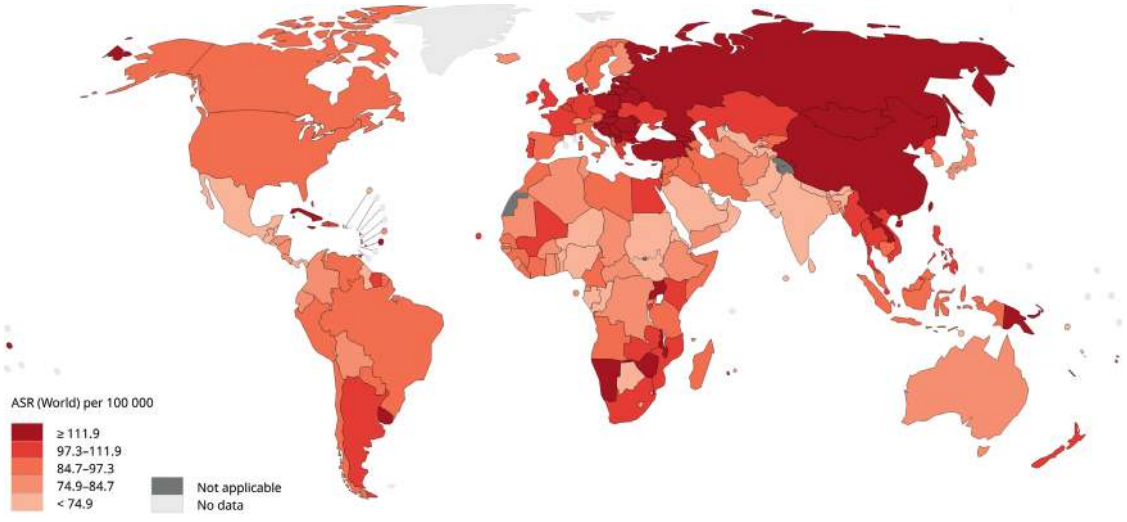
1 Lessons from Epidemiology



Global mortality rates for 2020. The darker the colour, the higher the rate. Data source: GLOBOCAN 2020. Graph production: IARC (http://gco.iarc.fr/today), World Health Organization.

Epidemiology is the study of the distribution and determinants (causes and risk factors) of health-related states and events. This chapter focuses on the distribution of cancers across the world; the next chapter deals with causes. We begin by looking at global patterns. These are of interest because they show marked variations in the forms of the disease that afflict different populations. These differences indicate the importance of environmental factors that include lifestyle – for example, what we eat and tobacco use – in determining both the type of cancer and the frequency of occurrence.

Although variation in cancer types occurs, there is a broad trend of rising incidence of all types across the world, for which a major driving force is increasing longevity. In the developed world, lung, breast, bowel and prostate cancers head the mortality table. Taking all cancers together, the last 40 years has seen a gradual increase in survival rates, although significant variations remain between nations and even within some countries. For the developing world, the outlook is more depressing: not only is the annual number of new cases rising, but inadequate screening programmes often mean that diagnosis is delayed until tumours have spread to secondary sites in the body and therefore become very difficult to treat. Analysis of cancer mortality in different age groups revealed many years ago that the additive effects of about half a dozen discrete events drive cancer development – the first direct evidence that the accumulation of mutations is the underlying cause.

1.1 Incidence of Cancer

Every year, over 18 million people worldwide are diagnosed with cancer (Fig. 1.1). Europe, with one-eighth of the world's population, has 25% of the global total of cancer cases. Together with North America, Europe contributes about 40% of new cancer cases from a combined population that is just 14% of the world figure of 7.8 billion. Hence, the rate of cancer diagnosis is higher in developed regions compared with less developed areas – by about two and a half times. The **age-standardised rates (ASRs)** are 296 cases of cancer diagnosed per 100,000 people in developed regions versus 115 per 100,000 for less developed regions, respectively.

The four major types of cancer that contribute to these figures are:

1. Breast cancer: 2.3 million new cases annually (12%)
2. Lung cancer: 2.2 million (11%)
3. Colorectal (bowel) cancer: 1.9 million (10%)
4. Prostate cancer: 1.4 million (7%)

These four cancers will be familiar to American and British readers because they are also in the top four of their national figures for both incidence and deaths due to cancers. For summaries of the major features of these and other cancers see Appendix D.

