Pancreatic Cancer: A Multidisciplinary Approach

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Springer

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Foreword: The Evolution of Pancreatic Cancer Care

I saw my first CT scan of a patient with pancreas cancer in 1981; I was a second-year medical student on my first surgical rotation. Body CT scans had entered widespread clinical practice about 1980, the year I started medical school. I stood together with the surgery team in a dark room, facing a row of films on a rotator—a series of small, grainy images. The radiologist pointed out the organs, which appeared as vaguely identifiable blobs of varying shades of gray—the liver, the stomach, the spleen—and *there*, the pancreas, and *there*, the cancer. It was a revelation, but I had no idea at the time how much during my professional lifetime not only imaging but also so many aspects of care of patients with pancreatic cancer would improve. Of course, despite those advances, we still have a very long way to go to substantively improve outcomes and quality of life for most patients with this still far too deadly disease.

During my early medical training, surgical care of pancreas cancer patients was primitive. This was before high-quality imaging; before clinical use of CA19-9; before endoscopy, EUS, FNA, preoperative tissue diagnosis, endobiliary stents, or diagnostic laparoscopy. This was our experience: evaluate a jaundiced patient, consider doing a poorly informative imaging study (CT or an angiogram), do a laparotomy a day or so later, find metastatic disease in most patients. Close and talk to their family. Occasionally you would encounter a patient without metastases, and you would mobilize the duodenum and head of the pancreas, put your hand behind the pancreatic head and try to feel for a plane between the tumor and the SMA. You would then proceed with the operation, hope the vein was free and that your impression of SMA interface had been accurate. If you were very lucky and surgery went well, you prayed for no leak, because there was no interventional radiology. Postop evaluation was primarily based on clinical examination, and if the drain you placed in the operating room did not work, the only way to drain a significant leak was to go back to the operating room.

As a fellow and subsequently as a faculty member at MD Anderson I was very fortunate to be introduced to and then became a member of a tremendous multidisciplinary pancreas program. I had the chance to experience and eventually contribute to an organized, coordinated TEAM that challenged each other to rethink and investigate the disease, and reevaluate our treatment strategies and treatment sequencing; in doing so I am proud to be able to say that we helped improve care for patients with pancreatic cancer.

Of course, we did not do this in a vacuum, as a single program or institution. Many advances were made elsewhere, including early on that pancreatic surgery could be performed safely at high volumes by experienced teams, and more recently proof through randomized trials that adjuvant systemic therapy for patients with surgically resected pancreatic cancer could improve survival.

Now 3 decades after I first arrived at MD Anderson, the approaches and techniques that were developed here and other places have been widely and successfully adopted, implemented, and extended. One of the fundamentally important lessons of my career has been: you can teach a medical student, a resident, a fellow, and a surgical partner to do things as well as you, and often they will find ways to do to them even better. Those from my generation accomplished some fundamental things: we significantly reduced the overall risk and morbidity of pancreatic surgery; we are much better at choosing for operation those we are more likely to help; our patients are living incrementally longer and doing better with the time they have.

Of course there is so much more to be done and that is already being done—as described by my colleagues in the chapters that follow: defining the molecular mechanisms that drive pancreatic cancer development, progression, and response to therapy including through identification of clinically important tumor biomarkers, liquid biopsy technologies and imaging-based biomarkers; better strategies for early detection and prevention of pancreatic cancer; development of novel approaches to systemic, targeted and immune-based therapies including exploitation of the patient and tumor microbiome; intelligent treatment sequencing and more precise implementation of radiation therapy; sophisticated approaches in diagnostic and interventional endoscopy; improved management of challenging patient categories, including borderline resectable and locally advanced disease; advances in surgical techniques, including minimally invasive and robotic surgery, and extended operative approaches including vascular resection and reconstruction; new approaches to palliation and improvements in quality of life through evaluation and intervention, including advances in nutrition, pain management, and integrative medicine. The future of pancreatic cancer care is being written, and the outline is contained in these chapters.

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Jeffrey E. Lee

Preface

Pancreatic cancer is a dreadful disease with an increasing impact on cancer-related mortality worldwide. This disease is the unfortunate exception to the general trend of improvement in cancer-related mortality. Pancreatic cancer is projected to become the second leading cause of cancer-related deaths worldwide by 2030. There is a significant need for better treatment options to improve the survival and quality of life of pancreatic cancer patients.

In the last decade, management of pancreatic cancer has shifted towards a multidisciplinary approach with encouraging results. There have been several recent advances, from screening high-risk cohorts to emerging precision medicine paradigms, as well as recently reported practice-changing data for surgically resected patients.

This book provides a comprehensive, state-of-the-art review of this field and will serve as a valuable resource for physicians and researchers with an interest in pancreatic cancer. The book describes data about risk factors and genetic predisposition for pancreatic cancer and highlights current screening strategies and preliminary results. The diagnosis and staging of pancreatic cancer is reviewed, with focus on imaging evaluations, laparoscopy, endoscopic ultrasound-guided biopsies, and biomarkers. For locally advanced and metastatic disease, systemic therapy, radiation, and chemoradiation approaches are discussed. For resectable and borderline resectable disease, surgical management and perioperative therapy are reviewed.

Given the multimodality approach of pancreatic cancer, the role of gastroenterologists in the management of the disease is reviewed with emphasis on screening, diagnosis, symptoms management, and endoscopic ultrasound-guided local therapies and fiducial markers placement. Emerging paradigms in pancreatic cancer management are presented, such as minimally invasive surgical approaches, local ablative technologies, emerging radiation approaches, image-based biomarkers, liquid biopsies, and molecular profiling of pancreatic cancer. This book also provides a valuable insight into nutrition and early integration of supportive/palliative care for pancreatic cancer patients.

This textbook will serve as a very useful resource for physicians and scientists dealing with, or interested in, this challenging malignancy. Given the multidisciplinary approach of pancreatic cancer, this book has brought together experts from a variety of integrated disciplines such as gastroenterology, medical oncology, surgical oncology, radiation oncology, pathology, radiology, rehabilitation medicine, and nutrition. The audience for this book

includes medical oncologists, radiation oncologists, surgeons, gastroenterologists, research scientists with interest in pancreatic cancer, fellows and residents training in surgical, radiation, and medical oncology as well as gastroenterology.

