1

Global Cancer Control

1.1 Introduction: Needs and Prospects for Cancer Control

Cancer can quite easily be thought of as a *modern* disease but there are good reasons why this may only appear to be the case. Firstly, cancer and heart disease are the major diseases and causes of death in old age, and it was only really during the latter stages of last century that large proportions of people began living to the seventh, eighth and ninth decades of life—decades at which chronic diseases are commonest.

Life expectancy in Ancient Egypt was around 40 years; this fell during the Dark and Middle Ages before rebounding to the same level in the middle of the 19th century. The large increase in life expectancy to current levels (Table 1.1.1) has been brought about by the cure or control of a large number of otherwise fatal diseases such as plague, cholera, diabetes, malnutrition, diseases of infancy and other infectious diseases such as tuberculosis.

The declines in death rates over the roughly hundred-year period 1848–54 to 1971 in England and Wales are remarkable. Major killers such as tuberculosis have seen a drop in mortality from 2901 per million over the period 1848–54 to 13 per million in 1971. Scarlet fever, diphtheria, whooping cough, measles, smallpox, puerperal fever, syphilis, typhus and non-respiratory tuberculosis have been virtually eliminated as a cause of death (Table 1.1.2). This has been a golden era for medicine and public health.

A second point is that better clinical diagnosis has led to more cases of cancer being diagnosed, a proportion of which would have previously been missed. There has been a remarkable improvement in imaging [1] and other diagnostic techniques, which have contributed substantially to an increased chance of diagnosis and to a more accurate diagnosis of cancer.

While there are reasons for an artefactual increase in the cancer burden, there has undoubtedly been a real increase in the number of people who develop cancer due to an increased exposure to etiological agents. The impact of cigarette smoking on lung cancer is salutary in making what was an otherwise extremely rare form of cancer at the beginning of the twentieth century into the commonest cancer in many populations a century later.

Men			
Highest Life Expectancy		Lowest Life Expectancy	
Andorra	80.6	Swaziland	39.8
Iceland	80.2	Sierra Leone	41.0
Hong King	79.4	Angola	41.2
Japan	79.0	Mozambique	41.7
Switzerland	79.0	Zambia	42.1
Australia	78.9	Lesotho	42.0
Sweden	78.7	Central African Rep	43.3
Israel	78.6	Afghanistan	43.9
Macau	78.5	Zimbabwe	44.1
Canada	78.3	Rwanda	44.6
New Zealand	78.2	Liberia	44.8
Singapore	78.0	Guinea-Bissau	44.9
Norway	77.8	Congo	45.2
Spain	77.7	Nigeria	46.4
Cayman Islands	77.5	Somalia	46.9
Italy	77.5	Cote d'Ivoire	47.5
Netherlands	77.5	Burundi	48.1
Malta	77.3	Malawi	48.1
Women			
Highest Life Expectancy		Lowest Life Expectancy	
Andorra	86.6	Swaziland	39.8
Japan	86.1	Lesotho	42.3
Hong Kong	85.1	Mozambique	42.4
Spain	84.2	Zambia	42.5
Switzerland	84.2	Zimbabwe	42.7
France	84.1	Afghanistan	43.8
Australia	83.6	Sierra Leone	44.2
Italy	83.5	Angola	44.3
Iceland	83.3	Central African Rep	46.1
Virgin Islands (US)	83.3	Liberia	46.6
Sweden	83.0	Nigeria	47.3
Canada	82.9	Congo-Kinshasa	47.7
Faroe Islands	82.8	Rwanda	47.8
Israel	82.8	Guinee-Bissau	47.9
Macau	82.8	Malawi	48.4
Cayman Islands	82.7	Cote d'Ivoire	49.3
Puerto Rico	82.7	Somalia	46.9
Austria	82.6	South Africa	49.7

Table 1.1.1 *Countries with highest and lowest life expectancy in men and women, 2005-2010 (Abstracted from Pocket World in Figures (2008 Edition). The Economist, London).*

Isaac Adler (1849-1918) wrote the first major medical text dealing with the pathology and clinical aspects of primary lung cancer [2]. He wrote:

"Is it worthwhile to write a monograph on the subject of primary malignant tumours of the lung? In the course of the last two centuries an ever-increasing literature has accumulated around this subject. But this literature is without correlation, much of it buried in dissertations and other out-of-the-way places, and, with but a few notable exceptions, no attempt has been made to study the subject as a whole, either the pathological or the clinical aspect having been emphasised at the expense of the other, according to the special predilection of the author. On one point, however, there is nearly complete consensus of opinion, and that is that primary malignant neoplasms of the lungs are among the rarest forms of the disease. This latter opinion of the extreme rarity of primary tumours has persisted for centuries."

Similar to lung cancer, several other major modern diseases were newly described and evolved rapidly during the twentieth century. For example, according to Poole-Wilson et al. [3], myocardial infarction was first described in a patient in 1910 by Obrastzow and Straschenko [4] and by Herrick [5]. Acute appendicitis was first described by Reginald Fitz in 1886 [6].

Cancer is not a modern disease

Cancer is not a modern disease but has clearly existed for many centuries. It is however a more common phenomenon in man nowadays than previously, in large extent due to the growth of the world's population and the relatively advanced age to which people now live, since it is a disease that is more common in elderly ages than in younger ages.

Researchers have attempted to seek early evidence of cancer from study of fossil remains. A tumour has been reported from the tail of a dinosaur, but there remains some doubt as to whether this is a true malignant tumour or a callous consequent to an injury to the animal's tail, some 80 feet from its brain [7]. Moodie and Abel [8] then described a tumour of the dorsal vertebrae in a cretaceous mosasaur (a large lizard) but there was never conclusive proof of malignancy. This, once again, could likely have been the result of injury as was another lesion, described as an osteosarcoma, found in the fossilised remains of the femur of a cave bear [9].