Incidence varies widely around the world, with Australia, New Zealand, Ireland, the USA and Denmark having the highest rates for both men and women combined (Table 1.1 right column). For all forms of cancer the lowest rates are about four times less than the USA figure (e.g. in Niger and The Gambia, Table 1.1, left column), although some specific cancers show much greater variation (e.g. there are about 300 new skin cancer cases in some parts of Australia for every one case in Kuwait).

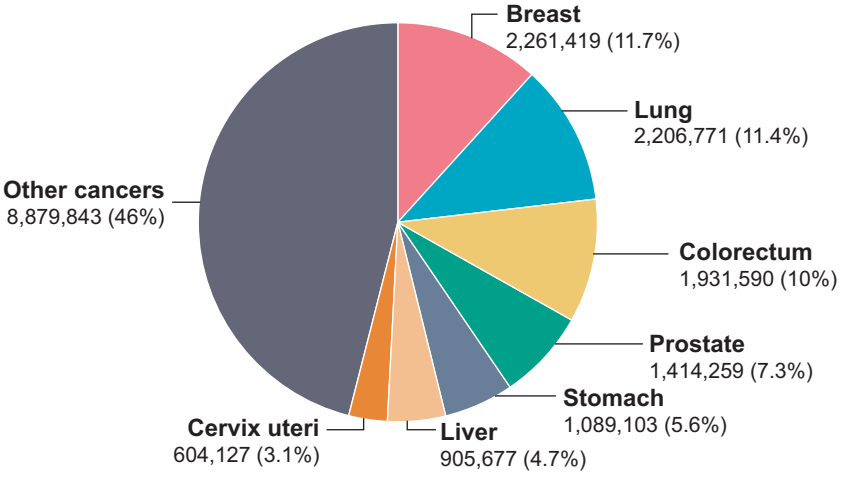


Figure 1.1 Incidence of major cancers worldwide for both sexes and all ages in 2020. Data show the number of new cases only. The percentage of the total number (19,292,789) is in parentheses. Data source: GLOBOCAN 2020. Graph production: Global Cancer Observatory (http:gco.iarc.fr/) © International Agency for Research on Cancer 2022.

Table 1.1 The best and the worst nations for cancer incidence: the lowest (left) and highest (right) rates per 100,000 people, for all ages and both sexes.

Niger	78 (62)	Australia	452 (83)
The Gambia	80 (62)	New Zealand	423 (82)
Nepal	81 (71)	Ireland	373 (82)
Bhutan	82 (72)	USA	362 (79)
Republic of Congo	84 (64)	Denmark	351 (81)

Figures in parentheses are life expectancies (years).
Data source: GLOBOCAN 2020.

Niger has the distinction of coming top of the incidence table (i.e. with the *lowest* rate in the world of 78 new cases per 100,000 people). Australia props up the table with the *highest* rate of 452, closely followed by New Zealand (423), with Ireland (373) in third place. The UK and USA are in the upper reaches (320 and 362, respectively). Notably, life expectancy is substantially longer in countries with the highest rates. In Australia, one in three men and one in four women are diagnosed with cancer by the age of 75, most commonly breast cancer followed by bowel cancer, prostate cancer and melanoma. Australia and New Zealand have the world's highest skin cancer rates and, although fourth in the overall rankings, melanoma is their most common cancer in men aged 25–49. Influential factors include the large percentage of the population with fair skin, making them prone to skin cancers, and the high levels of ambient ultraviolet radiation. National advertising campaigns, notably featuring the Australian cricketer Richie Benaud who enjoined television viewers to 'slip on a shirt, slop on sun cream, and slap on a hat', may have had some effect, as melanoma mortality has begun to decline since 2012.

In the UK in 2020, there were 458,000 new cancer cases, and for the USA the figure was 2,282,000. For women, breast cancer is the most common: 54,000 British women were diagnosed in 2020 and one in six Americans will get it, which means over 254,000 in 2020, about the same percentage in the two populations. For men, prostate cancer is the leading type with 56,800 UK cases and 210,000 American cases.

