Chapter 2
Epidemiology of Pancreatic Cancer

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Take Home Messages

- Regarding overall incidence, pancreatic cancer is a less common cancer globally.
- Due to its high case fatality, it ranks seventh in worldwide cancer mortality.
- As a result of the worldwide increase of lifespan it can be expected that incidence and mortality will rise further globally.
- Major risk factors associated with pancreatic cancer, such as smoking, diabetes and obesity are potentially modifiable, providing excellent opportunity for prevention.

Pearls and Pitfalls

- Age is a very important risk factor for cancer, hence, aging populations will drive the increase in incidence.
- As other countries strive to increase their productivity and economic prosperity it can be expected that this will also influence life expectancy and percentage of overweight in their population.

Further Perspectives

- Health statistics are vital for international comparison.
- Differences in incidence, survival and mortality between countries or regions are influenced by means for cancer detection, the quality of cancer registries, medical therapy and cause-of-death notification in the single countries.

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K. Søreide, S. Stättner (eds.), *Textbook of Pancreatic Cancer*,
https://doi.org/10.1007/978-3-030-53786-9_2

2.1 Introduction

Pancreatic cancer is ranks as the 12th most common malignancy, with an estimated 459,000 new cases globally in 2018 [1]. This corresponds to 2.5% of all new cancer cases worldwide. The small difference between the number of new cases and the number of deaths (an estimated 432,000) from this cancer confirms the poor prognosis of this disease (Fig. 2.1). This puts pancreatic cancer in the seventh rank (4.5%) in global cancer mortality after cancers of the lung, stomach and liver, breast, colon, and oesophagus [1]. The epidemiological characteristics (Box 2.1) of pancreatic cancer makes it nonetheless a public health burden, as a cancer with a very high case-fatality rate as the incidence and mortality almost approaches 100%. This chapter will detail some epidemiological features of pancreatic cancer worldwide, with examples from selected countries and regions.

2.2 Worldwide Incidence

Considering the geographical distribution, the highest age-standardized rates of incidence are found in the high-income regions of the world (North America, Western Europe, Asia Pacific and Central Europe [2]. The age-standardised incidence rate was 5.0/100,000 (4.9–5.1/100,000) in 1990 and increased to 5.7/100,000 (5.6–5.8/100,000, World Standard Population) in 2017 [2]. The highest incidence is observed in high income countries (Fig. 2.2), showing a positive correlation with

Box 2.1 Definition of Terms

Incidence: The number of new cases of a disease within a timespan (usually 1 year) gives information about the hazardousness and about the spreading of a disease, usually expressed as a number relative to the population.

Prevalence: The total number of cases living with a certain disease (within a region or a country and within a timespan, also usually calculated for one specific year), usually expressed as a number relative to the population.

Morbidity: The number of cases living with a certain disease irrespective of the time of onset (can not be calculated, is sort of a summative term if one does not want to differentiate between incidence and prevalence).

Mortality: The number of deaths from a certain disease (or group of diseases, e.g. "cardiovascular mortality"), usually expressed as a number relative to the population.

Case-fatality (Lethality): The number of deaths from a specific disease relative to the number of cases gives information about the deadliness of a disease, usually expressed as a percentage.

Fig. 2.1 Incidence and mortality of pancreatic cancer in Austria, 1983–2016, age standardized. (Data source: Statistics Austria, 2019 [5])

the Human Development Index (HDI), as well as with the Gross Domestic Product (GDP) of a country [3]. The highest incidence is found in Eastern Europe (males 9.9/100,000, females 5.8/100,000) and Western Europe (males 9.5/100,000, females 7.2/100,000), followed by Northern America (males 8.7/100,000, females 6.5/100,000), and Southern Europe (males 8.6/100,000, females 5.9/100,000), the lowest in Western Africa (males 2.4/100,000, females 1.9/100,000), Eastern Africa (males 1.4/100,000, females 1.4/100,000), and South Central Asia (males 1.1/100,000, females 1.0/100,000; all numbers: year 2018, age-adjusted to the World Standard Population) [1]. Figure 2.2 shows the incidence (n/100,000) of pancreatic cancer by World Areas, sorted by incidence in females [4].