Cause of Death	1848–54	1971
Tuberculosis	2901	13
Bronchitis, influenza	2239	603
Scarlet fever, diphtheria	1016	0
Whooping cough	423	1
Measles	342	0
Smallpox	263	0
URT infections	75	2
Cholera, dysentery	1819	33
Typhoid (typhus)	990	0
Non-Respiratory TB	753	2
Infections in Infants	1322	0
Puerperal fever	62	1
Syphilis	50	0
Other Infections	635	52

Table 1.1.2 *Death rates (per million) from various causes in England and Wales in 1848–1854 and 1971 (Data abstracted from Cairns [59])*

Evidence has been found in bony (skeletal) remains of both true bone tumours and destructive lytic lesions, and radiographic examination has also been able to detect smaller, occult deposits suggestive of disseminated disease [10]. The femur of a *homo erectus* (Pithecanthropus) dating from 450 000 BC initially gave the appearance of a tumour but could equally likely to have been *myositis ossificans*. There is also the possibility that a lesion found in the calvarium of a skeleton from the Twentieth Dynasty of Ancient Egypt (c. 1200 BC) exhibits malignant destruction of the jaw, sinus and palate with a surrounding zone of osteitis. Radiography has revealed 26 lesions in the skull of a man (aged around 30 years) with the appearance of multiple myeloma (or at least multiple secondary deposits) [11].

While there is suggestive but little conclusive evidence of cancer in fossilised or bony remains, there is clear evidence of the existence of cancer from study of Egyptian mummies. Granville [12] reported the dissection of an ancient Egyptian female mummy that revealed widespread disease of the ovaries with abdominal extensions, considered as bilateral malignant cystadenoma. Interestingly, while analysis of 88 adult and 5 child mummies revealed tumours of the bone, nasopharynx and mouth, they failed to find common modern-day tumours such as breast, colon, stomach and lung.

Cancer has been described by writers in ancient Greece, Rome and Persia, and it has been noted and treated in medieval texts. The American Egyptologist Edwin Smith brought to light what has become to be known as the Edwin Smith Surgical Papyrus, dating from about 2500 BC, which is devoted to surgical case histories, and number 45 in this series contains some of the earliest writings on cancer:

".....if thou examinest a [woman] having bulging tumours on [her] breast and thou findest that swellings have spread over [her] breast, it thou puttest they hand upon [her] breast upon these tumours thou findest them very cool, there being no fever at all therein when thy hand touches [her], they have no granulation, they form no fluid, they do not generate secretions of fluid and they are bulging to thy hand. Thou shouldest say concerning [her], "One having bulging tumours. There is no treatment."

(Translated by Professor James Breasted in 1930 [13]).

Another papyrus describes a tumour of the uterus treated by local vaginal application of fresh dates and limestone with and without pig's brain. Writings from ancient India (Ayuruedic books) suggest that cancer was able to be diagnosed correctly over 2500 years ago but was considered incurable. Tumours of the oral cavity, pharynx, oesophagus, pelvis and rectum are described, but no mention is made of cervix, breast, lung or bone cancers.

The aphorisms of Hippocrates of Cos (born 460 BC) contain a variety of references to malignant disease. Number 38 states: *"Every cancer not only corrupts the part it has seized but spreads further"*. Galen (131-200 AD) noted that *"cancerous tumours develop with greatest frequency in the breasts of women"*. He described a tumour raised above the skin, extending along the lymphatic vessels radially on all sides and often with red streaks: such tumours may ulcerate and discharge a dark, reddish, evil-smelling secretion. Galen likened the lesion to a crab: *karkinos* in Greek and *cancer* in Latin. He recognised that surgery was the only chance of cure and must be done at an early stage when excision of the whole lesion was possible.

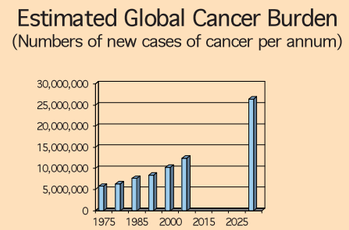
The captured Greek physician, Democedes, was called upon by King Darius of Persia to treat Atossa, the Queen, who had a lump in her breast that increased in size and eventually ulcerated: modesty had prevented her showing it to anyone until it had reached a large size.

Little progress or mention was made of cancer until the 18th century, when Bernard Peyrihle proposed a viral theory of cancer. John Hunter gave a long account of surgery for cancers of the female breast, uterus, lips and stomach and advised that tumours may be hereditary, and that palpitation of the mass should be gentle in case rough handling spread the disease. He noted that *"no cure has been found"*. In 1775, Percival Pott [14] described the occupational cancer of the scrotum that occurred in chimney sweeps. In 1761, John Hill suggested that snuff was responsible for nasal cancer and polyps [15]. Prior to this, in 1743 Ramazzini [16] had reported an excess of breast cancer in nuns in Padua.

Treatment advances came in the nineteenth century. In 1881, Billroth performed a successful gastrectomy for stomach cancer and in 1884, Godlee removed a brain tumour. William Marsden founded his Cancer Hospital in 1851 with two aims: care of the cancer patient and cancer research. The century closed with the discoveries of Roentgen and the Curies, which led to radiological diagnosis and radiotherapy, and the work of Beatson on hormonal manipulation in breast cancer.

Different forms of cancer have been recognised and treated for centuries, and it is advances in civilisation and the associated improvement in life expectancy that has contributed to making cancer such a common disease worldwide. In the United Kingdom in 1880 approximately half of the population died before 45 years of age and this decreased to around 3% in 1980. In 1880 in the United Kingdom, 25% of the population reached the age of 70; in 1990 the corresponding figure was 70% [17]. More recently, the effective prevention of cardiovascular diseases led to an acceleration of the decline of premature mortality and an increase in life expectancy and, inadvertently, cancer. More and more men and women are alive today at ages when cancer is more common than ever before, and the phenomenon is not restricted to a handful of developed countries.

Is such an increase as estimated for the year 2030 in the global cancer burden consistent with current trends? In 1975 it was estimated [1] that the global cancer burden was 5.9 million. The figure contains subsequent estimates made for 1980 [2], 1985 [3], 1990 [4], 2000 [5], 2002 [6] and 2030 (in this chapter). The global burden doubled in the last third of the twentieth century and the trend from this year (2008) to 2030 looks feasible when the long-term trends are examined.