1.2 Mortality from Cancer

In 2020, cancers caused 9,958,133 deaths, with over 70% being in low- and middle-income countries. Unsurprisingly, the death toll that results from the avalanche of new cases also has lung cancer at the top of the list (Fig. 1.2). The top five causes of cancer deaths are:

1. Lung cancer: 1.8 million deaths annually (18%)
2. Colorectal (bowel) cancer: 0.9 million (9%)
3. Liver cancer: 0.8 million (8%)
4. Stomach cancer: 0.8 million (8%)
5. Breast cancer: 0.7 million (7%)

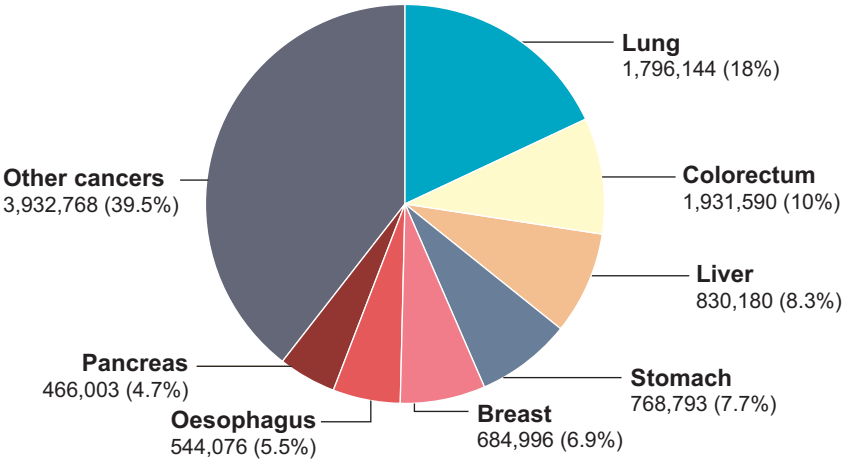


Figure 1.2 Cancer deaths worldwide for both sexes and all ages in 2020. The number of deaths is shown, with the percentage of the total number (9,958,133) in parentheses. Data source: GLOBOCAN 2020. Graph production: Global Cancer Observatory (http:gco.iarc.fr/) © International Agency for Research on Cancer 2022.

To put cancer in its place, we might note that humanity's biggest scourge is heart disease, which claims about 18 million deaths per year (about 31% of total mortality), including the total caused by ischaemic heart disease, cerebrovascular disease and hypertension. After heart disease, the next biggest killers all fall some way behind cancer, namely, human immunodeficiency virus (**HIV**)/acquired immunodeficiency syndrome (**AIDS**) (1 million), tuberculosis (1.4 million) and malaria (0.4 million). Much less well known is the figure of about 800,000 children who will die from diarrhoea this year – largely caused by ingesting germs through living in unsanitary conditions.

Pause and Recap

A brief survey of the global cancer picture reveals:

- In the table of incidence rates, the USA is fourth highest. Canada and the UK are a little lower (eighth and 12th, respectively).
- The current death rate is nearly 10 million a year. In the mortality table of 183 nations, the USA, Canada and the UK are 92nd, 80th and 70th, respectively. The improvement from their incidence rates reflects relatively better detection and treatment.
- The lowest and highest incidence rates differ by almost sixfold.
- The level of newly diagnosed cancers is disproportionally high in the developed world.
- The four most common cancers are lung, breast, bowel and prostate cancers.
- The major causes of death are lung, bowel, stomach, liver and breast cancers. The prominence of stomach and liver cancers reflects the global impact of infection on cancer mortality.

(cont.)

The Story Continues…

We now review cancer patterns across the major regions of the world and consider where we may be heading. We begin with the UK before turning to the USA and, in particular, to the socioeconomic factors that play a major role in these countries and that also reflect many aspects of the global cancer problem. We conclude by looking at global trends, reviewing the successes in dealing with cancer and summarising areas that require action if we are to reduce the cancer burden.

1.3 Global Patterns of Cancer Incidence and Mortality

By comparison with the incidence figures, the mortality ASRs reveal an almost complete change of nations at the top and bottom of the table, with Saudi Arabia (51 deaths per 100,000 people) in top spot and Mongolia (176) at the other end (Table 1.2). The UK (101) and the USA (86) are near the middle. Of the European nations, Hungary (149) is the worst performer (see Table 1.7 for European figures). The relative positions of countries in the tables of incidence and mortality are one measure of how well each country is doing in terms of cancer treatment. It is noticeable that the positions of both the UK and the USA are little changed, despite their resources. In contrast, Australia, with the worst incidence rate, has lifted itself to 68th (out of 185) in the mortality statistics.

