

# 1

## Cancer Epidemiology

*The art of war is of vital importance to the State. It is a matter of life and death, a road either to safety or to ruin. Hence it is a subject of inquiry which can on no account be neglected.*

– Sun Tzu

Cancer is not a new disease. Humans are not the only species to get cancer. In fact, cancer is found throughout the animal kingdom. Therefore, hominids were likely to have suffered from cancer before the advent of *Homo sapiens*.

The history of cancer is evidenced by traditional medicines used by many cultures around the world. These “folk remedies” actually serve as the basis of many medical treatments used today. Many of these natural products are discussed in subsequent chapters of this book.

Perhaps the earliest reference to cancer can be found in the writings of the ancient Egyptian physician Imhotep from around 2600 BCE (see Figure 1.1). In papyrus documents dating from this period, Imhotep describes treating breast tumors with cauterization. The procedure was evidently less than successful since he instructs the reader, “Tumor against the god Xenus ... do thou nothing there against.” Unfortunately, even today we are left with questions about whether side-effects of some treatments are worse for patients than the disease.

Regardless of its history, cancer is a huge problem today, and is likely to become an even larger problem tomorrow. About 14 million people were diagnosed with cancer in 2012, and 18 million in 2018. This trend is daunting, with the number of new cases expected to reach 24 million by 2035.

### 1.1 Cancer Incidence and Mortality

Over 14 million people around the world are diagnosed with cancer each year, and this number is expected to rise. By current estimates, more than one in three



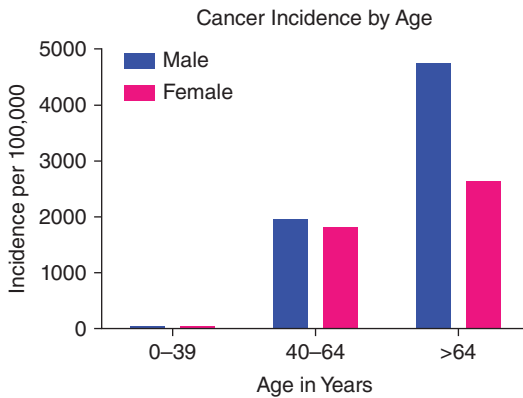
**Figure 1.1** Statue of the Egyptian physician Imhotep (ca. 2600 BCE).

Source: <https://upload.wikimedia.org/wikipedia/commons/d/d2/Imhotep.JPG>.

people will develop a form of cancer at some point in their lifetime. Around 10 million people died from cancer in 2018. Thus, cancer kills an average of over 15 people every minute. A comprehensive understanding of cancer incidence and outcomes is an important step toward decreasing these numbers.

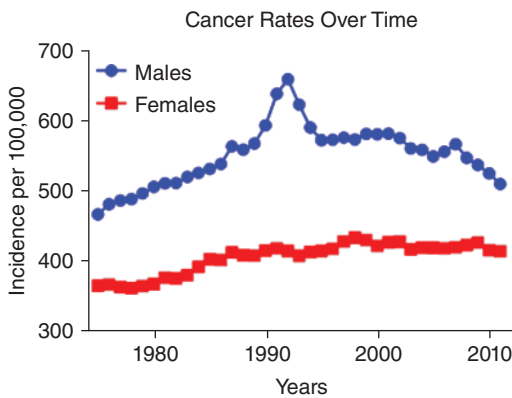
Cancer incidence, defined as the number of new cases arising in a period of time, is gender and age specific. In males, prostate cancer is the most prolific, where over 1 million new cases were diagnosed in 2018, accounting for around 8% of all new cancer cases and 15% of all new cancer cases in men. In females, breast cancer continues to be the most common tumor type. Over 2 million new cases were diagnosed in 2018, making it the second most common cancer. Breast cancer represents about 12% of all new cancer cases, and 25% of all cancers in women.