1. Parkin DM, Stjernswärd J and Muir CS. Estimates of the worldwide frequency of twelve major cancers. Bull World Health Organ. 1984;62(2):163-82

2. Parkin DM, Läärä E, Muir CS. Estimates of the worldwide frequency of sixteen major cancers in 1980. Int J Cancer. 1988 Feb 15;41(2):184-97.

3. Parkin DM, Pisani P, Ferlay J. Estimates of the worldwide incidence of eighteen major cancers in 1985. Int J Cancer. 1993 Jun 19;54(4):594-606

4. Parkin DM, Pisani P, Ferlay J. Estimates of the worldwide incidence of 25 major cancers in 1990. Int J Cancer. 1999 Mar 15;80(6):827-41

5. Parkin DM. Global cancer statistics in the year 2000. Lancet Oncol. 2001 Sep;2(9):533-43.

6. Ferlay J, Bray F, Pisani P and Parkin DM. GLOBOCAN 2002: Cancer Incidence, Mortality and Prevalence Worldwide IARC CancerBase No. 5. version 2.0, IARCPress, Lyon, 2004.

Priority setting requires knowledge of the cancer burden

Priority setting for cancer control and cancer services in any region needs to be based on knowledge of the cancer burden and the local mix of predominant cancer types. Unfortunately, neither the number of new cases of cancer nor the number of deaths caused by cancer is available from many parts of the world—in 2000, less than 20% of the world's population was covered by Cancer Registration and 35% by vital statistics schemes based on medically-certified cause of death. Furthermore, this coverage was not spread equally over the globe: in Africa less than 13% of the population was covered by such schemes, and in Asia about 9% was covered; by contrast, 95% of the population of Latin America was covered. The corresponding figures for cancer incidence statistics was 8% for Africa, 7% for Asia and 13% in Latin America.

The International Agency for Research on Cancer (IARC) estimated that for the year 2008 there were 12.4 million incident cases of cancer, 7.6 million deaths from cancer and 28 million persons alive with cancer within five years from initial diagnosis. IARC also estimated that just over half of incident cases and two thirds of cancer deaths arise in low- and medium-income countries. In 2008, the world population was estimated to be 6.7 billion and was expected to rise to 8.3 billion by 2030 [18]. During this period the populations of high-income countries are expected to increase by 4% while the increase is expected to be approximately 30% in low- and medium-income countries. Additionally, the proportion of the population in low- and medium-income countries aged over 65 is expected to increase by 5% to 10%. In view of the strong association between cancer rates and age, these will combine to increase the cancer burden by 2030, with low- and medium-income countries most affected.

There are several clearly identified causes of cancer [19-22] and several strategies that can lead to reductions in cancer incidence and mortality [23]. Currently, the most common forms of cancer differ between high-income countries and the remainder. In high-income countries, cancers of the lung, breast, prostate and colorectum dominate, and one third of cancers are caused by tobacco use and 10% by chronic infection [24]. Cancer control priorities include tobacco control, (high-tech) screening for small tumours, and curative treatment.

In low-resource and medium-resource countries, cancers of the stomach, liver, oral cavity, and cervix dominate [25,26]. This pattern is changing rapidly, with large increases in many parts of the world where lung, breast, and colorectal cancer have been historically uncommon. One quarter of the cancer burden in low-resource countries appears to be attributable to chronic infection, but 12% is currently caused by tobacco, and this proportion is growing [26]. Cancer control priorities in these countries include tobacco control and (low-tech) screening for down-staging, with treatment frequently aimed at palliation.

The great problems facing low- and medium-resource countries into this century are the growth and ageing of the population and the *westernisation* of their lifestyle, particularly the growth in the prevalence of tobacco smoking [25]. Changes in lifestyle habits including changing nutritional practices, increase in sedentary lifestyle, weight gain and obesity and sociological changes, notably increasing age at first birth and decreasing parity in women, are leading to large increases in breast and colorectal cancer in particular.

Tobacco is the best identified human carcinogen and is carcinogenic in all its forms of use [27,28]. It is clear, and has been for several years now, that the effect of tobacco on cancer risk, and indeed on overall mortality, is far in excess of any other common risk factor or treatment effect [29]. Information nowadays taken for granted (*half of smokers die of a smoking-related disease; half of these deaths are in middle age; each smoking-related death in middle age loses over 20 years of a non-smoker's life expectancy; there are over twenty fatal diseases causally linked to cigarette smoking; even if a smoker stops smoking in middle age he starts to win back some of non-smokers' life expectancy*), has evolved from the extensive follow-up of the British Doctors study [30].

Tobacco use has taken hold in populations in low- and medium-resource countries, and substantial increases have taken place in smoking prevalence in recent years. Given the substantial delay—which approaches 40 years—between big changes in smoking prevalence in populations being reflected in big changes in disease rates, the peak of the tobacco-smoking related cancer epidemic in low- and medium-countries has still to materialise. The Tobacco Epidemic will be driving the Cancer Epidemic in low- and medium-resource countries for years to come.

Low-resource and medium-resource countries are, arguably, harder hit by cancer than the high-resource countries [25]. Low-income countries are those with annual gross national income per capita of less than US$765. Such countries often have a limited health budget and a high background level of communicable disease. Cancer treatment facilities are not universally available, and life-extending therapies are often unavailable generally for economic reasons. Cancer and other chronic diseases, which are becoming more common, can cause devastating damage.

Middle-resource countries are those with an annual gross national income *per capita* of less than US$9300. Such countries risk being somewhat overlooked as high-income countries

increasingly focus on (expensive) new technologies and drugs to treat cancer, and many seek to help provide basic diagnostic and treatment facilities in low-income countries.

Many middle-income countries have diagnostic and treatment structures in place but face severe economic pressure to upgrade equipment and to pay for the new drugs used to treat cancer. Many hospitals need to be upgraded to high-income country standards and there is a need to accelerate training and to increase in the complement of specialised oncologists, radiotherapists, oncology nurses and all other medical, paramedical and technical personnel necessary. The situation in two middle-income countries, Hungary and Turkey, is summarised in the boxes in this chapter.

The first big step towards cancer prevention and control world-wide is to understand the magnitude and nature of the cancer burden in different regions of the world and then move towards an understanding of avoidable causes and other priorities. Recent increases in data availability in low-income countries allow a better, although still imperfect, picture of the global cancer burden.