All chapters are written by experts in their fields and include the most up-to-date scientific and clinical information. This comprehensive and yet concise state-of-the-art review of this field will help guide patient management and stimulate investigative efforts. This book outlines *The MD Anderson Approach to managing pancreatic cancer,* written mostly by experts from UT MD Anderson Cancer Center with some collaborative colleagues from other institutions. We are extremely grateful to all the contributors for their time and effort in this endeavor.

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Pancreatic Cancer at a Glance

1

Dema Maher Shobaki and Manoop S. Bhutani

Introduction

Cancer incidence and mortality are increasing worldwide, with expectations of becoming the leading cause of death and the biggest inhibitor to increase the life expectancy in every country in the twenty-first century [1]. Since the first description of pancreatic cancer in Giovanni Battista Morgagni's *De Sedibus et Causis Morborum per Anatomen Indigatis* in the 1760s, its global burden continues to rise due to aging, growth in the world's population, and high-risk lifestyles, such as smoking, physical inactivity, and "westernized" diets [2–4]. Known for its very poor prognosis, pancreatic cancer has a low 5-year survival rate of about 5%, regardless of the income status of all countries affected, and the incidence of pancreatic cancer is particularly high within the 60 and 80 years of age [5–7].

The Global Burden of Disease (GBD) study reported the incidence and mortality rates and its risk factors of pancreatic cancer across 195 countries and territories located across 21 regions, for both sexes and 20 age groups, from 1990 to 2017. The GBD reported the number of newly diagnosed pancreatic cancer cases increased from 195,413 in 1990 to 447,664 in 2017, a 129.1% increase observed globally [8]. There was a 125.2% increase in pancreatic cancer deaths worldwide, from 195,861 in 1990 to 441,082 in 2017 [8]. After stratifying 195 countries and territories into five sociodemographic index (SDI) groups, including low, low-middle, middle, high-middle, and high, the most prevalent age-standardized incidence rate (ASIR) occurred in low-middle SDI countries, and the highest increase in pancreatic deaths was detected in the middle SDI quintile [8].

The International Agency for Research on Cancer (IARC), a global institution established by the World Health Organization (WHO), gathered estimates of pancreatic cancer incidence and mortality rates across 185 countries across 21 regions as defined by the United Nations (UN) and published its reporting in the GLOBOCAN 2020 database [9]. Under the GLOBOCAN 2020 project, IARC collected the epidemiological variables of malignant pancreatic neoplasms, with the tenth edition of the International Classification of Diseases (ICD-10 version 2010) category of C25, from various international registries based on each cancer registry's definition of malignancy [9]. Pancreatic incidence and mortality rates by sex and 18 age groups (0–4, 5–9, 10–14,

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15–19 … 75–79, 80–84, 85 and over) were estimated for 185 countries and territories in 2020 [9]. The epidemiological information presented in this chapter is based on data available on Globocan 2020 on March 01, 2021 (December 2020, version 1.0).

Incidence

The incidence rate of new cases of pancreatic cancer was estimated among both sexes and across all ages. In 2020, 495,773 new cases of pancreatic cancer were identified worldwide, with the 13th highest incidence rate among all cancers, representing 2.6% of registered new cases of cancer [10]. Northern America and Europe observed the highest incidence age-standardized rate (ASR), the rate adjusted to account for difference in ages seen in the population, of pancreatic cancer at 8.00 and 7.80 per 100,000 people, respectively, in 2020 when compared to the world at 4.90 per 100,000 people (Table 1.1) [1, 10]. The lowest incidence ASR at 2.30 was seen in Africa followed by Asia with an incidence ASR of 4.00 [1, 10].

Table 1.1 The incidence age-standardized rates (ASR) of pancreatic cancer, the ranking of the pancreatic cancer, and the percentage of new cancer cases in both sexes across six continents when compared to the world in 2020. Data Sourced: GLOBOCAN 2020

Incidence age-standardized rates, world ranking, and percent of new cases of pancreatic cancer, both sexes, across six continents, in 2020				
Populations	Number of New Cases	Incidence, ASR[a]	Cancer Ranking	Percent of New Cases (%)
World	495,773	4.9	13	2.6
Africa	17,070	2.3	18	1.5
Asia	233,701	4.0	13	2.5
Europe	140,116	7.8	8	3.2
Latin America and the Caribbean	37,352	4.5	12	2.5
Northern America	62,643	8.0	11	2.4
Oceania	4891	6.6	11	1.9

[a]Per 100,000 people

Majority of the countries with the highest incidence of pancreatic cancer are located in Europe [10]. The average of the 15 countries with the highest ASR is 9.26, almost twice as much as that seen in the world collectively [10]. Hungary had the highest ASR in the world with 11.20 per 100,000, followed closely by the South American country of Uruguay with an ASR of 10.7 (Table 1.2A). The East African country of Malawi has the lowest incidence in the world, with 0.63 per 100,000, with the Melanesian country of Vanuatu estimated to have an ASR of 0.64 per 100,000 (Table 1.2B) [10]. There is a 178.7% difference in incidence rates between Hungary and Malawi [10].

There is a minor difference in the incidence of pancreatic cancer observed among men and women as well as noticeable difference in geographic distribution [1, 11]. There were more new cases of pancreatic cancer in men (5.70 per 100,000 people) than in women (4.10 per 100,000). The highest incidence rate in males was seen in Hungary, with an incidence rate of 13.70 per 100,000, whereas the lowest incidence rate was seen in Malawi with incidence rate of 0.46 per 100,000 (Table 1.3A, B) [10]. Similar to its male counterparts, the highest incidence rate in females was seen in Hungary with 9.20 per 100,000, a rate of 76.7% more than the world's average rate (Table 1.3C) [10]. Conversely, the lowest rate in females is estimated to be 0.30 per 100,000 in the South-Central Asian country of Pakistan (Table 1.3D) [10].