Cancer incidence may be further defined by the lifetime risk of developing the disease. For instance, in females, the risk of developing breast cancer is 1 in 8. In males, the risk of developing prostate cancer is 1 in 6; however, 80% of men who are 80 years old are likely to have some stage of prostate cancer. Some other tumor types also show considerable gender-related differences in cancer risk. For example, males are over twice as likely to develop lung cancer as women worldwide. However, lifestyle can be a factor for some of these differences. For instance, the chance of women getting lung cancer increases in countries such



**Figure 1.2** Worldwide cancer incidence by age. Statistics are shown for 2012.

Source: Data from <http://gco.iarc.fr/today>.



**Figure 1.3** Cancer rates over time. Invasive cancers from SEER 9 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, and Atlanta) age adjusted to 2000 USA population.

Source: Data from <http://gco.iarc.fr/today>.

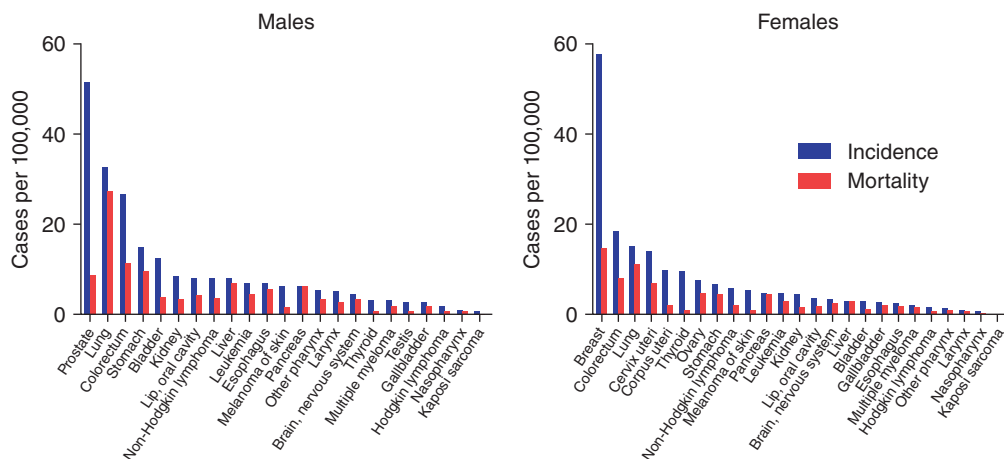
as the USA where women are more likely to smoke tobacco than in some other regions of the world.

In general, cancer risk increases with age, as shown in Figure 1.2. For example, less than 50 people per 100 000 under 39 years old were diagnosed with cancer in 2012. This number increased to over 1800 people between 40 and 64 years old, and over 3500 people older than 64 years. The rate of diagnosis in males 65 years or older rises most sharply with an incidence of over 4700 per 100 000.

Cancer is a major public health problem and is expected to become even worse. Cancer incidence rates have been steadily increasing over time. This is true for both males and females. However, regional spikes and dips can be seen in trends over time. For example, a spike in male cancers is seen in the 1990s in some areas of the United States, as shown in Figure 1.3. This spike has ebbed but incidence is still higher now than it was 40 years ago. In contrast, female cancer incidence has steadily climbed in these same areas over time.

Incidence rates of some types of cancer appear to be increasing more than others. Sites with annual cancer incidence increases of 1% or more include

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**Figure 1.4** Cancer incidence and mortality by tumor site. Numbers from IARC member countries (Germany, France, Italy, United Kingdom, USA, Australia, Austria, Belgium, Brazil, Canada, Denmark, Finland, India, Ireland, Japan, Norway, Netherlands, Qatar, Republic of Korea, Russia, Spain, Sweden, Switzerland, and Turkey) are shown for 2012.

Source: Data from <http://gco.iarc.fr/today>.