Evolution of the global cancer burden

Around the year 2000, less than 20% of the world's population was covered by cancer registration and 33% by mortality schemes based on medically certified deaths. However, this is not equally spread over the globe: in Africa less than 13% of the population is covered by a death certificate scheme, in Asia only 8.5% of the population is covered, and 95% of the population of Latin America is covered. The corresponding population coverage for cancer incidence statistics is 8% in Africa, 7% in Asia and 10% in Latin America.

In the absence of data from large portions of the population, it is necessary to make estimations; the methods used to compute these are described in detail in *GLOBOCAN 2002* [31]. In summary, incidence and mortality rates (number of cases or deaths per 100 000 persons per year) were estimated by country, sex and cancer site, for 5 age groups (0-14, 15-44, 45-54, 55-64, 65+) using the most recently available data collected at the IARC up to the year 2004 or 2005 wherever possible [32-34]. The numbers of cases and deaths were computed by multiplying these estimated rates by the estimated 2008 population estimates for the corresponding country [18]. The results are presented according to World Health Organization Region.

Mortality data are available from the WHO Mortality Database [35] are available by sex and cancer site up to 2005 for many countries of the world, although the degree of detail and quality of the data vary considerably. Only regional mortality data are available for some countries, and these data were used to estimate national rates. For countries where mortality data were unavailable or were known to be of poor quality, estimates of mortality were made from incidence, by use of country or region-specific survival.

Various methods were used to estimate the sex- and age-specific incidence rates of cancer for a country. Wherever available, the most recent national incidence rates or estimates have been used. For countries where local or regional incidence and national mortality data were available, national incidence was estimated by applying a set of age-, sex- and site-specific incidence/mortality ratios, obtained from the aggregation of representative cancer registries data, to the country's national mortality. Incidence/mortality ratios are obtained from a Poisson regression model of the selected registry incidence data offset by corresponding mortality data, including terms for sex and age. This method is regularly used by the Descriptive Epidemiology Group of IARC, and has been shown to estimate cancer incidence accurately. Where local and/or regional incidence data are available and no information on death is available, regional rates were used to estimate national rates. For those countries for which no data were available, the country-specific rates were calculated from the simple average of those of neighbouring countries as described in *GLOBOCAN 2002* [31].

Global Cancer Burden

It has been estimated that 58.8 million people died in 2004 [36]. Half of these deaths involved people less than 60 years of age, and there were 22 million deaths in people aged 70 years and older and 10.7 million deaths in people aged 80 years and over. Approximately one death in five was in a child under 5 years of age. Deaths from cancer represent around one eighth of all deaths, although there will be more people who will have died *with cancer* although it was not the direct cause of death.

Mortality data provide important information but are restricted to giving insight into the absolute lack of health in any population. Cancer incidence data have the substantial advantage of providing a clearer picture of the cancer problem and have a key role to play in service planning and related activities. It is also clear, at least in qualitative terms, that the cancers which are common in certain parts of the world are not so common in others. It is essential to have estimates of the burden of cancer and its different types in different parts of the world.

WHO African Region (AFRO)

The estimated population of the AFRO Region in 2008 was 812 million (404 million men and 408 million women), most of whom are young (Figure 1.1.1a). The effectiveness of national population censuses in several African countries is not reliable, and a very small proportion of the total population of the AFRO Region is covered by medically-certified causes of death (7.2% of the population) or is covered by population-based cancer registries which provide incidence data (8.3% of population). The estimates of population and cancer burden for AFRO have a large measure of inaccuracy present.

It is estimated that there were 667 000 incident cases of cancer in 2008 (314 000 in men and 353 000 in women) and 518 000 deaths from cancer (approximately 252 000 in men and 266 000 in women) (Figure 1.1.1b). In men, the commonest cancer, and the commonest cause of cancer-related mortality, was Kaposi Sarcoma, which is an undoubted consequence of the HIV/AIDS epidemic, followed by cancers of the liver, prostate and oesophagus. In women, cervix cancer was the most common form of cancer and cancer death. Breast cancer was second most common in incidence and mortality, followed by liver cancer and Kaposi Sarcoma (Figure 1.1.1b).

WHO Region of the Americas (AMRO/PAHO)

Each country in the Region of the Americas (AMRO/PAHO) has a national census. In North America (United States of America and Canada) the entire population is covered by a national death certificate scheme and 90% of the population by population-based cancer registration. In Central and Latin America, 95% of the population is covered by a national mortality scheme and 13% by population-based cancer registration. Estimates will be better in North America than in Central and Latin America.

The estimated population of the AMRO/PAHO region was 831 million in 2000, with marginally more women than men (Figure 1.1.2a). The population pyramid demonstrates a population that contains a significant number of middle-aged men and women, quite dissimilar to the young population of the AFRO Region (Figure 1.1.2a).

There were an estimated 2 617 000 incident cases of cancer in 2008, 1.338 million in men and 1.279 million in women. Overall, there were an estimated 1 258 000 deaths from cancer in 2008: in men there were an estimated 651 000 deaths from cancer and 607 000 cancer deaths in women. Prostate cancer was the commonest incident cancer in men although there were more deaths from lung cancer (Figure 1.1.2b). Lung cancer was the second commonest incident form of cancer in men followed by cancer of the colorectum, stomach and

Fig. 1.1.1 *Population pyramid (Figure 1.1.1a), Cancer Incidence and Mortality (Figure 1.1.1b) in World Health Organization African Region (AFRO).*