2.3 Trends in Incidence

Trend analysis of incidence shows a small but steady increase of incidence globally. The number of incident cases of pancreatic cancer in both sexes increased 2.3 times from 195,000 incident cases in 1990 to 448,000 cases in 2017 globally [2].

The sex distribution globally is slightly to the disadvantage of men, in 2017, 51.9% (232,000) of the total incident cases occurred in males, compared with 52.1% (102,000) in 1990 [2]. The number of incident cases peaked at the ages of 65–69 years in males, whereas the peak in females was observed at the ages of 75–79 years.

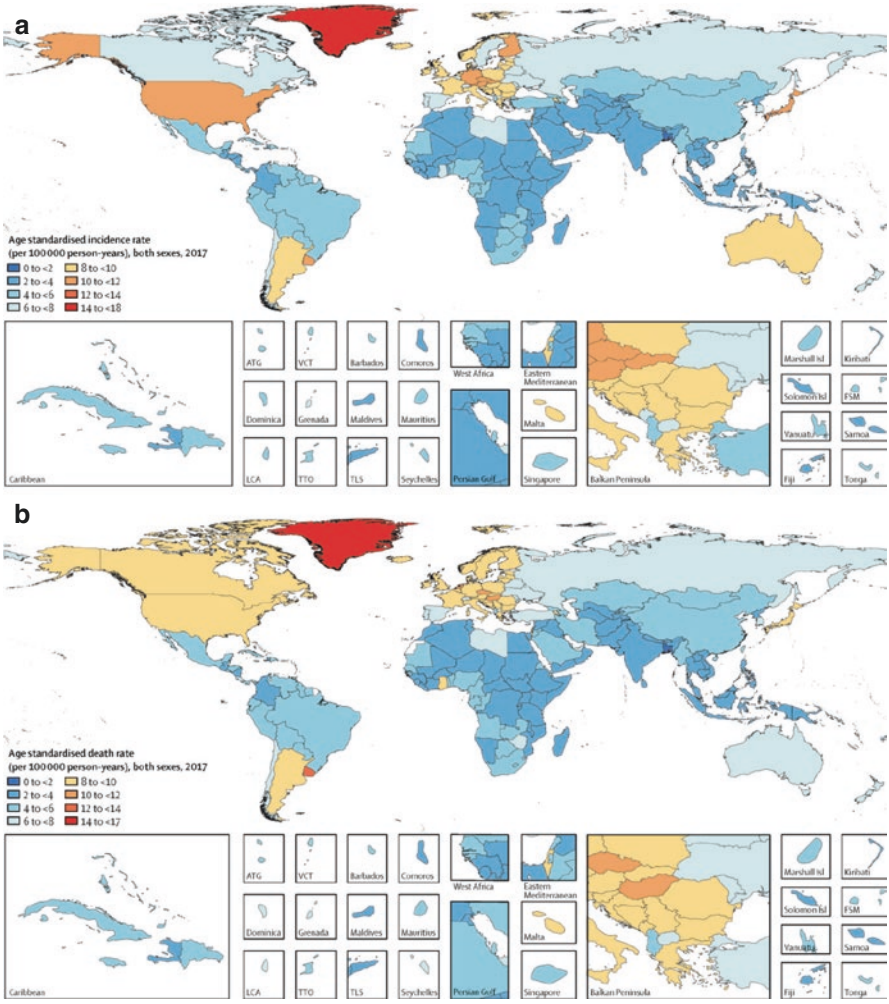

Fig. 2.2 Age-standardised rates of incidence (**a**) and death (**b**) of pancreatic cancer across 195 countries and territories in both sexes, 2017. (Reproduced with permission from GBD 2017 Pancreatic Cancer Collaborators. The global, regional, and national burden of pancreatic cancer and its attributable risk factors in 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Gastroenterol Hepatol. 2019 Dec;4(12):934–947)

2.3.1 Data from The Netherlands

In a Dutch national cohort of 36,453 patients with pancreatic ductal adenocarcinoma (PDAC), the incidence increased from 12.1 (1997–2000) to 15.3 (2013–2016) per 100,000, whereas median overall survival increased from 3.1 to 3.8 months. Resection rates and use of adjuvant or palliative chemotherapy increased with

improved survival in these patients. Since the majority of patients only received supportive care, in all patients with PDAC the survival benefit of 3 weeks was negligible [5].

