incidence rates in the country.

**Liver Cancer**

Liver cancer in men is the fifth most frequently diagnosed cancer worldwide but the second most frequent cause of cancer death. In women, it is the seventh most commonly diagnosed cancer and the sixth leading cause of cancer death. An estimated 748,300 new liver cancer cases and 695,900 cancer...
deaths occurred worldwide in 2008 (Fig. 2). Half of these cases and deaths were estimated to occur in China. Globally, rates are more than twice as high in males as in females. The highest liver cancer rates are found in East and South-East Asia and in Middle and Western Africa, whereas rates are low in South-Central and Western Asia, as well as Northern and Eastern Europe (Fig. 9). Among primary liver cancers, hepatocellular carcinoma (HCC) represents the major histological subtype, accounting for 70% to 85% of the total liver cancer burden worldwide. Cholangiocarcinomas that arise primarily from the epithelial lining of the bile duct (intra- and extrahepatic bile duct) are relatively rare, but high incidence rates are found in Thailand and other parts of Eastern Asia largely due to the elevated prevalence of liver fluke infection.

The high liver cancer (HCC) rates in parts of Asia and sub-Saharan Africa largely reflect the elevated prevalence of chronic hepatitis B virus (HBV) infection, with over 8% of the populations in these regions chronically infected with the virus. HBV infection accounts for about 60% of the total liver cancer in developing countries and for about 23% of cancer in developed countries; the corresponding percentages for hepatitis C virus (HCV) infection are 33% in developing countries and 20% in developed countries. Interaction of aflatoxin B1 (AFB) exposure with chronic HBV infection has been noted to increase liver cancer. However, the contribution of AFB exposure to the liver cancer burden in parts of Africa and Asia, where the exposure is prevalent, is unknown. In the United States and several other low-risk Western countries, alcohol-related cirrhosis and possibly nonalcoholic fatty liver disease, associated with obesity, are thought to account for the majority of liver cancer.

Liver cancer incidence rates are increasing in many parts of the world including the United States and Central Europe, possibly due to the obesity epidemic and the rise in HCV infection through continued transmission by injection drug users. In contrast to the trend in the low-risk areas, rates decreased in some historically high-risk areas, possibly due to the HBV vaccine. Universal infant hepatitis vaccination programs in Taiwan reduced liver cancer incidence rates by about two-thirds in children and young adults.

As of 2008, a total of 177 countries (91%) had introduced the HBV vaccine into their national infant immunization schedules (Fig. 10), although in 2006 only 27% of infants worldwide received the first dose within 24 hours of birth, as recommended by the WHO. Preventive strategies against HCV, for which no vaccine is available, include screening of donor’s blood for antibodies to HCV, instituting adequate infection control practices during medical procedures including the use of oral delivery of medicines where possible, and needle exchange programs among injection drug users. Crop substitution and improved grain storage practices have been shown to reduce contamination with AFB in sub-Saharan Africa.

Cervical Cancer

Cervical cancer is the third most commonly diagnosed cancer and the fourth leading cause of cancer death in females worldwide, accounting for 9% (529,800) of the total new cancer cases and 8% (275,100) of the total cancer deaths among females in 2008 (Fig. 2). More than 85% of these cases and deaths occur in developing countries. India, the second most populous country in the world, accounts for 27% (77,100) of the total cervical cancer deaths. Worldwide, the highest incidence rates are in Eastern, Western, and Southern Africa, as well as...
South-Central Asia and South America. Rates are lowest in Western Asia, Australia/New Zealand, and North America (Fig. 11).

The disproportionately high burden of cervical cancer in developing countries and elsewhere in medically underserved populations is largely due to a lack of screening that allows detection of precancerous and early stage cervical cancer; the health care infrastructure in these countries does not support Papanicolaou testing or other types of screening tests. The most efficient and cost-effective screening techniques in low-resource countries include visual inspection using either acetic acid or Lugol’s iodine and DNA testing for human papillomavirus (HPV) DNA in cervical cell samples. A recent clinical trial in rural India, a low-resource area, found that a single round of HPV DNA testing was associated with about a 50% reduction in the risk of developing advanced cervical cancer and associated deaths.