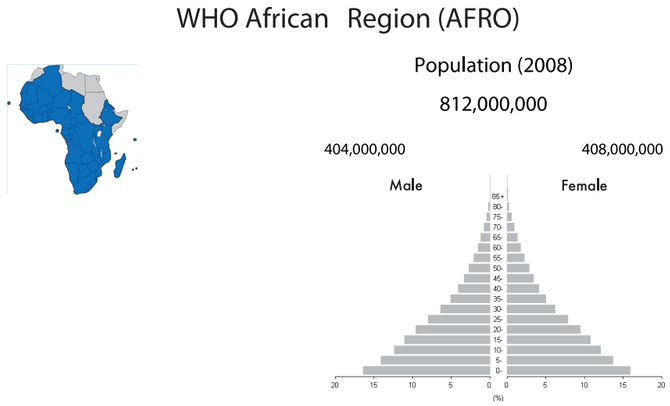


Fig. 1.1.1a

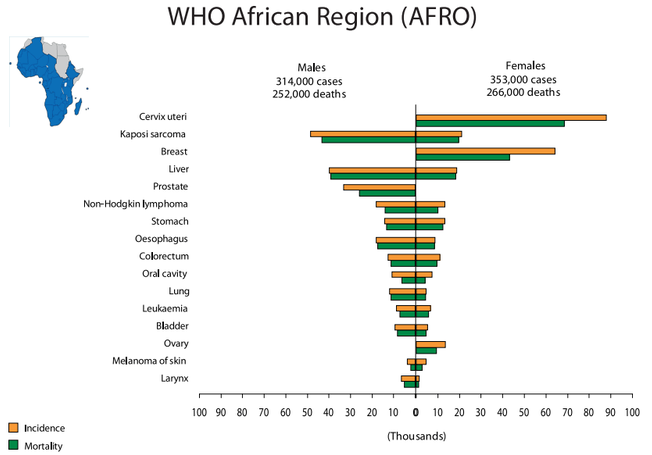


Fig. 1.1.1b

lymphoma (Figure 1.1.2b). In women, breast cancer was the commonest incident form of cancer although, as in men, there were more deaths from lung cancer. Lung cancer was the second commonest form of cancer in women followed by colorectal cancer, cervix cancer and cancer of the corpus.

There are substantial differences between North America (United States and Canada) and Central and South America. The population pyramids of these regions are remarkably different. In North America (total population 346 million) there is a clearly ageing population (Figure 1.1.3a) while in Central and Latin America (total population 577 million) there is a young population (Figure 1.1.3b).

In North America there were an estimated 1 606 000 incident cases of cancer (849 000 in men and 757 000 in women) and 669 000 deaths from cancer (349,000 in men and 320,000 in women) in 2008. Prostate cancer clearly predominates incidence, followed by lung cancer, colorectal cancer, bladder cancer, melanoma and lymphoma (Figure 1.1.3c). Lung cancer is the commonest form of death from cancer, followed by prostate cancer and colorectal cancer (Figure 1.1.3c). In women, breast cancer is the commonest incident form of cancer, followed by cancer of the lung, colorectal cancer and cancer of the corpus (Figure 1.1.3c). Lung cancer is the commonest cause of cancer death in women, followed by breast cancer and colorectal cancer (Figure 1.1.3c).

In the southern part of the PAHO Region (Central and South America and the Caribbean) in 2008 there were 1 011 000 incident cases of cancer (489 000 in men and 522 000 in women) and 589 000 cancer deaths (302 000 in men and 287 000 in women). In men the commonest incident form of cancer is prostate cancer followed by lung cancer, stomach cancer and colorectal cancer (Figure 1.1.3d). Lung cancer is the most frequent cancer cause of death followed by prostate, stomach and colorectal (Figure 1.1.3d). In women, the commonest form of cancer is breast cancer followed by cervix

Fig. 1.1.2 *Population pyramid (Figure 1.1.2a), Cancer Incidence and Mortality (Figure 1.1.2b) in World Health Organization PAHO Region (PAHO).*

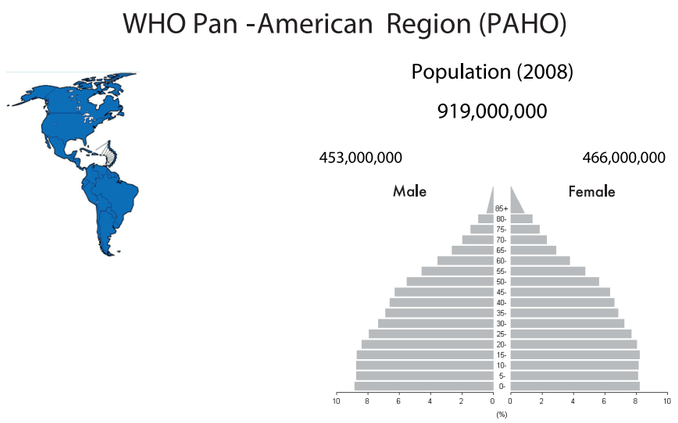


Fig. 1.1.2a

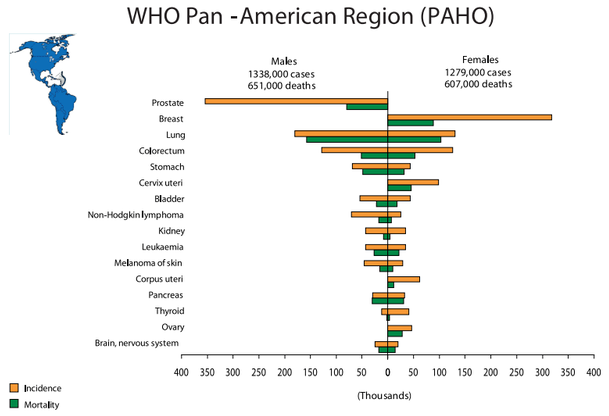


Fig. 1.1.2b

Fig. 1.1.3 *Population pyramid for Northern American component (Figure 1.1.3a) and Central and Latin American component (Figure 1.1.3b) and Cancer Incidence and Mortality for Northern American component (Figure 1.1.3c) and Central and Latin American component (Figure 1.1.3d) for World Health Organization PAHO Region.*