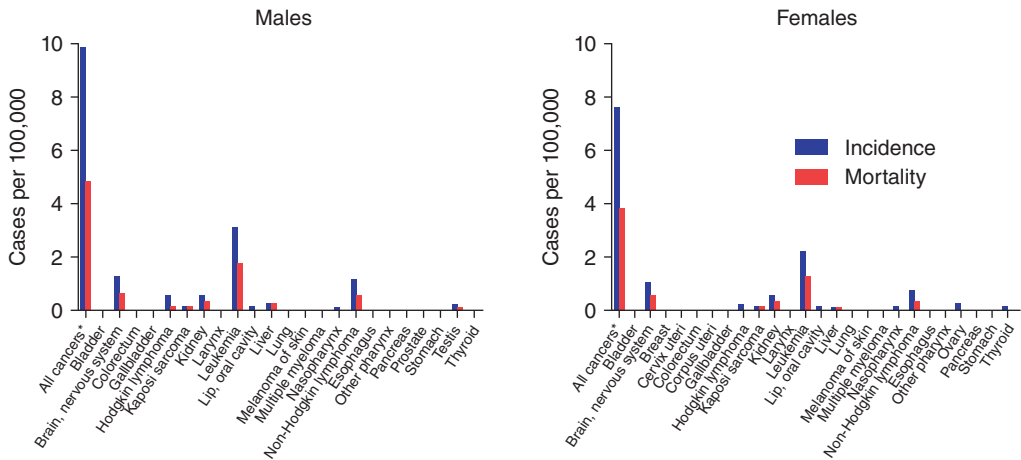
melanoma, renal, thyroid, pancreas, and liver. Meanwhile, although incidence rates are less than 1% per year, cancers such as non-Hodgkin lymphoma, certain childhood cancers, leukemia, myeloma, testicular, and oral cancers are still on the increase. Cancer is the second leading cause of death in the USA and UK (behind heart disease). In fact, cancer causes about 25% of all the deaths in these countries.

There are more than 200 different types of cancer but four particular tumor types constitute over half of all new cases diagnosed: breast, lung, colorectal, and prostate. In 2012, there were 14.1 million new cases of cancer diagnosed worldwide. As shown in Figure 1.4, these four cancers account for nearly 50% of these new cases (6.9 million), and are responsible for about half of all cancer deaths.

## 1.2 Childhood Cancer

Cancer in children is relatively rare. Less than one out of 1 million cancers are found in children under 15 years old. Nonetheless, children do get cancer. In 2012, over 160 000 children were diagnosed with cancer, and cancer killed about 80 000 children.

Leukemia is the most common form of pediatric cancer, followed by lymphomas and cancers of the central nervous system. These cancers were responsible for about 8 million deaths of children under 15 years old around the world



**Figure 1.5** Childhood cancer incidence and mortality by tumor site. Worldwide numbers for males and females up to 14 years old are shown for 2012. \* All cancers exclude nonmelanoma skin cancer.

Source: <http://gco.iarc.fr/today>, August 2014.

in 2012. As shown in Figure 1.5, 35% of these deaths were caused by leukemias, compared to 12% by lymphomas and 14% by brain tumors.

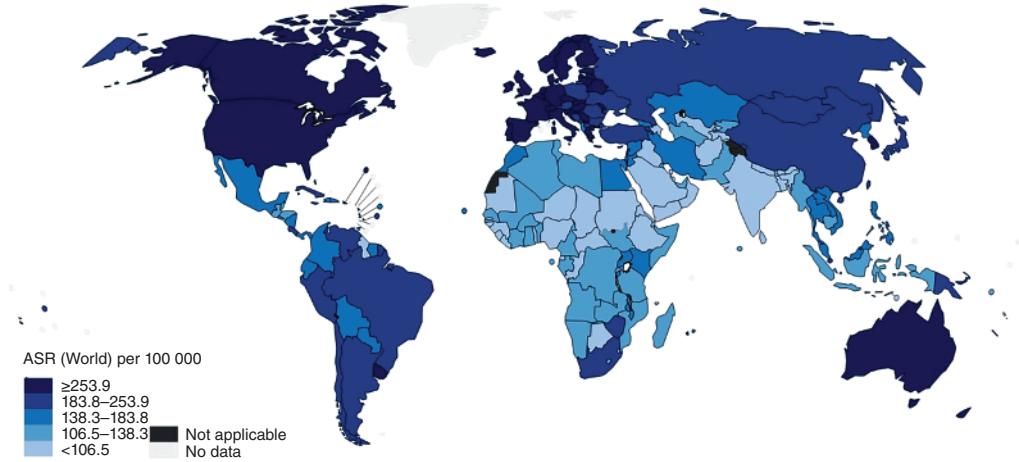
Although pediatric cancers are rare compared to adult cancers, they can be devastating. Whereas adult patients who remain cancer free for five years are often considered to be “cured” since their chance of mortality after this time is consistent with other causes, this is not the case with children. Pediatric cancer patients can undergo remission only to have cancer emerge again at a relatively young age. Thus, consequences from childhood cancers can be especially brutal.