In contrast to incidence rates, lifespan is not significantly different between the extremes of the mortality spectrum, other than for the Republic of Congo, indicating the importance for survival of factors relating to detection and treatment. Gradual shifts have occurred in the worldwide cancer pattern over the last century due to changes in lifestyle. The most dominant factor is indeed longevity, providing more time to develop the disease. This, together with other factors including increased exposure to risk factors, has led the World Health Organization (WHO) to predict that between 2008 and 2030 the number of new cancer cases will increase

Table 1.2 The best and the worst nations for cancer mortality: lowest (left) and highest (right) rates per 100,000 people for all ages and both sexes.

Saudi Arabia	51 (75)	Mongolia	176 (70)
Nepal	55 (71)	Serbia	152 (76)
United Arab Emirates	56 (78)	Hungary	149 (76)
Republic of Congo	57 (64)	Montenegro	145 (77)
Sri Lanka	57 (77)	Slovakia	141 (77)

Figures in parentheses are life expectancies (years).
Data source: GLOBOCAN 2020.

more than 80% in low-income countries – double the rate expected in high-income countries – and that the global cancer death toll will rise by 45%.

To examine cancer patterns in more detail, we'll begin with a comparison of the global picture with data for the USA and UK as representatives of the developed world (Fig. 1.3).

In general, shifts in global cancer statistics are gradual, but it is notable that some have impacted the top ten groups in Fig. 1.3 since it was originally drawn from the 2008 WHO data for the 1st edition of this book. In global incidence, thyroid cancers have displaced **non-Hodgkin's lymphoma** (to 11th). In the USA, thyroid cancers have also appeared together with cancers of the endometrium, supplanting ovarian and cervical cancers (now 16th and 21st). In the UK, leukaemias have displaced oesophageal cancers to 12th in the table. The mortality data show no global changes in the top ten since 2008, but for the USA, brain cancers appear at the expense of ovarian cancers (now 13th). For the UK, liver cancer and leukaemias have appeared in the top ten causes of cancer death, displacing stomach and ovarian cancers to 13th and 14th, respectively.

The reasons for the relative rise in incidence of some cancers are unclear. The thyroid cancer increase has been ascribed to overdiagnosis, but other factors, such as obesity, could be involved – being overweight has been estimated to account for up to 60% of all endometrial cancers. The appearance of brain cancer in the USA mortality table reflects the fact that, although the incidence of brain cancer is gradually declining, there is a rising, unexplained, trend of **glioblastoma multiforme**, the most aggressive type of brain cancer. Also unexplained are the rates of acute myeloblastic leukaemia (**AML**) and chronic lymphocytic leukaemia (**CLL**), which are significantly outpacing those of other cancers. One cancer stands out as appearing in both of the global lists but in neither of the USA or UK tables – stomach cancer. This provides an informative example of how human endeavour can affect cancers. Go back 90 years in the USA and stomach cancer was the biggest cancer killer, albeit that in 1930 the total death toll was only approximately 120,000. Nowadays, nearly two-thirds of stomach cancers occur in the developing world. We'll come back to this in a moment, but here too the incidence is declining, as it has done in the USA. The reasons are not clear but may include the increasing availability of fresh fruit and vegetables and of meat preserved by refrigeration rather than by salting, together with a decline in smoking and reduced viral infection. Nevertheless, although it has declined to 15th in the mortality table, 11,438 people died of stomach cancer in the USA in 2018.

One other significant point in Fig. 1.3 is that oesophageal cancer is the 6th most common cause of cancer death in the UK even though it is only 11th in incidence, reflecting the fact that it is usually detected only after it has **metastasised** and become very difficult to treat. The two major types of this cancer are oesophageal **squamous-cell carcinoma** (OSCC) and oesophageal **adenocarcinoma** (OAC). A large increase in OAC has appeared in England since the 1970s, but this appears to be levelling off. OSCC rates are declining. Improved screening (Chapter 10) is beginning to offer hope for this disease.