The expectations that vaccines which primarily protect against the most common strains of HPV infections (HPV types 16 and 18), which cause about 70% of cervical cancers, may prevent cervical cancer worldwide are at present high. However, affordable pricing is the most critical factor to facilitate the introduction of HPV vaccines in low- and medium-resource countries in the short term. It is also extremely important that women continue to receive screening services because the current vaccines are being given to adolescent girls only, and


even vaccinated girls should begin screening when they reach the recommended screening age since the vaccines do not provide protection for the 30% of chronic infections by HPV types other than HPV 16, 18, 6 and 11 that cause cervical cancer. 

Esophageal Cancer

An estimated 482,300 new esophageal cancer cases and 406,800 deaths occurred in 2008 worldwide. Incidence rates vary internationally by nearly 16-fold, with the highest rates found in Southern and Eastern Africa and Eastern Asia and lowest rates observed in Western and Middle Africa and Central America in both males and females (Fig. 12). Esophageal cancer is 3 to 4 times more common among males than females.

Esophageal cancer usually occurs as either squamous cell carcinoma in the middle or upper one-third of the esophagus, or as adenocarcinoma in the lower one-third or junction of the esophagus and stomach. In the highest risk area, stretching from northern Iran through the central Asian republics to North-Central China, often referred to as the “esophageal cancer belt,” 90% of cases are squamous cell carcinomas. Major risk factors for squamous cell carcinomas in these areas are not well understood, but are thought to include poor nutritional status, low intake of fruits and vegetables, and drinking beverages at high temperatures.

In low-risk areas such as the United States and several Western countries, smoking and excessive alcohol consumption account for about 90% of the total cases of squamous cell carcinoma of the esophagus. Smoking, overweight and obesity, and chronic gastroesophageal reflux disease, which triggers Barrett’s esophagus, are thought to be the major risk factors for adenocarcinoma of the esophagus in the United States and some Western countries. A number of studies also found smokeless tobacco products and betel liquid (with or without tobacco) as risk factors for esophageal cancer in certain parts of Asia.

Temporal trends in esophageal cancer rates for the 2 major histological types vary within countries and across countries. Incidence rates for adenocarcinoma of the esophagus have been increasing in several Western countries, in part due to increases in the prevalence of known risk factors such as overweight and obesity. In contrast, rates for squamous cell carcinoma of the esophagus have been steadily declining in these same countries because of long-term reductions in tobacco use and alcohol consumption. However, squamous cell carcinoma of the esophagus has been increasing in certain Asian countries such as Taiwan, probably as a result of increases in tobacco use and alcohol consumption.

Bladder Cancer

An estimated 386,300 new cases and 150,200 deaths from bladder cancer occurred in 2008 worldwide. The majority of bladder cancer occurs in males and there is a 14-fold variation in incidence internationally. The highest incidence rates are found in the countries of Europe, North America, and Northern Africa (Fig. 13). Egyptian males have the highest mortality rates (16.3 per 100,000), which is twice as high as the highest rates in Europe (8.3 in Spain and 8.0 in Poland) and over 4 times higher than that in the United States (3.7). The lowest rates are found in the countries of Melanesia and Middle Africa (Fig. 13).

Smoking and occupational exposures are the major risk factors in Western countries, whereas chronic infection with *Schistosoma hematobium* in developing countries, particularly in Africa and the Middle East, accounts for about 50% of the total burden. A majority of bladder cancers associated with schistosomiasis are squamous cell carcinoma,
while those associated with smoking are transitional cell carcinoma.\textsuperscript{113}

It is easier to interpret trends in bladder cancer mortality rates than trends in incidence rates because trends in mortality are affected less by differences in reporting of low-grade tumors. In the United States, mortality rates have stabilized in males and decreased in females from 1997 through 2006,\textsuperscript{18} and in Europe declines have been observed in most countries since the 1990s,\textsuperscript{114} due in part to reductions in smoking prevalence and reductions in occupational exposures known to cause bladder cancer. Bladder cancer continues to be the most common cancer among males in Egypt,\textsuperscript{2} despite the large decreases in \textit{schistosoma}-associated bladder cancer.\textsuperscript{115,116} This is likely the result of a reduction in \textit{schistosoma}-related bladder cancers being offset by an increase in tobacco-related bladder cancers.\textsuperscript{115}