When stratifying the incidence of disease into 21 United Nations (UN) regions, the risk of developing pancreatic cancer is highest in Western Europe (8.6), then in the Northern America (8.0), followed closely by 7.5 per 100,000 in Central and Eastern Europe [10]. The lowest incidence rates were observed in Southern-Central Asia (1.2), in Middle Africa (1.5), and in Eastern Asia (1.8) (Fig 1.1a–f) [10]. The highest rates of new pancreatic cases in men are in Western Europe (9.9) and Central and Eastern Europe (9.9), followed by Northern America (9.3) [10]. Conversely, the lowest incidence rates in men are in the regions of Southern-Central Asia (1.5), Eastern Africa, and Middle Africa

Table 1.2 (A) The 15 countries with the highest incidence rate (ASR) in 2020, compared to the incidence rate seen in the world. (B) The 15 countries with the lowest incidence rate (ASR) in 2020, compared to the world's incidence rate. Data Sourced: GLOBOCAN 2020

Populations	Cancer—Incidence Ranking	Incidence, ASR[a]
(A) Countries with the highest incidence age-standardized rates of pancreatic cancer in 2020		
World	Not Applicable	4.9
Hungary	1	11.2
Uruguay	2	10.7
Japan	3	9.9
Slovakia	4	9.6
Czechia	5	9.5
Austria	6	9.0
Armenia	7	8.9
Estonia	8	8.9
Malta	9	8.9
Germany	10	8.8
Finland	11	8.8
Latvia	12	8.8
Republic of Moldova	13	8.7
France	14	8.6
Slovenia	15	8.6
(B) Countries with the lowest incidence age-standardized rates of pancreatic cancer in 2020		
World	Not Applicable	4.90
Malawi	1	0.63
Vanuatu	2	0.64
Botswana	3	0.66
Eswatini	4	0.69
Pakistan	5	0.73
Mozambique	6	0.77
Sri Lanka	7	0.81
Rwanda	8	0.88
India	9	0.94
Viet Nam	10	0.97
Guinea	11	0.98
Bangladesh	12	1.00
Angola	13	1.00
Namibia	14	1.00
Djibouti	15	1.00

[a]Per 100,000 people

Table 1.3 (A) The six countries with the highest incidence rates in the male population compared to the world's incidence. (B) The six countries with the lowest incidence rates in the male population. (C) The six countries with the highest incidence rates in the female population when compared to the world's incidence rate of pancreatic cancer. (D) The six countries with the lowest incidence rates in females when compared to the world's incidence rate of pancreatic cancer. Data Sourced: GLOBOCAN 2020

(A) Countries with the highest incidence age-standardized rates of pancreatic cancer, males, all ages, in 2020	
Populations (male)	**Incidence, ASR[a]**
World	5.7
Hungary	13.7
French Guiana	13.0
Uruguay	12.8
Slovakia	12.0
Armenia	11.9
Latvia	11.9
(B) Countries with the lowest incidence age-standardized rates of pancreatic cancer, males, all ages, in 2020	
Populations (male)	**Incidence, ASR[a]**
World	5.70
Malawi	0.46
Eswatini	0.57
Botswana	0.82
Pakistan	1.1
Bangladesh	1.1
Sri Lanka	1.1
Mozambique	1.1
(C) Countries with the highest incidence age-standardized rates of pancreatic cancer, females, all ages, in 2020	
Populations (female)	**Incidence, ASR[a]**
World	4.1
Hungary	9.2
Uruguay	8.9
Japan	8.2
Czechia	8.0
Austria	8.0
Sweden	7.9

(continued)

Table 1.3 (continued)

(D) Countries with the lowest incidence age-standardized rates of pancreatic cancer, females, all ages, in 2020

Populations (female)	Incidence, ASR[a]
World	4.10
Pakistan	0.30
Comoros	0.47
Mozambique	0.53
Rwanda	0.55
Sri Lanka	0.61
Djibouti	0.61

[a]Per 100,000 people

(2.0), followed closely by Western Africa (2.2) [10]. The highest risk in developing pancreatic cancer in women was observed in Western Europe (7.4), in Northern America (6.9), and in Northern Europe and Australia and New Zealand (6.7), while the lowest rates are in Southern-Central Asia (0.88) and in Middle Asia (1.2) [10].

The rate of developing pancreatic cancer increases with age in both the male and female populations (Fig. 1.2, Table 1.4) [1, 11–13]. The age-standardized rates of new cases of pancreatic cancer drastically increase after the age of 54 in both men and women [10]. This may be the result