To a considerable extent, the mortality rankings reflect the very limited progress that has been made in treating some cancer types, such as lung, pancreas, liver and oesophageal cancers, the latter being the 11th highest in the USA. However, some cancers – prostate and breast – remain

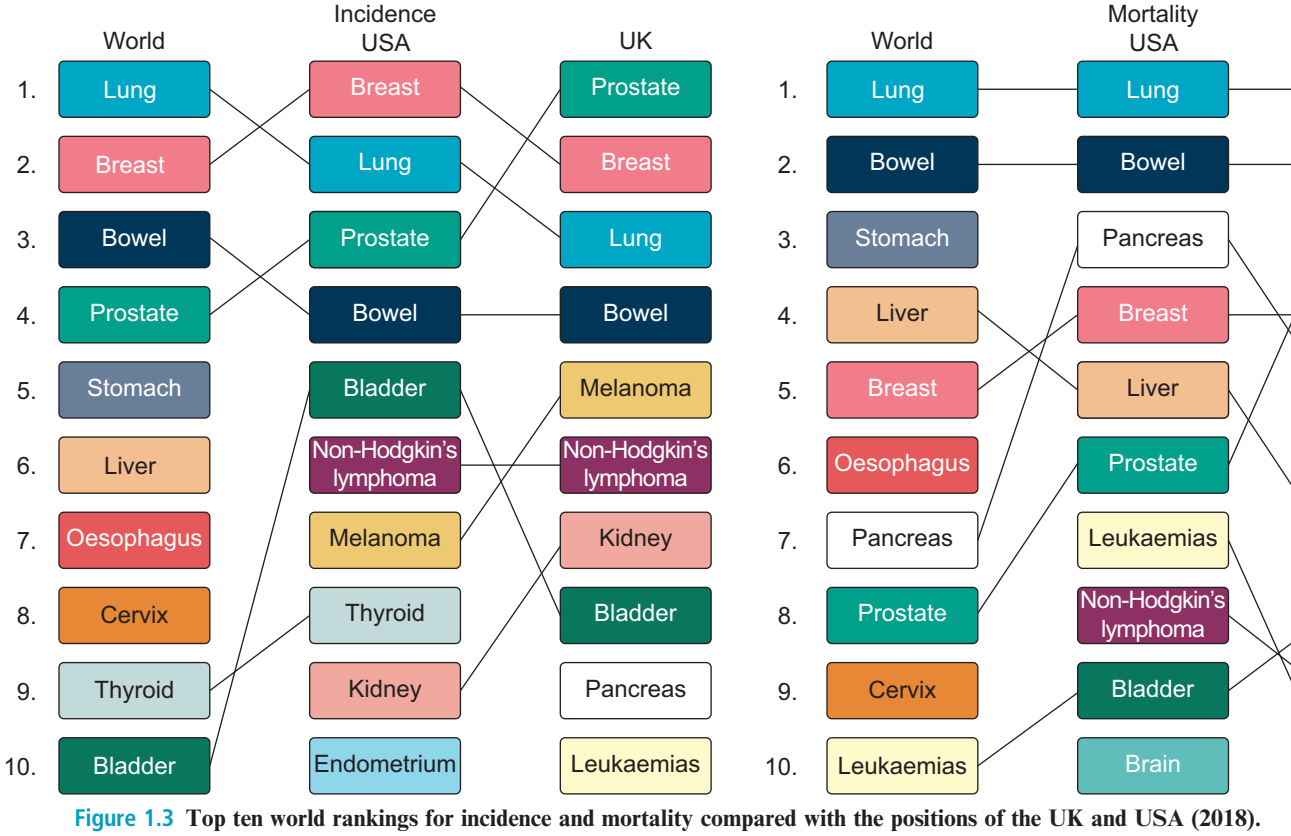


Figure 1.3 Top ten world rankings for incidence and mortality compared with the positions of the UK and USA (2018).