### 1.3 Global Epidemiology

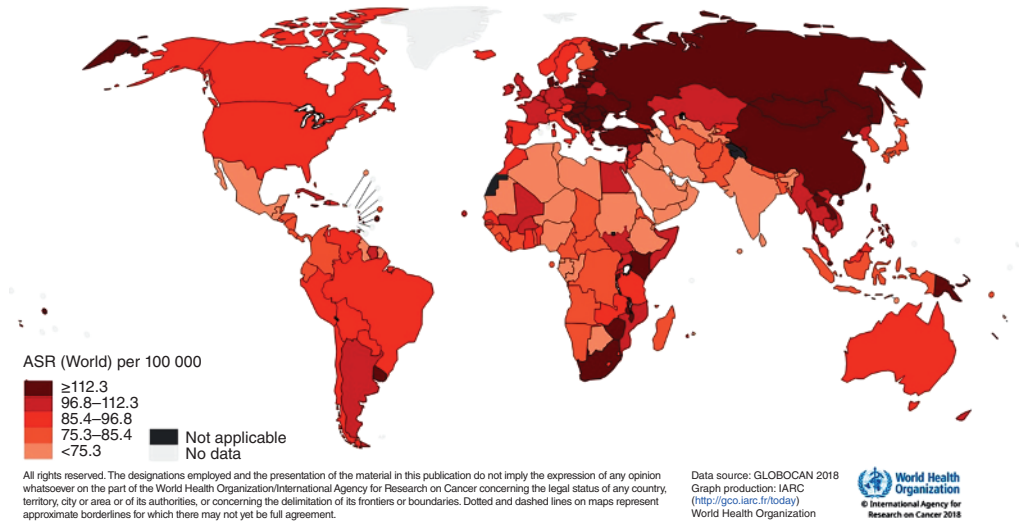
Cancer is a global problem, but it is a larger problem in some countries than in others (Figure 1.6). North America, western Europe, Australia, and New Zealand have the highest incidence, while India, along with some countries in the Middle East and Central Africa, have lower incidences. These differences can result from population demographics and lifestyle factors. Age is also a primary risk factor. For example, India has a median age of 27 years, while the median age in the USA is 38 years. This difference in age demographics may account for the higher cancer incidence in the USA compared to India, though other factors such as a chemopreventive diet and exercise may also affect cancer incidence. For example, although Japan has a relatively high median age of 48 years, its cancer incidence rate is lower than that of the USA. This relatively low cancer rate of an

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Estimated age-standardized incidence rates (World) in 2018, all cancers, both sexes, all ages



Estimated age-standardized mortality rates (World) in 2018, all cancers, both sexes, all ages



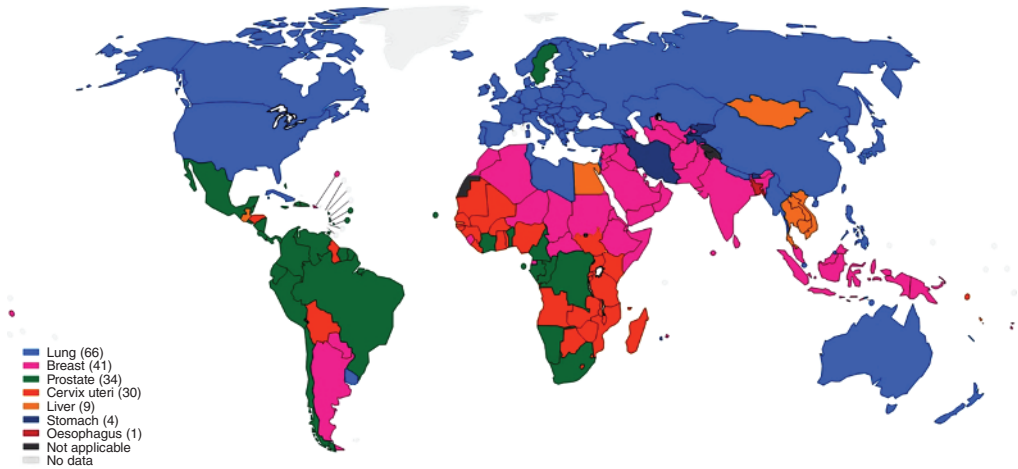
**Figure 1.6** Cancer incidence and mortality by country. Incidence (*top*) and mortality (*bottom*) per 100 000 people for all cancers are shown for 2018.