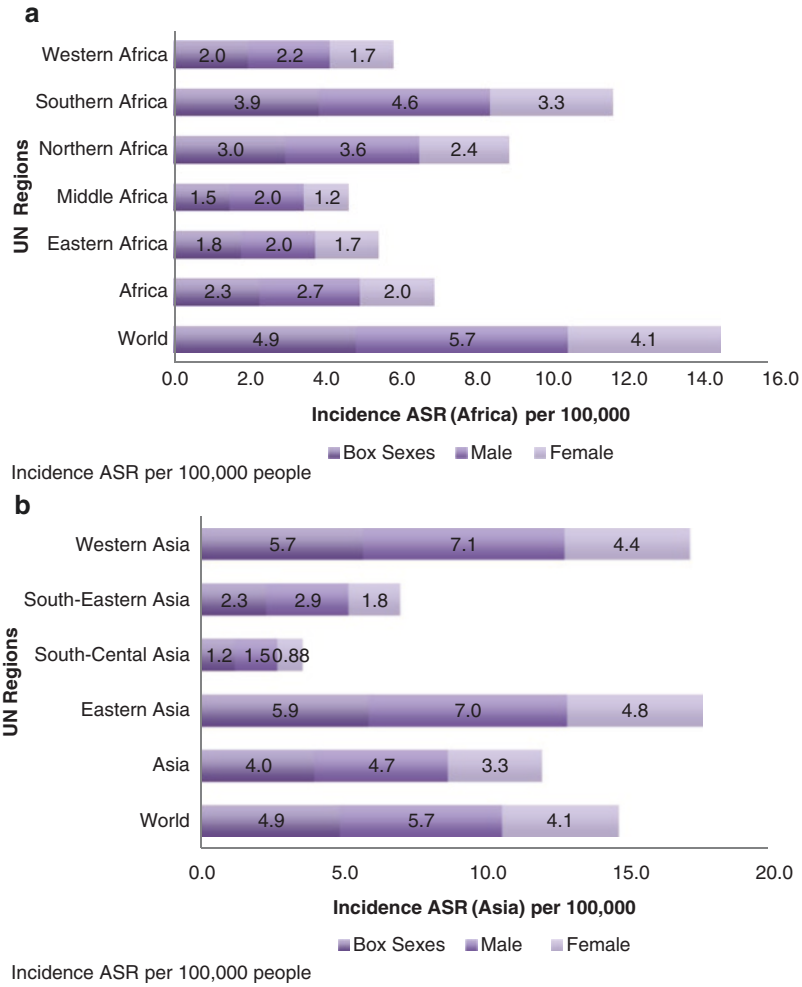
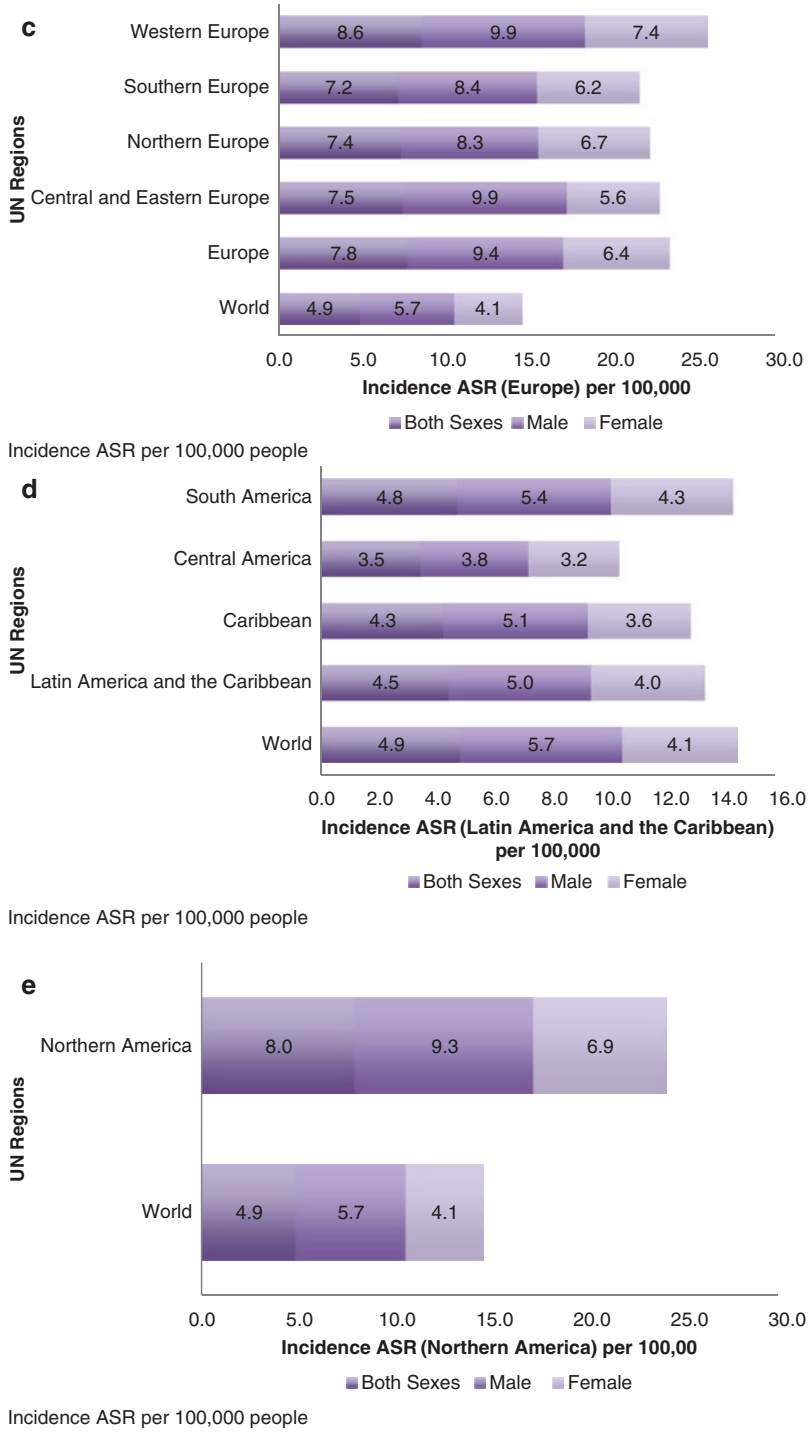


Fig. 1.1 (**a**) The estimated rates of new pancreatic cancer in UN African regions, including both sexes, males, and females, in 2020. (**b**) The estimated rates of new pancreatic cancer in UN Asian regions, including sexes, males, and females, in 2020. (**c**) The estimated rates of new pancreatic cancer in UN European regions, including both sexes, males, and females, in 2020. (**d**) The estimated rates of new pancreatic cancer in UN Latin America and the Caribbean regions, including both sexes, males, and females, in 2020. (**e**) The estimated rates of new pancreatic cancer in UN Northern American regions, including both sexes, males, and females, in 2020. (**f**) The estimated rates of new pancreatic cancer in UN Northern American regions, including both sexes, males, and females, in 2020. Data Sourced: GLOBOCAN 2020



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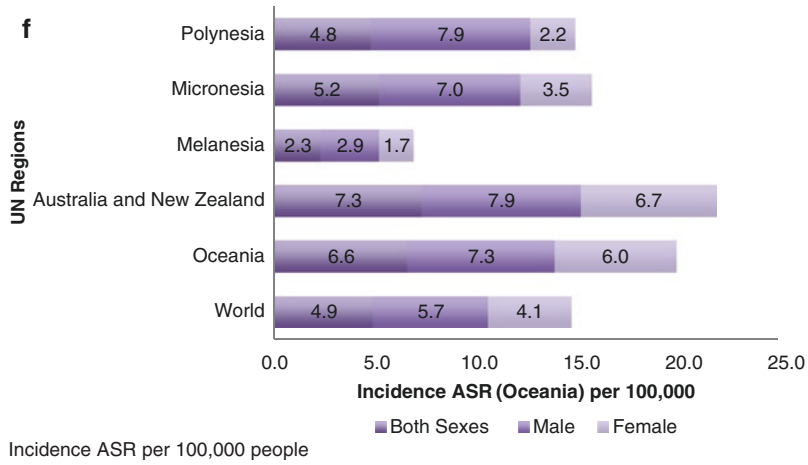

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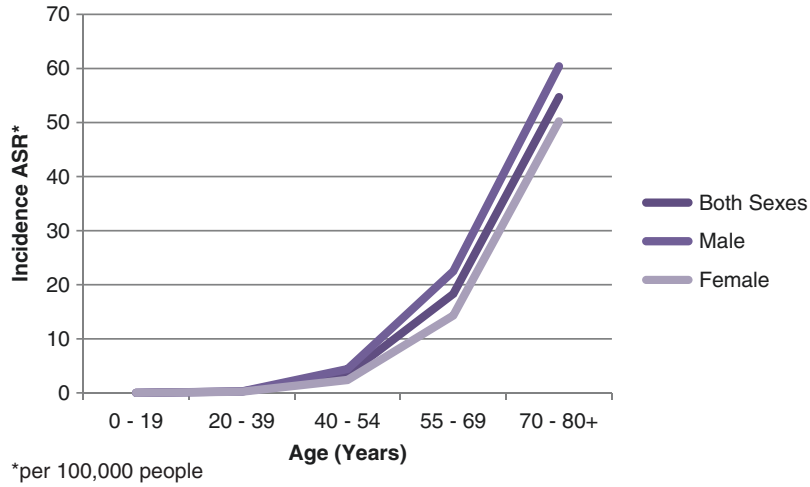