\textbf{Non-Hodgkin Lymphoma}

An estimated 355,900 new cases and 191,400 deaths from non–Hodgkin lymphoma (NHL) occurred in 2008. NHL encompasses a wide variety of disease subtypes for which incidence patterns vary. NHL is more common in developed areas, with the highest incidence rates found in North America; Australia/New Zealand; and Northern, Western, and Southern Europe. The lowest rates are found in South-Central and Eastern Asia and the Caribbean (Fig. 14). In general, the incidence of NHL is low in Africa with the exception of some areas with a high incidence of Burkitt’s lymphoma (a subtype of NHL caused by Epstein-Barr virus [EBV]) among children. In addition to EBV and other infections such as the human immunodeficiency virus (HIV), NHL is associated with occupational exposures to herbicides and chlorinated organic compounds.\textsuperscript{117}

The incidence rate of NHL increased in most developed countries during the 1990s and has leveled off in recent years.\textsuperscript{18,118,119} The increases prior to 1990 may be due in part to improvements in diagnostic procedures and changes in classification,\textsuperscript{120} as well as the onset of the acquired immune deficiency syndrome (AIDS) epidemic, particularly among white males. Subsequent declines in AIDS–related NHL subtypes after the 1990s are partly due to the declining incidence of HIV infection and the success of antiretroviral therapies that delay the onset of AIDS.\textsuperscript{121} However, non–AIDS–associated NHL subtypes continued to increase or stabilize during the same time period.\textsuperscript{121} NHL incidence rates are also increasing in developing countries such as Thailand and Uganda,\textsuperscript{122,123} due in part to the AIDS epidemic.
Increases in NHL, particularly among older age groups, have also been observed in Egypt, where the AIDS epidemic is less prominent. The exact causes for this increase are not entirely clear but could be related to altered immune function associated with older age as well as HCV infection, which is prevalent among older Egyptians and has recently been classified by the IARC as having a causal link to NHL.124,125

Cancers of the Lip and Oral Cavity

An estimated 263,900 new cases and 128,000 deaths from oral cavity cancer (including lip cancer) occurred in 2008 worldwide. Generally, the highest oral cavity cancer rates are found in Melanesia, South-Central Asia, and Central and Eastern Europe and the lowest in Africa, Central America, and Eastern Asia for both males and females (Fig. 15). Smoking, alcohol use, smokeless tobacco products, and HPV infections are the major risk factors for oral cavity cancer, with smoking and alcohol having synergistic effects.126,127 The contribution of each of these risk factors to the burden varies across regions.126,128-131 Worldwide, smoking accounts for 42% of deaths from cancers of the oral cavity (including the pharynx) and heavy alcohol consumption for 16% of the deaths; the corresponding percentages in high-income countries are about 70% and 30%, respectively.132 Smokeless tobacco products and betel quid with or without tobacco are the major risk factors for oral cavity cancer in Taiwan, India, and other neighboring countries.128,133,134 The rise in the incidence rate of oral cancer in Taiwan may have been in part due to the increased consumption of betel quid and alcohol.135

Oral cavity cancer mortality rates among males decreased significantly in most countries, including those of Europe and Asia, over the past decades.136,137 But rates continued to increase in several Eastern European countries, including Hungary and Slovakia.136 The increase in females in most European countries largely reflects the ongoing tobacco epidemic.136 This contrasts with the decreasing trends at all ages in both males and females in the United States and United Kingdom,56,136,138 where the tobacco epidemic began and declined earlier. However, incidence rates for oral cancer sites related to HPV infections, such as the oropharynx, tonsil, and base of the tongue, are increasing in young adults in the United States and in some countries in Europe,139-143 which is hypothesized to be in part due to changes in oral sexual behavior.130,144

Nasopharyngeal Cancer

The term nasopharyngeal carcinoma (NPC) is used here as a surrogate for nasopharyngeal cancers (International Classification of Diseases, 10th revision [ICD-10] code C11), given that carcinomas represent the vast majority of nasopharyngeal tumors. There were an estimated 84,400 incident cases of NPC and 51,600 deaths in 2008, representing about 0.7% of the global cancer burden, and the disease may be considered one of the rarer cancer forms globally, ranking as the 24th most frequently diagnosed cancer form worldwide and 22nd within the developing world. The global statistics by world region reveal the distinct features of its descriptive epidemiology, however, and the contrasting geographical and ethnic variations in the distribution of incidence worldwide.