Source: <http://gco.iarc.fr/today>.

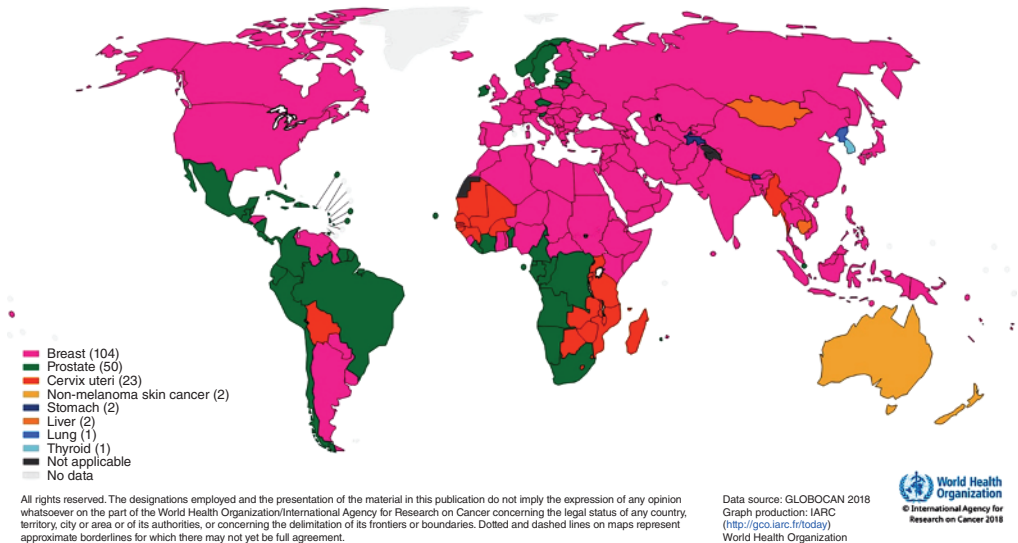
elderly population has been attributed to the chemopreventive properties of soy beans and other foods in the Japanese diet.

Overall, cancer mortality rates correlate with incidence, an effect shown in Figure 1.6. However, some intriguing observations arise from these comparisons. For example, the demarcation line between North and South Korea

Top cancer per country, estimated age-standardized mortality rates (World) in 2018, both sexes, all ages



Top cancer per country, estimated age-standardized incidence rates (World) in 2018, both sexes, all ages



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Data source: GLOBOCAN 2018  
Graph production: IARC  
(<http://gco.iarc.fr/today>)  
World Health Organization



**Figure 1.7** Most common cancers by country. Most common cancers for each country are shown as measured by incidence (*top*) and mortality (*bottom*) for 2018.

Source: <http://gco.iarc.fr/today>.

appears to delineate a difference in incidence and mortality between the two countries. While North Korea has a lower cancer incidence, it reports a higher mortality rate than South Korea. This apparent paradox may arise from incongruent options between healthcare systems in each country.

Figure 1.7 illustrates cancer incidence rates by site and country. Lung cancer has the highest incidence in most countries, followed by colorectal cancer in Russia, Australia, and regions of Africa and South America. Lung cancer also causes the most mortality around the world, followed by liver cancer in Mongolia, Thailand, and regions of Africa. However, some unique patterns arise from these data. For example, Papua New Guinea shows high levels of oral cancer that are not as prevalent in more western parts of the Indonesian islands, a difference attributed to the chewing of betel nut with tobacco by much of the population. Thus, lifestyle factors play a major role in the types of cancers seen, as well as cancer incidence and mortality rates.