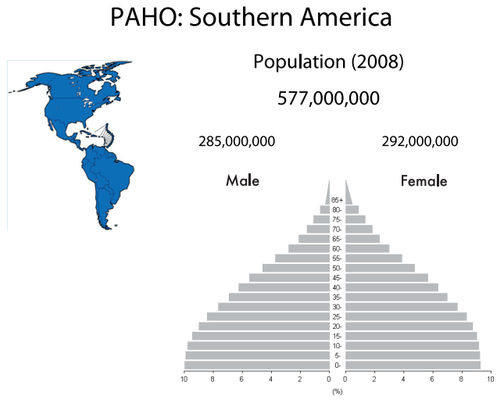


Fig. 1.1.3a

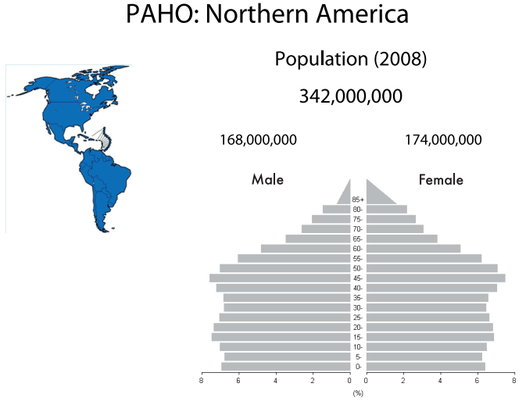


Fig. 1.1.3b

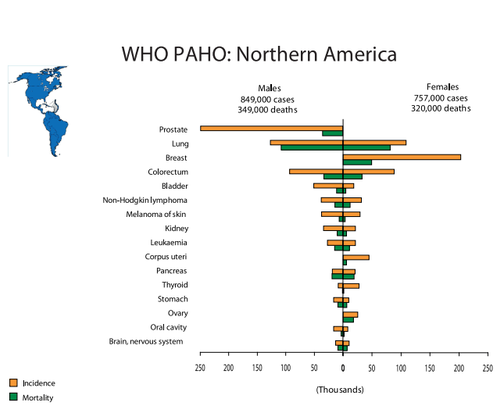


Fig. 1.1.3c

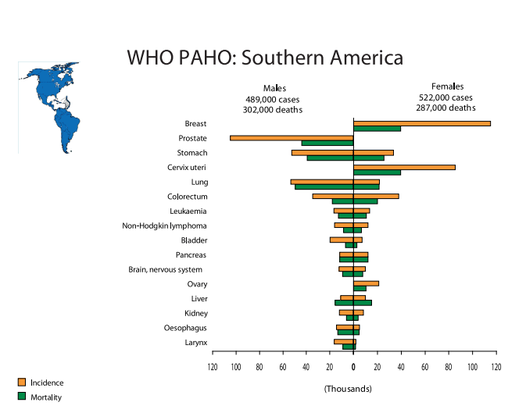


Fig. 1.1.3d

cancer, colorectal cancer, stomach cancer and lung cancer. Breast cancer, cervix cancer, stomach cancer, lung cancer and colorectal cancer are the commonest forms of cancer death (Figure 1.1.3d).

WHO South East Asia Region (SEARO)

The effectiveness of national population census in several Asian countries is uncertain, and only a small proportion of the total population of the SEARO Region has mortality data available or is covered by population-based cancer registries which provide incidence data. When considering the estimates of population and cancer burden for SEARO, these observations must be taken into account while also noting that the overall burden and the cancer pattern is dominated by India, which comprises 67% of total population of the Region.

It is estimated that the population of the SEARO Region in 2008 was 1.768 billion, with a slight predominance of men than women. The population pyramid demonstrates a young population (Figure 1.1.4a).

It is estimated that in 2008, there were 1 589 000 incident cases of cancer in 2008 (758 000 in men and 831 000 in women) and 1 072 000 deaths from cancer (approximately 557 000 in men and 515 000 in women) (Figure 1.1.4b). In men, the commonest cancer was lung cancer, followed by oral cancer, pharyngeal cancer, oesophagus cancer, stomach cancer, colorectal cancer, liver cancer and larynx cancer (Figure 1.1.4b). Lung cancer was the commonest form of cancer deaths in men (Figure 1.1.4b). If oral cavity and pharynx are combined, then this site is the predominant site of incident cancer and cancer death in men. In women, cervix cancer and breast cancer were the commonest incident and fatal forms of cancer by a considerable margin (Figure 1.1.4b). The different case mix between men and women results in more deaths in men than in women, based on fewer incident cases.

Fig. 1.1.4 *Population pyramid (Figure 1.1.4a), Cancer Incidence and Mortality (Figure 1.1.4b) in World Health Organization South-East Asia Region (SEARO).*

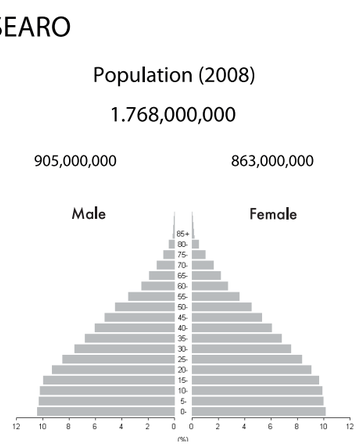


Fig. 1.1.4a

Fig. 1.1.4b

WHO Eastern Mediterranean Region (EMRO)

As in SEARO and WPRO, the effectiveness of national population census in several countries is uncertain, and only a small proportion of the total population of the EMRO Region has mortality data available or is covered by population-based cancer registries that provide incidence data. When considering the estimates of population and cancer burden for EMRO, these must be taken into account.

The estimated 2008 population of the EMRO Region was 561 million, with a slight predominance of men over women. The population pyramid demonstrates a young population (Figure 1.1.5a).

It is estimated that in 2008, there were 467 000 incident cases (228 000 in men and 239 000 in women) and 323 000 deaths from cancer (approximately 228 000 in men and 153 000 in women) (Figure 1.1.5b). In men, the commonest cancers were lung cancer and bladder cancer, although there were more deaths from lung cancer (Figure 1.1.5b). In women, breast cancer was the commonest incident and fatal form of cancer by a considerable margin from cervix cancer (Figure 1.1.5b).

WHO Western Pacific Region (WPRO)

The effectiveness of national population census in several Asian countries is uncertain, and only a small proportion of the total population of the WPRO Region has mortality data available or is covered by population-based cancer registries that provide incidence data. When considering the estimates of population and cancer burden for WPRO, these observations must be taken into account while simultaneously noting that the cancer pattern and burden are driven by China, which comprises 75% of the total population of the Region, and where there is a high frequency of cancers with a poor prognosis (lung, liver, oesophagus, stomach). A high mortality/incidence ratio should be expected in this region.