Fig. 1.2 The estimated incidence age-standardized rates of new pancreatic cancer with age, for both sexes, in 2020. Data Sourced: GLOBOCAN 2020

Table 1.4 The estimated incidence age-standardized rates of new pancreatic cancer with age, for both sexes, in 2020. Data Sourced: GLOBOCAN 2020

Estimated incidence age-standardized rates of pancreatic with age, male and female, in 2020			
Populations (age)	Incidence ASR (both sexes)[a]	Incidence ASR (male)[a]	Incidence ASR (female)[a]
0–19	0.01	0.01	0.01
20–39	0.25	0.27	0.22
40–54	3.4	4.4	2.4
55–69	18.3	22.5	14.3
70–85+	54.7	60.4	50.2

[a]Per 100,000 people

of the lack of pancreatic cancer diagnoses prior to the age of 55 [11, 13, 14].

Although the etiology for the incidence rates of pancreatic cancer is not apparent, the exposure to particular risk factors from the environment may explain the difference observed in geographic (see Chap. 2) [11]. The use of various forms of diagnostic modalities and the accuracy, completeness, and coverage of the registries completed in developed and underdeveloped countries may contribute to these differences [11, 15, 16].

Prevalence

Per the International Agency for Research on Cancer, the prevalence of pancreatic cancer is the number of diagnosed individuals who are still alive at a given point in time [10, 17]. The prevalence rate, presented as the proportion of the population with pancreatic cancer per 100,000 people is estimated over 1-year, 3-year, and 5-year time period in 2020. The estimated proportions of the world's cases of pancreatic cancer in 2020 are 2.80 per 100,000 people in a 1-year time period, 4.30 in a 3-year time period, and 4.90 in a 5-year time period [10].

Majority of the countries with the highest prevalence ratios are located in Europe [10]. Within the 1-, 3-, and 5-year time periods, the largest proportion of a population with pancreatic cancer diagnoses is observed in Japan (14.00, 21.00, 23.80), followed by Hungary (10.90, 16.70, 19.20), Germany (10.90, 16.50, 18.70), and Finland (10.80, 16.40, 18.60) (Table 1.5A–C) [10].

Djibouti has the lowest pancreatic cancer prevalence ratio of 0.10 per 100,000 people in their population, followed by Botswana (0.13) and Guinea-Bissau and the Solomon Islands (0.15) within a 1-year time period in 2020 (Table 1.6A) [10]. In reference to a 3-year time period, Malawi and the Solomon Island have the lowest ratio with 0.29 per 100,000 individuals, followed closely by Botswana (0.30) (Table 1.6B) [10]. Botswana has the lowest prevalence ratio of pancreatic cancer in 2020 within a 5-year time period (0.30), with Vanuatu estimating to have 0.33 per 100,000 of their populations living or surviving pancreatic cancer, followed by Malawi (0.36) (Table 1.6C) [10].

Table 1.5 The 15 countries with the highest age-specific ratios of incidence of pancreatic cancer. (A) 1-year estimated prevalence of pancreatic cancer in 2020. (B) 3-year estimated prevalence of pancreatic cancer in 2020. (C) 5-year estimated prevalence of pancreatic cancer in 2020. Data Sourced: GLOBOCAN 2020

(A) Countries with the highest sex-, age-specific ratios of incidence of pancreatic cancer in 2020, 1-year estimated prevalence

Populations	1-Year Ranking	1-Year Prevalence[a]	Proportions[b]
World	Not Applicable	214,471	2.80
Japan	1	17,753	14.00
Germany	2	9168	10.90
Hungary	3	1055	10.90
Finland	4	601	10.80
Czechia	5	1079	10.10
Austria	6	878	9.70
Malta	7	43	9.70
Slovenia	8	199	9.60
Switzerland	9	823	9.50
Estonia	10	124	9.30
Sweden	11	930	9.20
France, Guadeloupe	12	37	9.20
France	13	5951	9.10
Italy	14	5523	9.10
Denmark	15	528	9.10

(continued)

Table 1.5 (continued)

(B) Countries with the highest sex-, age-specific ratios of incidence of pancreatic cancer in 2020, 3-year estimated prevalence

Populations	3-Year Ranking	3-Year Prevalence[c]	Proportions[b]
World	Not Applicable	331,348	4.30
Japan	1	26,553	21.00
Hungary	2	1616	16.70
Germany	3	13,799	16.50
Finland	4	907	16.40
Czechia	5	1648	15.40
Austria	6	1335	14.80
Malta	7	65	14.70
Slovenia	8	302	14.50
Switzerland	9	1244	14.40
Estonia	10	187	14.10
Sweden	11	1409	14.00
France	12	9036	13.80
Denmark	13	798	13.80
Italy	14	8264	13.70
Latvia	15	258	13.70

(C) Countries with the highest sex-, age-specific ratios of incidence of pancreatic cancer in 2020, 5-year estimated prevalence

Populations	5-Year Ranking	5-Year Prevalence[d]	Proportions[b]
World	Not Applicable	379,958	4.90
Japan	1	30,137	23.80
Hungary	2	1851	19.20
Germany	3	15,698	18.70
Finland	4	1032	18.60
Czechia	5	1875	17.50
Austria	6	1521	16.90
Slovenia	7	342	16.50
Malta	8	73	16.50
Switzerland	9	1419	16.40
Estonia	10	212	16.00
Sweden	11	1604	15.90
France	12	10,313	15.80
Denmark	13	910	15.70
Latvia	14	296	15.70
Italy	15	9386	15.50
Greece	16	1611	15.50
Lithuania	17	422	15.50

[a]Computed using sex-, site-, and age-specific ratios of incidence to 1-year prevalence from Nordic countries for the period 2006–2015

[b]Proportions of the population per 100,000 persons

[c]Computed using sex-, site-, and age-specific ratios of incidence to 3-year prevalence from Nordic countries for the period 2006–2015

[d]Computed using sex-, site-, and age-specific ratios of incidence to 5-year prevalence from Nordic countries for the period 2006–2015