## 1.4 Cancer Survival Rates

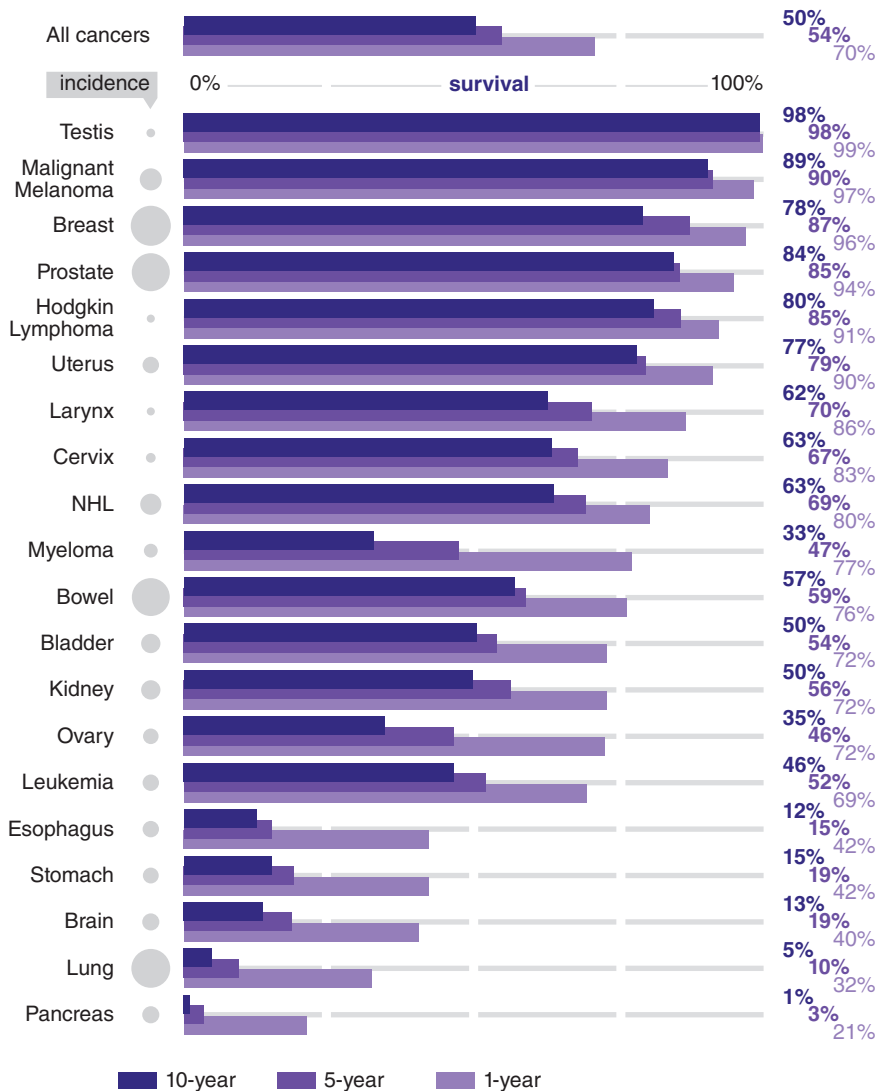
Cancer is a unique malady. While infectious diseases can be obliterated by medicines such as antibiotics, cancer treatments are not that simple and recurrence is far too common. Some consider a patient who is treated and still alive for some amount of time – generally five years – to be “cured.” However, current shifts in thought do not consider most patients to be cured of their cancer. Instead of being cured, these patients are called “survivors.” The question then becomes, “how long do they survive”?

As shown in Figure 1.8, the one-, five-, and 10-year survival rates for all cancers average out to around 70%, 54%, and 50%, respectively. However, survival depends greatly on the type of cancer involved. Figure 1.8 shows one-, five-, and ten-year survival rates for common cancers. Relatively high survival rates of 80% or more are seen in patients with some cancers including testicular, melanoma, breast, prostate, and Hodgkin lymphoma.