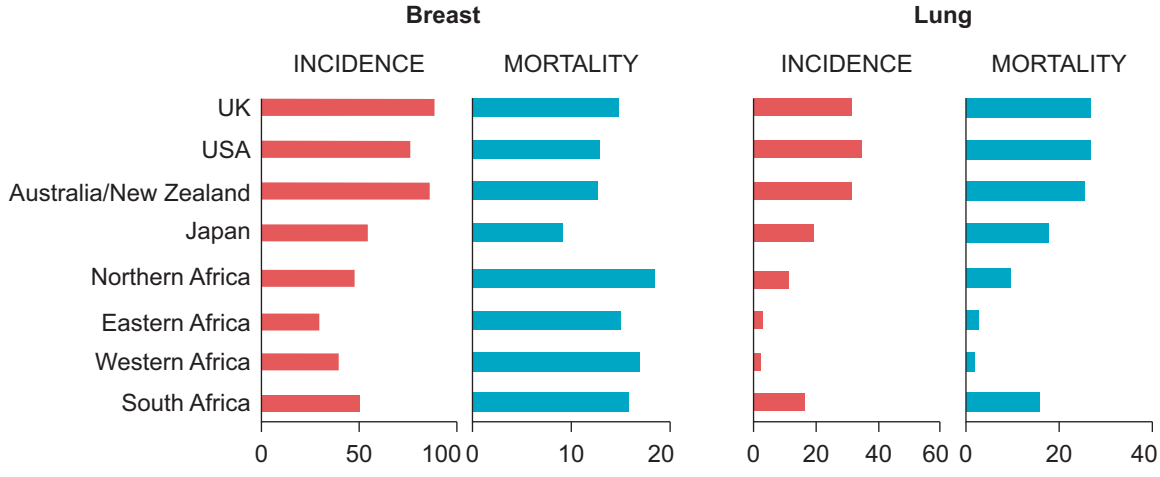


Figure 1.4 Global variation in breast (left) and lung (right) cancer. The numbers are rates per 100,000 of the population. The total figures (in 2020) for incidence were 2,261,000 (breast) and 2,207,000 (lung) and for mortality were 685,000 (breast) and 1,800,000 (lung). Data source: GLOBOCAN 2018 and Cancer Research UK.

prominent, even though there have been huge increases in survival over the last 40 years, largely because the incidence is so high.

We've already seen that big contrasts occur in the prevalent types of cancer across the world. In fact, most forms of cancer show marked variation between countries that differ significantly in what might broadly be called lifestyle. Thus, for example, as recently as 2002, the chances of a woman developing or dying from breast cancer were about three times lower in Japan than in the UK or USA, although that difference has now narrowed to about twofold (Fig. 1.4). Lung cancer, which is the highest incidence, biggest killer in the developed world, is rare in Eastern and Western Africa.

We know that these differences reflect lifestyle because of what has happened when significant numbers of people have emigrated. Thus, for example, after the Second World War a considerable number of Japanese moved to the USA and within a generation the women had acquired the statistical profile for breast cancer of American women. Similar shifts have been observed in the incidence and mortality of colon cancer following group migrations. Even so, the gap in breast cancer incidence between the USA and Japan is closing, presumably as Western habits swamp traditional Japanese lifestyles.

The picture is complicated, however, by the fact that such differences occur not only between countries (Fig. 1.5) but also within national populations. Thus, for example, we noted that in the USA, stomach cancer is 13th on the list of killers, but for every white person that this disease claims, 2.5 African Americans will die, despite 66% of the population being white with only 14% being African American. A further 15% of the US population is Hispanic or Latino, originating mainly from Mexico, Puerto Rico, Central and South America, Cuba and Dominica, with 60% of these having been born in the USA. For this group, overall cancer death rates are lower than for non-Hispanic whites (370 versus 505 per 100,000 in the period