NPC is more frequent in males than females in both the developing and developed world, with incidence rates commonly 2 to 3 times higher in males in higher resource countries, with male-to-female rate ratios often considerably higher in developing regions (Table 1) (Fig. 16). The geographical disparities in the burden of NPC in relation to
resource are noteworthy, with an estimated 92% of new cases occurring within economically developing countries. According to world area, incidence rates are highest in South-Eastern Asia, in both sexes (Fig. 16), with the disease being the sixth most common among males in the region. Indeed in global terms, the 3 highest national incidence rates are estimated in Malaysia, Indonesia, and Singapore, where rates are high among the Chinese and Malay populations.24 Elsewhere in Asia, high incidence rates are observed in a number of provinces in South-Eastern China, including Guangdong and Hong Kong, and in other parts of Southern Asia (the Philippines and Thailand).145-147 Rates are also elevated in Polynesia, Southern Africa, and Northern Africa (Fig. 16), particularly within the latter region in Tunisia and Algeria. Other populations where NPC is relatively frequent include the Inuit populations of Alaska, Greenland, and North Canada, as well as Chinese and Filipinos living in the United States.145-147 Rates of this malignancy tend to be considerably lower in most populations living elsewhere within the Americas, Europe, Africa, and Central and Eastern Asia (Fig. 16).

NPC has viral, environmental, and genetic components to its etiology.148,149 Migrants from high- to low-risk countries retain incidence rates intermediate to natives of their host country and their country of origin,150 implicating a role for environmental and/or genetic factors, and a possible interaction with EBV. While the virus is considered an important step in NPC progression, only a fraction of the EBV-infected population develops the disease. Moreover, infection with the virus is considered both lifelong and ubiquitous in most areas of the world.151

Many studies have reported increased risks associated with certain foods eaten within high-risk areas including salted fish and certain preserved foods and hot spices, all of which are high in nitroso compounds and volatile nitrosamines.149 Exposure to such foods during the time window that includes weaning and childhood may be important, as may be the timing of infection with EBV in early life.152 While trends in NPC have been reported as reasonably stable in high-risk areas of Southern China,153 declines have been observed in several populations of Chinese origin over the last 2 decades.154-156 NPC in higher resource settings is more associated with lifestyle-related risk factors; the decreasing smoking prevalence among US males, for example, has been postulated as a contributor to the overall decline in NPC incidence.157

**Kaposi Sarcoma**

KS is a cancer of cells that line lymph and blood vessels and is unusual in that, unlike most other cancers, it is multifocal in origin, growing in several areas of the body at once. Before the AIDS epidemic, KS was regarded as extremely rare in nearly all areas of the world, with exceptionally elevated rates observed in certain populations of Mediterranean, middle Eastern, or eastern European descent, predominantly in males aged older than 50 years,158 and, more notably, in sub-Saharan Africa populations.159,160 The African form of KS (sometimes termed “endemic”) has been diagnosed at younger ages than has been the case in European populations and affects proportionally more females, although the male-to-female ratio may still be as high as 9 to 1.159,161 KS is also diagnosed in immunosuppressed patient populations, including transplant recipients and, especially, people infected with HIV. The diagnosis of KS is regarded as AIDS-defining in those who are HIV positive and, for many years, KS was the most common cancer observed in AIDS patients and indeed this, in part, initially defined the AIDS epidemic.162 However, since the advent of highly active antiretroviral
therapies (HAART) for HIV in the 1990s, this is no longer the case. In populations where HAART is readily available to those infected with HIV, KS has again become a rare diagnosis. Due to the limited availability of HAART, this is not the case in much of sub-Saharan Africa, where KS can now be one of the most common forms of cancer and the age range at diagnosis can include young children.

The rare occurrence of KS in many areas of the world and the rapid increase in incidence following the emergence of AIDS, followed by the rapid decrease associated with HAART, means that it is not possible to provide meaningful estimates of the global burden of KS apart from in sub-Saharan Africa. An estimated 22,000 cases in males and 12,000 cases in females were diagnosed in 2008 (Table 3). The corresponding estimated age-standardized incidence rates were 8.1 and 3.6 per 100,000, respectively. The majority of these cases occurred in the countries of Eastern Africa (which includes Ethiopia, Rwanda, Uganda, Zambia, and Zimbabwe). In the countries of Eastern Africa overall, there were an estimated 16,000 cases in males and 9,000 cases in females and corresponding estimated age-standardized incidence rates were 14.9 and 6.8 per 100,000, respectively. KS was, therefore, the most common cancer in males and the third most common in females (after breast and cervical cancers) in Eastern Africa. In Zimbabwe, rates reached as high as 40.9 and 21.9 per 100,000, respectively, based on an estimated 1500 and 1100 cases in males and females, respectively. The countries of Southern Africa (including Botswana, Namibia, and South Africa) had the highest rates of KS (11.5 and 5.1 per 100,000, respectively) after Eastern Africa, followed by Middle Africa (4.1 and 0.6 per 100,000, respectively) and Western Africa (1.9 and 1.2 per 100,000, respectively).