However, some caveats arise from these numbers. Individual cases for each cancer should be taken into account. For example, while the survival rate for malignant melanoma is 90%, this survival rate drops to 16% after melanoma has metastasized to other sites beyond lymph nodes. Later chapters discuss cancer metastasis and the challenges this key element of cancer biology presents.

In contrast to early testicular, skin, and prostate cancers, some other cancer types including cancers of the esophagus, stomach, brain, lung, and pancreas are notoriously lethal. For example, pancreatic cancer has a five-year survival rate of only 3%. These relatively low survival rates may result from the aggressive nature of these cancers combined with challenges in early detection technologies.

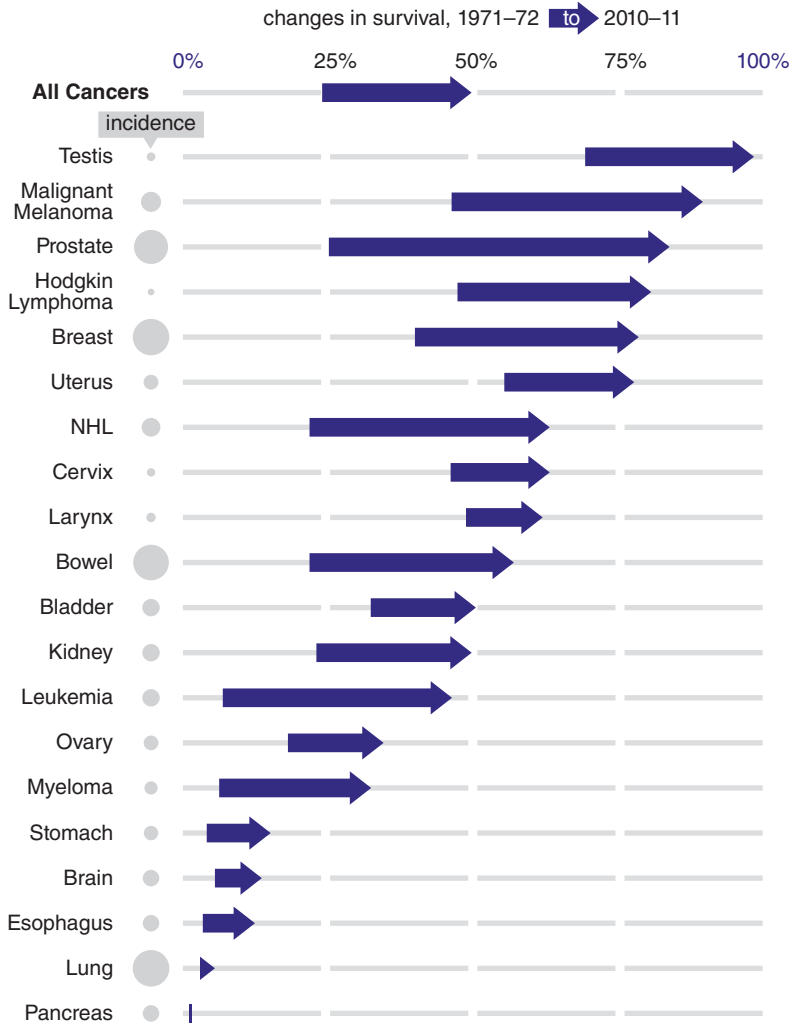
Progress in the early diagnosis and treatment of cancer has positively affected cancer survival rates, leading to a doubling of 10-year overall cancer survival rates from 25% to 50% in the past 40 years (Figure 1.9). For example, tests for the biomarker prostate specific antigen (PSA) have increased the diagnosis of



**Figure 1.8** Cancer survival rates. Age-standardized one-, five-, and 10-year net survival rates are shown for common cancers in adults (aged 15–99) in England and Wales in 2010–2011. Breast and laryngeal data are shown for female and male only, respectively. NHL, non-Hodgkin lymphoma.

Source: [www.cancerresearchuk.org/cancer-info/cancerstats/survival/common-cancers](http://www.cancerresearchuk.org/cancer-info/cancerstats/survival/common-cancers), August 2014. Reproduced with permission of Cancer Research UK.