2.3.2 Data from Austria

Pancreatic cancer ranks sixth in the list of the most common cancers in Austria, representing 2.3% of the total incidence of cancer of roughly 41,000 cases (population 2016: 8.7 million) [6].

The number of newly diagnosed cases in Austria rose from 1045 in 1983 to 1799 in 2016, an increase of 72% within these 34 years. This corresponds to age-standardised rates of 18.0 per 100,000 in 1983 to 21.1 per 100,000 in 2016 (males: 20.9 in 1983–22.5 in 2016; females: 15.8 in 1983–19.8 in 2016, European Standard Population 2013), also showing a rising trend in incidence over the years [7].

In Austria, the sex distribution is also slightly to the disadvantage of men, age-standardized rates in men are 22.5 per 100,000 in 2016 (20.9 in 1983) compared to 19.8 per 100,000 in women (15.8 in 1983). According to the larger number of women in Austria as a consequence of a high life expectancy, 47.1% (848 in 2016) of the total incident cases occurred in males, compared with 52.9% (951 cases in 2016) in women [7]. In Austria the number of new cases peaks at ages 65–74 in men and at 75–84 in women, while age-specific incidence peaks at age 75–84 years in both sexes [8].

According to the Austrian Cancer Registry, 2660 cases with pancreatic cancer accounted for 0.7% of the total cancer prevalence (Persons living in Austria with cancer in 2016). Of these, 54.5% had their diagnose within the past 3 years, 12.7% within 3–5 years, 14.8% within 5–10 years and only 18% were diagnosed 10 or more years ago.

With respect to the registered tumour stage, only 5.6% of all cases (2014–2016) were at stage "localised" at time of diagnosis, 21.6% were at stage "regional" and 33.0% were at stage "distant", respectively (26.1% were of "unknown" stage and 13.7% of incident cases were DCO, death certificate only) [7].

2.3.3 Data from Canada

A recent publication from Canada [9] describes age-standardized cancer-incidence trends in Canada between 1971 and 2015. The most striking results from these analyses relate to increasing incidence trends among younger adults for breast, colorectal, pancreatic, endometrial and kidney cancers. Obesity is a risk factor for these cancer sites and the rising incidence runs parallel to the growing prevalence of

obesity in recent decades. In addition, increases in pancreatic cancer and non-Hodgkin lymphoma among women, a new finding, was observed [9].

2.3.4 Data from Puerto Rico

In Puerto Rico, between 2011 and 2015, 7.8 per 100,000 persons were diagnosed with pancreatic cancer. Higher rates were observed in men than in women (9.2 vs. 6.7 per 100,000, respectively) and in persons aged 65 years or older (42.7 per 100,000 persons). A lower risk of being diagnosed with pancreatic cancer was seen in Puerto Rico in comparison to in members of several racial/ethnic groups in the US [10].

2.3.5 Data from the USA

In an analysis of the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) database, trends in age-adjusted incidence of Stage IA PDAC between 2004 and 2016 were determined. The incidence of Stage IA PDAC cases diagnosed increased statistically significantly from 2004 to 2016 (annual percent change (APC): 14.5, 95% confidence interval (CI) [11.4, 17.7], $p < 0.001$). During the study period, average age at diagnosis for Stage IA and IB cases declined by 3.5 years (95% CI: 1.2–5.9 years; $p = 0.004$) and 5.5 years (95% CI = 3.4–7.6 years; $p < 0.001$), whereas average age increased for higher-stage cases (by 0.6–1.4 years). Among Stage IA cases the proportion of blacks was smaller (10.2% v. 12.5%), and the proportion of other non-Caucasians was higher compared to higher-stage cases (11.9% v. 8.4%, $p < 0.001$). The 5-year overall survival for Stage IA PDAC improved from 44.7% [95% CI = 31.4, 63.7] in 2004 to 83.7% [95% CI = 78.6%, 89.2%] in 2012; 10-year survival improved from 36.7% [95% CI = 24.1, 55.8] in 2004 to 49.0% [95% CI = 37.2%, 64.6%] in 2007 [11].