Outside of sub-Saharan Africa, populations in which KS had been reported to the ninth volume of Cancer Incidence in Five Continents with male age-standardized incidence rates of 1.0 per 100,000 per year or greater in the period between 1998 and 2002 were US Blacks (highest rate: 6.2 in the District of Columbia); Israel Jews (2.9); Colombia, Cali (2.5); US Whites (highest rate: 2.3 in the District of Columbia); Italy (highest rate: 2.2 in Brescia); Portugal (highest rate: 2.1 in South region); US Hispanic Whites (highest rate: 2.0 in Los Angeles); Brazil (highest rate: 1.8 in Sao Paolo); Switzerland (highest rate: 1.4 in Geneva); and Spain (highest rate: 1.3 in Canary Islands). Female rates of KS exceeded 1.0 per 100,000 in only one population (Italy, Sassari, with a rate of 1.2). The KS in these populations represents a mix of the pre-AIDS era and HIV-associated forms. It is noteworthy that no Asian populations reported incidence rates greater than 1.0 per 100,000.

It is now evident that the KS-associated herpes virus (human herpes virus type 8 [HHV–8]) is the major causative factor for KS but generally requires immunosuppressive conditions in which to function pathogenically. HHV-8 infection is common in sub-Saharan Africa, in those European populations at higher risk of KS, and in all HIV transmission high-risk groups. A combination of HIV and HHV-8 positivity confers an over 1000-fold risk of KS. Those areas of Africa where endemic KS and HHV-8 infection were relatively common have seen a rapid increase in the incidence of KS since the onset of the HIV epidemic. In recent decades, the incidence of KS has increased about 20-fold in Uganda, Zimbabwe, and other sub-Saharan African countries.

**Limitations**

The global and region-specific estimates presented here are built up from those for 182 countries or

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<th>TABLE 3. Estimated Number of Cases and Age-Standardized Incidence Rates for Kaposi Sarcoma in Regions of Sub-Saharan Africa, 2008</th>
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<tr>
<td><strong>MALES</strong></td>
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<td><strong>NUMBER OF CASES</strong></td>
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<tr>
<td>Eastern Africa*</td>
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<td>Southern Africa†</td>
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<td>Middle Africa‡</td>
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<td>Western Africa§</td>
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<td>Sub-Saharan Africa</td>
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*Burundi, Comoros, Djibouti, Eritrea, Ethiopia, France (La Réunion), Kenya, Madagascar, Malawi, Mauritius, Mozambique, Rwanda, Somalia, Tanzania, Uganda, Zambia, Zimbabwe.

†Botswana, Lesotho, Namibia, South African Republic, Swaziland.

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


Source: GLOBOCAN 2008.
Despite the provisos concerning data quality and the methods of estimation, the GLOBOCAN 2008 estimates represent the best available evidence and may be used in the setting of priorities for cancer control actions in different regions and countries of the world. The GLOBOCAN 2008 online tool\(^5\) can be used for making forward projections of estimated numbers of new cancer diagnoses and deaths by country and region to 2030 using the 2008 baseline and utilizing the UN estimates for future population changes. These projections make the assumption that the incidence and mortality rates estimated for 2008 will not change and while this allows for the development of scenario planning, a review such as that contained in this publication is most robust if built from the 2008 baseline.

**Conclusions**

The global burden of cancer continues to increase largely because of the aging and growth of the world population and an increasing adoption of cancer-causing behaviors, particularly smoking, within economically developing countries. Female breast, lung, and colorectal cancers are occurring in high frequencies in many economically developing countries, in addition to the disproportionately high burden of cancers related to infections. A significant proportion of the worldwide burden of cancer could be prevented through the application of existing cancer control knowledge, and by implementing programs for tobacco control, vaccination (for liver and cervical cancers), and early detection and treatment, as well as public health campaigns promoting physical activity and healthier dietary patterns. Much remains to be learned about the causes of several major cancers including prostate and colorectal cancers. Implementing and sustaining such actions requires concerted efforts among private and government public health agencies and the pharmaceutical industry, as well as individual and government donors. \(^\square\)

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