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**Figure 1.9** Changes in cancer survival rates over time. Age-standardized 10-year net survival rates are shown for common cancers in adults (aged 15-99) in England and Wales from 1971-1972 to 2010-2011. Breast and laryngeal data are shown for female and male only, respectively. Ten-year survival for 2005-2006 and 2010-2011 was predicted by an excess hazard statistical model. Survival for bowel cancer is a weighted average derived from data for colon and rectum cancer. NHL, non-Hodgkin lymphoma.

Source: [www.cancerresearchuk.org/cancer-info/cancerstats/survival/common-cancers/#Trends](http://www.cancerresearchuk.org/cancer-info/cancerstats/survival/common-cancers/#Trends), August 2014. Reproduced with permission of Cancer Research UK.

early asymptomatic prostate tumors. This early detection combined with better treatments has dramatically increased prostate cancer survival rates. This is reflected by the increase in 10-year survival rates over the last 40 years from about 25% in 1971 to over 80% in 2011, as shown in Figure 1.9. Indeed, after prostate cancer mortality rates increased by around 50% during the 1980s, these advances have decreased mortality rates by about 30% since 1990 in Europe.

Breast cancer provides another example of progress in cancer treatments. Breast cancer screening procedures can detect tumors at very early stages. This early detection followed by improved treatments has increased 10-year survival rates from about 40% in 1971 to nearly 80% in 2011, as shown in Figure 1.9.

Survival rates for some pediatric cancers have risen dramatically over time. Childhood cancer mortality rates decreased by an average of 2.6% per year between 1962 and 2001, essentially cutting the death rate in half. Nearly 72% of the childhood cancer cases diagnosed in the time period 1992–1996 survived over five years, and this number has increased to over 80% for patients diagnosed in the time period 2004–2010. Acute lymphoblastic leukemia provides a good example of how pediatric survival rates can be improved. The five-year survival rate for this form of cancer, which accounts for three out of four cases of childhood leukemias, has gone from less than 10% in the 1960s to 80% of those diagnosed between 1992 and 1996, and over 90% of those diagnosed between 2000 and 2005. Such improvements are attributed to improved diagnostic techniques and the continual refinement and validation of combination chemotherapy regimens made possible by the steady enrollment of children into clinical trials.

In contrast to progress made in the detection and treatment of cancers such as breast and prostate, some other cancers have remained stubbornly lethal. For example, 10-year survival rates for lung and pancreatic cancer have remained under 5% for the past 40 years. Nonetheless, progress in cancer detection and treatments has extended overall cancer survival rates and saves thousands of lives every year.

In clinical terms, cancer survival outcomes can be expressed in a number of ways. Overall survival simply notes patient survival, while “disease-free” survival requires that cancer not be detected in a patient, and will exclude other causes of mortality. Meanwhile, “progression-free” survival requires that the cancer may be detectable but does not progress or get worse. Thus, a patient may have a shorter disease-free survival period than a progression-free survival period. In clinical studies, overall survival is considered less specific as it can be affected by a variety of factors that can lead to death, including complications resulting from age and treatment-related side-effects.

## 1.5 Summary and Conclusions

- Cancer is not a new disease; it has been described in medical texts for thousands of years.
- Cancer is increasing from about 14 million cases per year to 24 million cases per year expected by 2035.
- Most cancers are found in people over 40 years old, but children can also get cancer.
- Lung, prostate, breast, liver, stomach, and skin are common cancer sites.
- Regional differences are seen in cancer incidence and type that can be related to genetics, lifestyles, and the environment.
- Improved methods for detection and treatment have increased cancer survival rates, particularly for certain cancers including prostate, breast, and lymphoma.
- Cancer survival depends on cancer types, and can be increased by improving methods for detection and treatment.

## Further Reading

[http://www.wcrf.org/cancer\\_statistics](http://www.wcrf.org/cancer_statistics)

<http://seer.cancer.gov/statfacts>

<http://globocan.iarc.fr>

<http://seer.cancer.gov>

<http://www.cancerresearchuk.org/cancer-info/cancerstats>