The following Fig. 2.3 shows age-specific counts and rates of incident cases (A), deaths (B), and DALYs (C) of pancreatic cancer by sex, 2017, on a global basis (DALYs = disability-adjusted life-years) [2].

2.4 Worldwide Mortality

There were an estimated 9.6 million cases of death in 2018 globally due to cancer [1], 4.5% of which were attributed to pancreatic cancer. Considering the geographical distribution, the highest age-standardized rates of mortality are found in the high-income regions of the world (Central Europe, High-income North America, Western Europe, and Southern Latin-America, the lowest in Oceania, Central

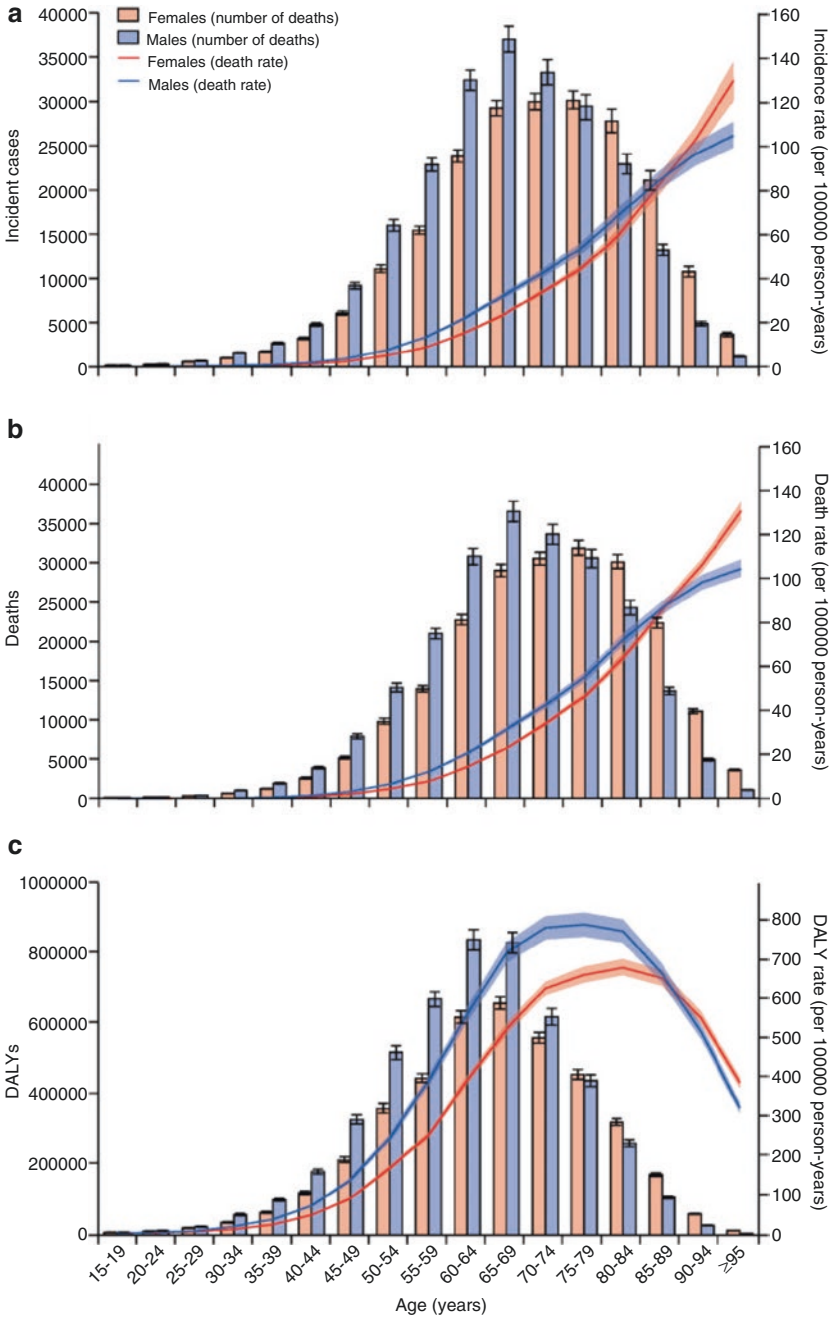

Fig. 2.3 Age-specific counts and rates of incident cases (**a**), deaths (**b**), and DALYs (**c**) of pancreatic cancer by sex, 2017. (Reproduced with permission from GBD 2017 Pancreatic Cancer Collaborators. The global, regional, and national burden of pancreatic cancer and its attributable risk factors in 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Gastroenterol Hepatol. 2019 Dec;4(12):934–947)

sub-Saharan Africa, Eastern sub-Saharan Africa, and South Asia [2].There was a 2.3 times (125%) increase in the number of deaths globally from 1990 to 2017, increasing from 196,000 deaths for both sexes combined in 1990 [2]. The global age-standardised death rate increased by 10.4%, from 5.1/100,000 in 1990 to 5.6/100,000 in 2017. The age-standardised mortality in males was 5.7/100,000 in 1990 and 6.3/100,000 in 2017. The equivalent findings for females were 4.5/100,000 in 1990 and 5.0/100,000 in 2017. In 2017, pancreatic cancer caused approximately 441,000 deaths globally, including roughly 226,000 deaths among males and about 215,000 deaths among females [2].