Fig. 1.1.5 *Population pyramid (Figure 1.1.5a), Cancer Incidence and Mortality (Figure 1.1.5b) in World Health Organization Eastern Mediterranean Region (EMRO).*

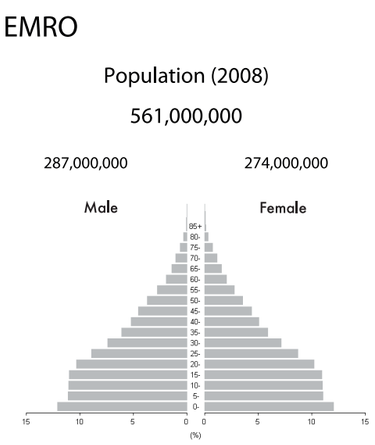


Fig. 1.1.5a

Fig. 1.1.5b

The population of the WPRO Region in 2008 was estimated to be 1.780 billion, with marginally more men than women (Figure 1.1.6a). The population pyramid demonstrates an ageing population with a bulge in the numbers in middle age (Figure 1.1.6a).

It is estimated that in 2008 there were 3 689 000 incident cases of cancer (2 213 000 in men and 1 476 000 in women) and 2 575 000 deaths from cancer (approximately 1 629 000 in men and 946 000 in women) (Figure 1.1.6b). In men, the commonest incident cancer was stomach cancer, closely followed by lung cancer and liver cancer and then oesophagus cancer and colorectal cancer (Figure 1.1.6b). Lung cancer, liver cancer, stomach cancer and oesophageal cancer were the commonest forms of cancer death in men (Figure 1.1.6b). In women, breast cancer was the commonest incident form of cancer, followed by stomach cancer, lung cancer, colorectal cancer, liver cancer and cervix cancer (Figure 1.1.6b). Lung cancer was the commonest cancer cause of death in women followed by stomach cancer, liver cancer, oesophagus cancer, breast cancer and colorectal cancer (Figure 1.1.6b).

WHO European Region (EURO)

National censuses of the population in countries of the EURO Region provide fairly good data. In addition, 98.3% of the population of the Region is covered by mortality statistics and 36.5% of the population is covered by population-based cancer registration.

The population of the EURO Region in 2008 was estimated to be 891 million, with marginally more women than men (Figure 1.1.7a). The population pyramid demonstrates an ageing population with a bulge in the numbers in middle-age and decreasing numbers of births in younger age categories (Figure 1.1.7a).

It is estimated that in 2008 there were 3 422 000 incident cases of cancer (1 821 000 in men and 1 601 000 in women) and 1 847 000 deaths from cancer (approximately 1 034 000 in men and 813 000 in women) (Figure 1.1.7b). In men, the commonest incident cancer was lung cancer followed by prostate cancer, colorectal cancer, bladder and stomach cancer (Figure 1.1.7b). Lung cancer, colorectal cancer, prostate cancer and stomach cancer were the commonest forms of cancer death in men (Figure 1.1.7b). In women, breast cancer was the commonest incident form of cancer, followed by colorectal cancer, lung cancer, corpus cancer and stomach cancer (Figure 1.1.7b). Breast cancer was also the commonest cancer cause of death in women, followed by colorectal cancer, lung cancer and stomach cancer (Figure 1.1.7b).

Countries of Central and Eastern Europe have experienced an ongoing economic transition for over a decade. It was decided to restrict attention to the countries of the WHO EURO Region that were outside the European Union and the European Economic Area. This provided a sub-region with a total population of 413 million. The population pyramid demonstrates a reduced number of births in recent years and a marked predominance of women at older age groups (Figure 1.1.8a).

There were an estimated 1 049 000 incident cases of cancer in 2008 (523 000 in men and 526 000 in women) and 644 000 cancer deaths (359 000 in men and 285 000 in women) (Figure 1.1.8b). The commonest incident forms of cancer in men were lung cancer, stomach cancer, colorectal cancer, prostate cancer and bladder cancer (Figure 1.1.8b). Lung cancer, stomach cancer and colorectal cancer were the commonest forms of cancer death (Figure 1.1.8b). In women, breast cancer was the commonest form of cancer followed by colorectal cancer, stomach cancer, cervix cancer and corpus cancer (Figure 1.1.8b). Breast, colorectal and stomach cancer were the commonest forms of cancer death in women (Figure 1.1.8b).

Fig. 1.1.6 *Population pyramid (Figure 1.1.6a), Cancer Incidence and Mortality (Figure 1.1.6b) in World Health Organization Western Pacific Region (WPRO).*

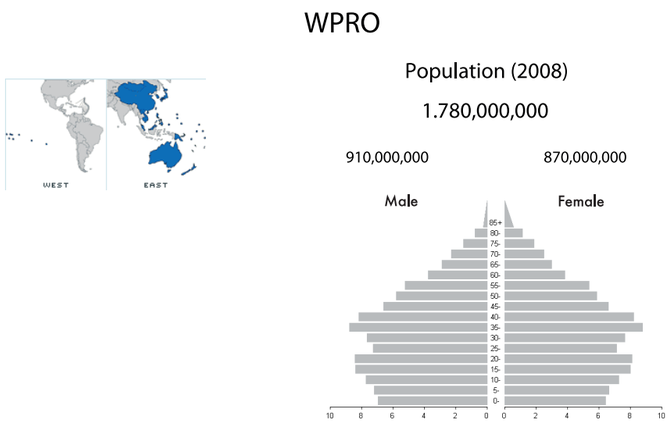


Fig. 1.1.6a

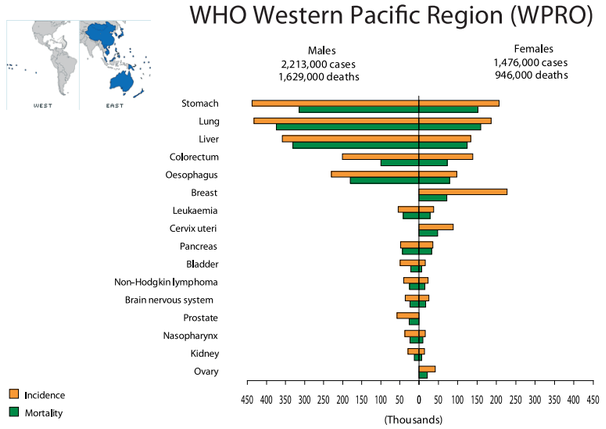


Fig. 1.16b

Fig. 1.1.7 *Population pyramid (Figure 1.1.7a), Cancer Incidence and Mortality (Figure 1.1.7b) in World Health Organization European Region (EURO).*