Table 1.6 The 15 countries with the lowest sex-, age-specific ratios of incidence of pancreatic cancer. (A) 1-year estimated prevalence of pancreatic cancer in 2020. (B) 3-year estimated prevalence of pancreatic cancer in 2020 (C) 5-year estimated prevalence of pancreatic cancer in 2020. Data Sourced: GLOBOCAN 2020

(A) Countries with the lowest sex-, age-specific ratios of incidence of pancreatic cancer in 2020, 1-year estimated prevalence

Populations	**1-Year Ranking**	**1-Year Prevalence[a]**	**Proportions[b]**
World	Not Applicable	214,471	2.80
Djibouti	1	1	0.10
Botswana	2	3	0.13
Guinea-Bissau	3	3	0.15
Solomon Islands	4	1	0.15
Malawi	5	33	0.17
Eswatini	6	2	0.17
Mozambique	7	62	0.20
Angola	8	68	0.21
Guinea	9	28	0.21
Timor-Leste	10	3	0.23
Namibia	11	6	0.24
Rwanda	12	32	0.25
Pakistan	13	579	0.26
Lesotho	14	6	0.28
Sudan	15	125	0.29
Zambia	16	53	0.29
Central African Republic	17	14	0.29

(B) Countries with the lowest sex-, age-specific ratios of incidence of pancreatic cancer in 2020, 3-year estimated prevalence

Populations	**3-Year Ranking**	**3-Year Prevalence[c]**	**Proportions[b]**
World	Not Applicable	331,348	4.30
Malawi	1	56	0.29
Solomon Islands	2	2	0.29
Botswana	3	7	0.30
Vanuatu	4	1	0.33
Angola	5	111	0.34
Guinea	6	46	0.35
Mozambique	7	111	0.36
Central African Republic	8	19	0.39
Eswatini	9	5	0.43
Rwanda	10	57	0.44
Eritrea	11	16	0.45
Pakistan	12	1010	0.46
Uganda	13	211	0.46
Sudan	14	206	0.47
Burundi	15	60	0.50

(C) Countries with the lowest sex-, age-specific ratios of incidence of pancreatic cancer in 2020, 5-year estimated prevalence

Populations	**5-Year Ranking**	**5-Year Prevalence[d]**	**Proportions[b]**
World	Not Applicable	379,958	4.90
Botswana	1	7	0.30
Vanuatu	2	1	0.33
Malawi	3	69	0.36
Angola	4	130	0.40

(continued)

Table 1.6 (continued)

Guinea	5	52	0.40
Mozambique	6	134	0.43
Eswatini	7	5	0.43
Solomon Islands	8	3	0.44
Central African Republic	9	23	0.48
Rwanda	10	66	0.51
Guinea-Bissau	11	10	0.51
Uganda	12	243	0.53
Sudan	13	242	0.55
Pakistan	14	1230	0.56
Burundi	15	67	0.56
Eritrea	16	20	0.56

[a]Computed using sex-, site-, and age-specific ratios of incidence to 1-year prevalence from Nordic countries for the period 2006–2015
[b]Proportions of the population per 100,000 persons
[c]Computed using sex-, site-, and age-specific ratios of incidence to 3-year prevalence from Nordic countries for the period 2006–2015
[d]Computed using sex-, site-, and age-specific ratios of incidence to 5-year prevalence from Nordic countries for the period 2006–2015

Mortality

The mortality rates of pancreatic cancer differ around the world. In 2020, the world had 466,003 deaths relating to pancreatic cancer, with a mortality age-standardized rate (ASR) of 4.5 per 100,000 people [10]. Moreover, pancreatic cancer is the world's seventh leading cancer-related death, comprising 4.7% of all cancer-related deaths [10]. Similar to what was observed for the incidence ASR, Europe and North America have the highest mortality ASR at 7.2 and 6.5 per 100,000 people, respectively, with the Oceania region experiencing the third highest mortality rate of 5.2 (Table 1.7) [10]. The lowest mortality rate was estimated to be 2.3 per 100,000 people in Africa, with pancreatic cancer as the 14th leading cause of cancer-related deaths, as of 2020 [10].

Similar to the incidence trends around the world, majority of the countries with the highest mortality age-standardized rates of pancreatic cancer are located in Europe. The Central and Eastern European country of Hungary and the South American country of Uruguay each have the highest mortality ASR in 2020 at 10.2 per 100,000, a difference of 77.6% when compared to the world's average rate, distantly followed by Armenia at 8.6 per 100,000 (Table 1.8A) [10]. The Eastern African country of Malawi has the lowest morality rate in the world, with 0.62 per

Table 1.7 The mortality age-standardized rates (ASR) of pancreatic cancer, the ranking of the pancreatic cancer deaths, and the percentage of cancer deaths in both sexes across six continents when compared to the world in 2020. Data Sourced: GLOBOCAN 2020

Mortality age-standardized rates, world ranking, and percent of new cases of pancreatic cancer, both sexes, across six continents, in 2020				
Populations	Number of Death Cases	Mortality, ASR[a]	Cancer Ranking	Percent of Cancer Deaths (%)
World	466,003	4.5	7	4.7
Africa	16,549	2.3	14	2.3
Asia	224,034	3.8	7	3.9
Europe	132,134	7.2	4	6.8
Latin America and the Caribbean	36,030	4.3	7	5.1
Northern America	53,277	6.5	2	7.6
Oceania	3979	5.2	5	5.7

[a]Per 100,000 people

Table 1.8 (A) The 15 countries with the highest mortality rate (ASR) in 2020, compared to the morality rate seen in the world. (B) The 15 countries with the lowest mortality rate (ASR) in 2020, compared to the world's mortality rate. Data Sourced: GLOBOCAN 2020

Populations	Cancer Mortality Ranking	Mortality, ASR[a]
(A) Countries with the highest mortality age-standardized rates of pancreatic cancer in 2020		
World	Not Applicable	4.5
Hungary	1	10.2
Uruguay	2	10.2
Armenia	3	8.6
Czechia	4	8.5
Finland	5	8.5
Republic of Moldova	6	8.3
Germany	7	8.2
Austria	8	8.1
Serbia	9	8.0
Israel	10	8.0
Slovakia	11	8.0
Montenegro	12	8.0
Estonia	13	7.8
Malta	14	7.8
France, Guadeloupe	15	7.8
(B) Countries with the lowest mortality age-standardized rates of pancreatic cancer in 2020		
World	Not Applicable	4.5
Malawi	1	0.62
Vanuatu	2	0.64
Botswana	3	0.66
Eswatini	4	0.69
Pakistan	5	0.71
Mozambique	6	0.75
Sri Lanka	7	0.80
Rwanda	8	0.85
India	9	0.90
Viet Nam	10	0.92
Bangladesh	11	0.98
Guinea	12	0.98
Angola	13	1.00
Namibia	14	1.00
Djibouti	15	1.00

[a]Per 100,000 people

100,000 people, followed by Vanuatu at 0.64 and Botswana at 0.66 (Table 1.8B) [10]. Asia experienced about 48.1% of the world's pancreatic cancer-related deaths [10, 11].