Age-specific rates for mortality increased with increasing age; this trend was similar between males and females. The number of deaths peaked at the ages of 65–69 years in males, whereas the peak in females was observed at the ages of 75–79 years [2]. Figure 2.3 shows the mortality (n/100,000) of pancreatic cancer by World Areas, sorted by mortality in females [4].

The Fig. 2.4 shows (A) the age-standardised incidence rates of pancreatic cancer in 2017. (B) The percentage change in age-standardised incidence rate of pancreatic cancer from 1990 to 2017. (C) The age-standardised death rates of pancreatic cancer in 2017. (D) The percentage change in age-standardised death rate of pancreatic cancer from 1990 to 2017. GBD = Global Burden of Diseases, Injuries, and Risk Factors Study [2].

2.4.1 Data from The Netherlands

Recent estimates have indicated that the number of deaths from pancreatic cancer overtook breast cancer mortality rates across the EU in 2017, meaning that the disease is now the EU's third leading cause of cancer-related death, behind lung and colorectal cancer [12]. According to GLOBOCAN 2018 [13] pancreatic cancer ranks seventh in women and ninth in men in the Netherlands. Overall, 6.3% of all cancer deaths can be attributed to this cancer. Among the 28 European countries the Dutch mortality ranks 20th.

2.4.2 Data from Austria

Pancreatic cancer ranks third in the list of the most common cancers in Austria, representing 8.6% of the total cancer mortality of roughly 20,000 cases (population 2016: 8.7 million).

The number of deaths due to pancreatic cancer in Austria rose from 1024 in 1983 to 1678 in 2016, an increase of 64% within these 34 years. This corresponds to an increase of age-standardised mortality rates of 17.5/100,000 in 1983 to