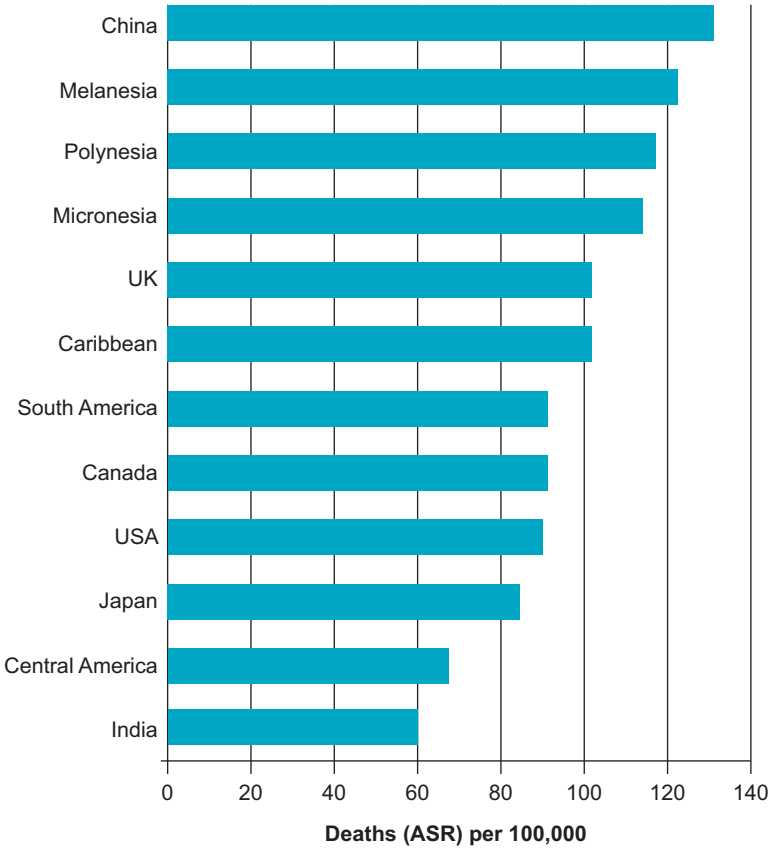


Figure 1.5 Cancer mortality rates across the world. ASR, age-standardised rates. Data source: GLOBOCAN 2018 and Cancer Research UK.

2012–2016). This is because the rates for the major cancers (prostate, breast, colorectal and lung) are lower, although Hispanic rates are higher for stomach, liver, cervix, acute lymphocytic leukaemia and gallbladder cancers. This difference appears to be more sustained than occurred in the cohorts of migrants mentioned earlier, but the cancer rates in descendants of Hispanics are nevertheless approaching those of non-Hispanic whites.

1.3.1 The UK

The annual British contribution to these statistics is 367,000 new cases – nearly 1000 a day – and around 180,000 deaths (490 every day). In line with the rest of the world, the four major types are breast, prostate, lung and bowel cancer (Table 1.3).

All told, cancers account for more than a quarter (28%) of all deaths in the UK. For many years, a little-publicised and lamentable fact has been that UK **cancer survival rates** lagged somewhere around 10% behind those for pretty well every other European country. In other words, for the last 50 years, you were significantly more likely to die of cancer in the UK than in

Table 1.3 The 10 most common causes of cancer death in the UK in 2020 for males and females.

Males	Females
Lung (19,109)	Lung (17,409)
Prostate (13,168)	**Breast (11,839)**
Colorectum (11,556)	Colorectum (10,116)
Oesophagus (5802)	Pancreas (5020)
Pancreas (5202)	**Ovary (4096)**
Bladder (4460)	Liver (2841)
Liver (4220)	Oesophagus (2648)
Leukaemia (3107)	**Uterus (2613)**
Non-Hodgkin's lymphoma (3107)	Non-Hodgkin's lymphoma (2512)
Kidney (3014)	Leukaemia (2195)

Numbers for each cancer are shown in parentheses. Broadly speaking, the pattern is the same for males and females (female cancers in bold type), with prostate and breast cancers occupying second place in the respective tables. Two other female cancers (ovarian and uterine) are the fifth and eighth leading causes of female cancer deaths in the UK. The total figures for male and female deaths are 95,968 and 83,680, respectively.
Data source: American Cancer Society and Centers for Disease Control and Prevention.

most European countries. In 1970, that 'significantly' was about 50%. However, the most recent study has shown that mortality rates have been falling since the early 1990s in both the European Union and the UK, but in the UK, the drop has been more pronounced. What's more, the pattern is similar for all cancers taken together. Thus, the gap has continued to narrow since 1970 such that now the UK and the European Union have similar overall cancer survival rates.

While that is good news, all is not well across the UK cancer scene. The National Cancer Intelligence Centre has produced a Cancer Atlas that compares incidence and death from the 21 most common cancers in 168 regions of the UK. The Atlas highlights those regions in northern England and Scotland that are cancer 'hot spots', notably Liverpool and Glasgow, where the cancer mortality rates are double those of the best-performing areas. Cancer is but one component of what has been called 'excess mortality' that reflects deprivation and poverty, the root causes of poor health in all societies. It has been pointed out that if you walk over Westminster Bridge from the House of Commons, the life expectancy of the denizens around you drops 5 years. Go in the other direction to Liverpool and twice as many people are dying of cancer as in West London.

1.3.2 The USA

In 2017, there were 1,701,315 new cases of cancer and 599,099 cancer deaths, corresponding to rates of 438 and 153 per 100,000 of the population, respectively. Men are slightly more susceptible than women (Table 1.4), male rates being 475 and 182 while the female figures are 413 and 131 (all per 100,000). Cancer mortality is exceeded only by that due to heart disease and it accounts for one in four of all USA deaths.