There was roughly a 33.0% difference in the pancreatic cancer mortality age-standardized rate between males and females in 2020, with the world's rate in males being 5.3 per 100,000 people and 3.8 observed in females [10]. The highest mortality rates in males were seen in the countries of Hungary (12.6) and Uruguay (12.2), whereas the lowest mortality age-standardized rates were seen in Malawi with incidence rate of 0.46 and in the Southern African country of Eswatini with 0.57 per 100,000, respectively (Tables 1.9A, B) [10]. The highest incidence rate in females was seen in Uruguay with 8.5 per 100,000, followed closely by Hungary with a rate of 8.4, and Finland at 7.3 (Table 1.3C) [10]. The lowest mortality rates in females were estimated to be 0.30 per 100,000 in the South-Central Asian country of Pakistan and in the Eastern African country of Comoros (0.47) (Table 1.9C, D) [10].

The world's mortality rates were also stratified into 21 United Nations (UN) regions, and mortality rates were highest in Western Europe with 7.8 per 100,000 people, in Central and Eastern Europe with a rate of 7.1, and in Southern Europe with a rate of 6.6 (Fig. 1.3a–f) [10]. The lowest mortality rates were observed in South-Central Asia (1.1), in Middle Africa (1.5), in and Eastern Africa (1.8) (Fig. 1.3a–f) [10]. The highest rates of pancreatic cancer-related deaths in males were in Central and Eastern Europe (9.6) and in Western Europe (9.1), both with rates higher than Europe's average of 8.8 [10]. The lowest mortality rates in men were in South-Central Asia (1.4) and in Eastern Africa and Middle Africa (2.0) [10]. The highest mortality rates in females were in Western Europe (6.6), in Northern Europe (5.7), and in Northern America and Southern Europe (each at 5.5), while the lowest rates are in South-Central Asia (0.86), in Middle Africa (1.1), and in Melanesia (1.6) [10].

The mortality rates increase with age in both the male and female populations (Fig. 1.4, Table 1.10). Roughly 90.0%, 419,597 out of 466,003 pancreatic cancer-related deaths occur after the age of 55 [1, 10, 11]. The mortality ASR increase was more pronounced in the female pop-

Table 1.9 (A) The six countries with the highest mortality age-standardized rates in the male population compared to the world's mortality rate. (B) The six countries with the lowest mortality age-standardized rates in the male population. (C) The six countries with the highest mortality age-standardized rates in the female population when compared to the world's mortality rate of pancreatic cancer. (D) The six countries with the lowest mortality age-standardized rates in females when compared to the world's mortality rate of pancreatic cancer. Data Sourced: GLOBOCAN 2020

(A) Countries with the highest mortality age-standardized rates of pancreatic cancer, males, all ages, in 2020

Populations (male)	Mortality, ASR[a]
World	5.3
Hungary	12.6
Uruguay	12.2
Armenia	11.5
Republic of Moldova	10.7
Latvia	10.6
Montenegro	10.6

(B) Countries with the lowest mortality age-standardized rates of pancreatic cancer, males, all ages, in 2020

Populations (male)	Mortality, ASR[a]
World	5.30
Malawi	0.46
Eswatini	0.57
Botswana	0.82
India	1.10
Pakistan	1.10
Bangladesh	1.10
Sri Lanka	1.10
Mozambique	1.10

(C) Countries with the highest mortality age-standardized rates of pancreatic cancer, females, all ages, in 2020

Populations (female)	Mortality, ASR[a]
World	3.8
Uruguay	8.5
Hungary	8.4
Finland	7.3
France, Guadeloupe	7.2
Austria	7.1
Czechia	7.0

Table 1.9 (continued)

(D) Countries with the lowest mortality age-standardized rates of pancreatic cancer, females, all ages, in 2020

Populations (female)	Mortality, ASR[a]
World	3.80
Pakistan	0.30
Comoros	0.47
Mozambique	0.52
Rwanda	0.52
Sri Lanka	0.60
Djibouti	0.61

[a]Per 100,000 people

ulation when compared to its male counterpart after the age of 55 [10].

Human Development Index

The incidence and mortality cases of pancreatic cancer were evaluated by low, medium, high, very high Human Development Index (HDI), which is a statistic composite index of life expectancy, education, and gross income. As reported in Table 1.11, pancreatic cancer's incidence and mortality ASRs are positively associated with human development for both sexes [10, 18]. The largest difference in incidence ASR was observed in the high HDI group from the medium HDI at 117.2% [10]. In parallel, there is a 121.4% difference in mortality ASR in the high HDI group [10].

Incidence Projections

The IARC provided their predicted number of new cases of pancreatic cancer in males, females, and both sexes, across the world and its six continents. The projected incidence of pancreatic cancer in the years 2025, 2030, 2035, and 2040 indicates upward trends in all