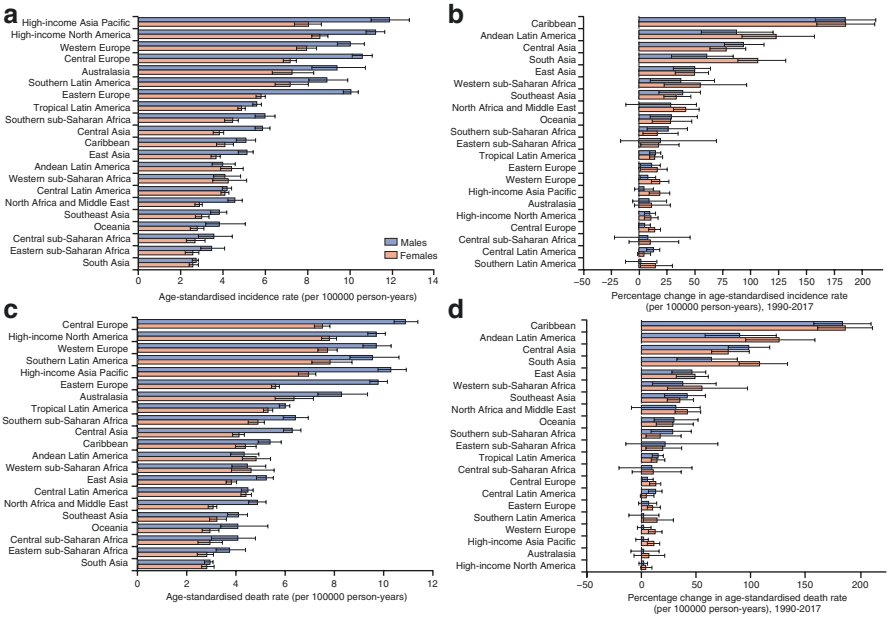

Fig. 2.4 Levels and trends in age-standardised incidence and death rates of pancreatic cancer across 21 GBD regions by sex. (Reproduced with permission from GBD 2017 Pancreatic Cancer Collaborators. The global, regional, and national burden of pancreatic cancer and its attributable risk factors in 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Gastroenterol Hepatol. 2019 Dec;4(12):934–947)

19.6/100,000 in 2016 (males: 20.2 in 1983–21.1 in 2016; females: 15.6 in 1983–18.1 in 2016, European Standard Population 2013), also showing a rising trend in mortality over the years [7].

In Austria, the sex distribution of age-standardized mortality rates is also slightly to the disadvantage of men, nevertheless according to the larger number of women in Austria as a consequence of a high life expectancy, 46.9% (787 in 2016) of the total incident cases occurred in males, compared with 53.1% (991 cases in 2016) in women [7]. In Austria the number of deaths peaks at ages 75–84 in both sexes, while age-specific mortality peaks at age 85+ years in both sexes [8].

A clear increase in 1-year survival can be observed in Austrian patients with pancreatic cancer, rising from 16.7% in the diagnose period 1989–1993 to 37.5% in the diagnose period 2014–2016, and 3-year survival rose from 7.0% in 1989–1993 to 14.6% in 2014–2016. In the survival of longer periods this increase is less pronounced, in the case of 5-year survival the rise is from 5.8% in 1989–1993 to 9.8% in 2014–2016, and the trend of 10-year survival is U-shaped from 5.2% in 1989–1993 to 5.7% in the diagnose period between 2014 and 2016. No distinct differences in survival between men and women can be observed [7].

2.4.3 Data from Canada

Long-term outcomes of Canadian patients affected by PC remain unsatisfactory, with only 9% of the patients surviving at 5 years [14]. The mortality rate is the highest among all the solid tumours with a case-to-fatality ratio of 0.93. The age-standardized 5-year relative survival in 2012 was 9.1% (95% confidence interval [CI], 8.3–10). There were geographic variations among provinces with the highest survival registered in Ontario (10.9%; 95% CI, 9.9–12) and the lowest survival reported in Nova Scotia (4.7%; 95% CI, 2.8–7.2) [14].

2.4.4 Data from Puerto Rico

In Puerto Rico, between 2011 and 2015, 6.7 per 100,000 persons died from pancreatic cancer, men and persons 65 years and older had higher mortality rates. Mortality trends in Puerto Rico increased from 2001 to 2015 (annual percent change [APC] = 1.9%). A lower risk of dying from pancreatic cancer was seen in Puerto Rico compared to members of several racial/ethnic groups in the US [10].

2.4.5 Data from the USA

According to analyses of the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) database, 7.8% of cancer deaths can be attributed to pancreatic cancer (as opposed to 3.2% of cancer incidence). The death rate was 11.0 per 100,000 men and women per year, showing a rather stable trend over the past 25 years [15]. The 5-year relative survival rose from around 2% in the 1970s to 8.6% in the year 2010.

2.5 Conclusion

From an epidemiological point of view, pancreatic cancer is not a very frequent tumour. The substantial case fatality rate makes pancreatic cancer important, however, as number of deaths will soon equal or exceed more common and prevalent cancers. The development of the prevalence of risk factors as well as the further increase in life expectancy will crucially determine the future development of this cancer's incidence and mortality.

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