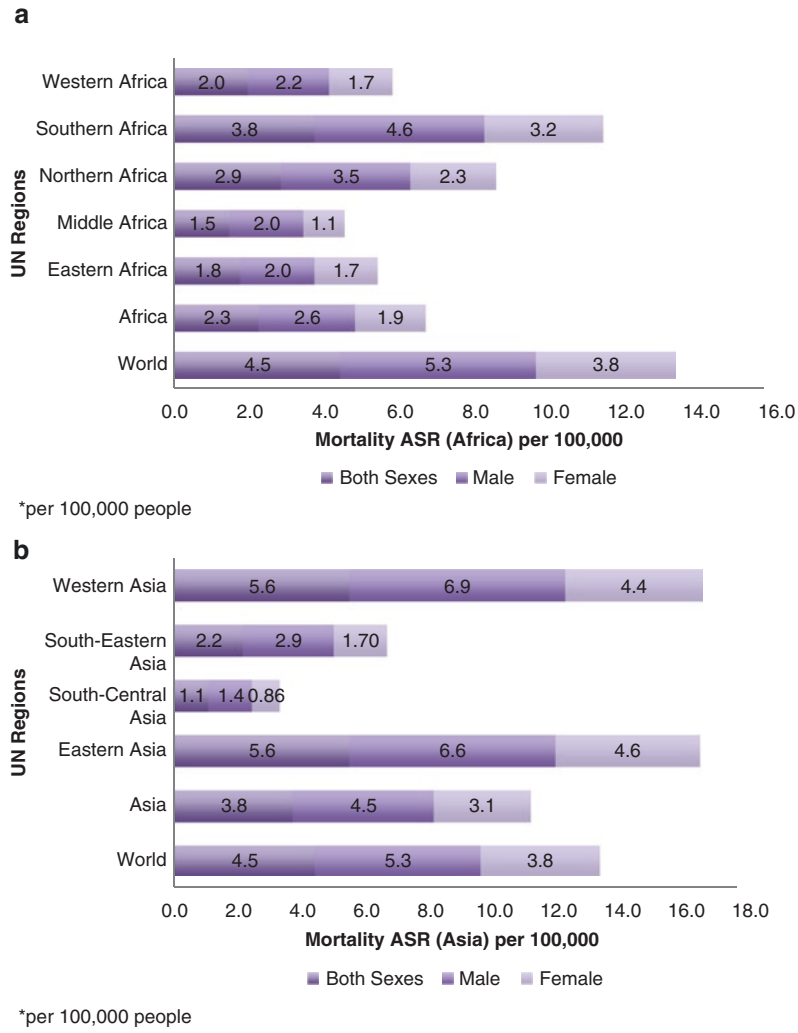

Fig. 1.3 (**a**) The estimated pancreatic cancer-related mortality age-standardized rates in UN African regions, including both sexes, males, and females, in 2020. (**b**) The estimated pancreatic cancer-related mortality age-standardized rates in UN Asian regions, including sexes, males, and females, in 2020. (**c**) The estimated pancreatic cancer-related mortality age-standardized rates in UN European regions, including both sexes, males, and females, in 2020. (**d**) The estimated rates of new pancreatic cancer in UN Latin America and the Caribbean regions, including both sexes, males, and females, in 2020. (**e**) The estimated pancreatic cancer-related mortality age-standardized rates in UN Northern American regions, including both sexes, males, and females, in 2020. (**f**) The estimated pancreatic cancer-related mortality age-standardized rates in UN Northern American regions, including both sexes, males, and females, in 2020. Data Sourced: GLOBOCAN 2020

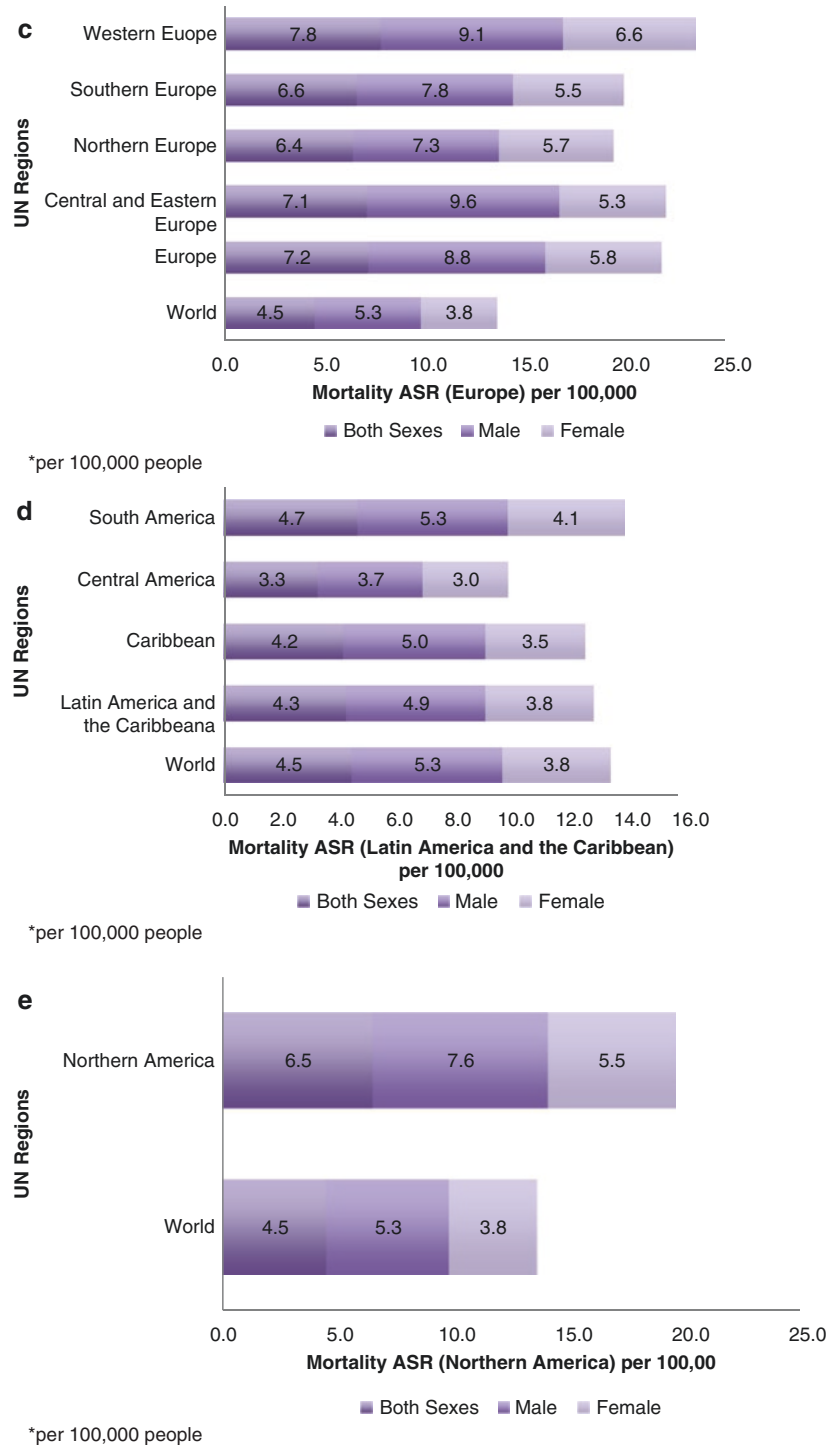

Fig. 1.3 (continued)