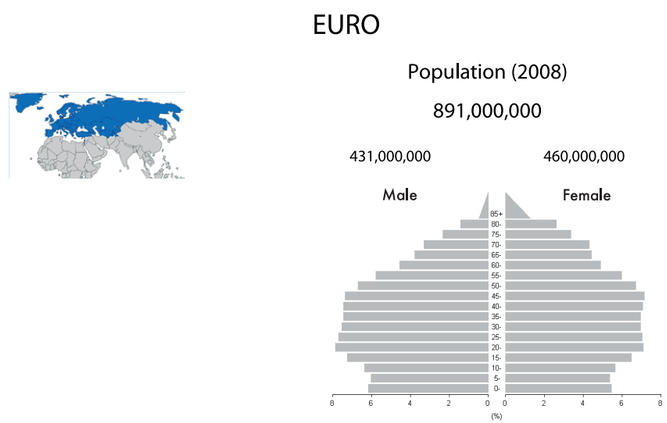


Fig. 1.1.7a

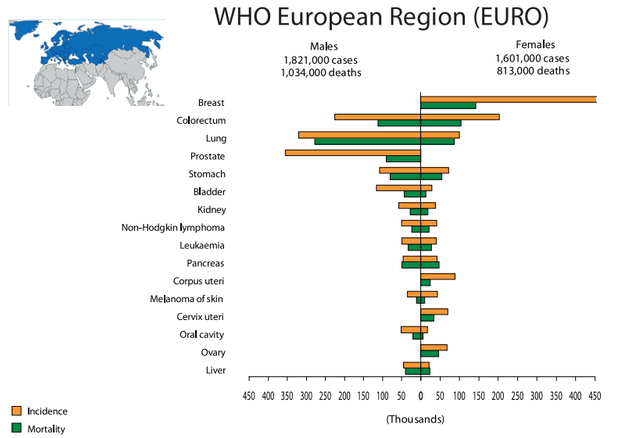


Fig. 1.1.7b

Worldwide

Globally, there were an estimated 12.4 million incident cases of cancer in 2008 (6 672 000 in men and 5 779 000 in women) and 7.6 million deaths from cancer (4 293 000 in men and 3 300 000 in women). Over half of the incident cases occurred in residents of four WHO regions with a large proportion of countries of low- and middle-income—AFRO, EMRO, SEARO and WPRO (Figure 1.1.9). Globally, lung cancer was the commonest incident cancer and cause of cancer-related mortality in men; in women, the most common incident cancer and cause of cancer-related death was breast cancer.

The global cancer burden: Factors driving the increase

There are three clear scenarios under which the global cancer burden could increase over time. First of all, the increase in the world's population anticipated from 6.1 billion in 2000 through 6.7 billion in 2008 to attain 8.3 billion by 2030 will lead to an increase in the cancer burden even if the age-specific rates remain constant. Secondly, given the very large increases in cancer risk with age, if the population size and the age-specific rates remain constant, then the burden will increase if the population ages. Figure 1.1.10 clearly shows that the world population will age considerably by 2030 as well as increasing significantly.

Aging is a major issue for the future cancer burden. Aging has proceeded more gradually in more developed countries than in less developed countries, affording these nations time to adjust to this structural change. Japan is the major exception, doubling its percentage of population age 65 or older in just 26 years. Other countries in East and Southeast Asia (especially China, South Korea, Taiwan and Thailand) are on a similarly rapid trajectory, fuelled by dramatic and relatively recent drops in fertility. It took 115 years for the proportion of France aged 65 and over to double from 7% (1865) to 14% (1980). In Singapore it will take

Fig. 1.1.8 *Population pyramid (Figure 1.1.8a), Cancer Incidence and Mortality (Figure 1.1.8b) in World Health Organization European Region (EURO) with European Union and European Economic Area countries omitted.*

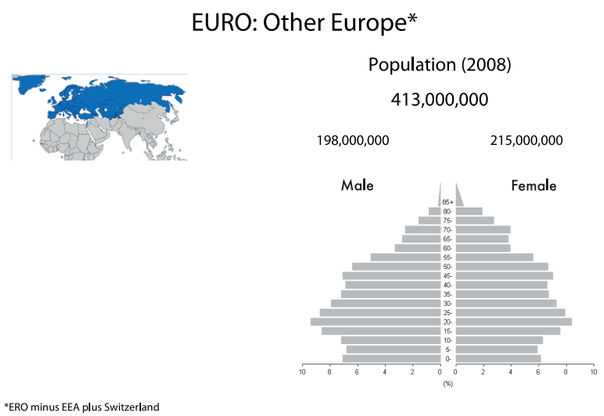


Fig. 1.1.8a *Population Pyramid for modified EURO Region, 2008*

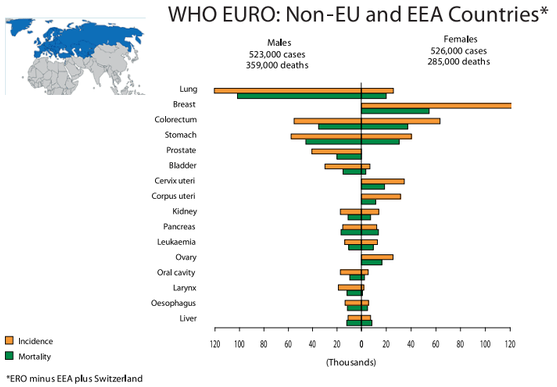


Fig. 1.1.8b

**WHO EURO Region minus European Union Member States (Austria, Belgium, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Poland, Portugal, Slovakia, Slovenia, Spain, Sweden and United Kingdom) and members of the European Economic Area (Iceland and Norway) and Switzerland.*

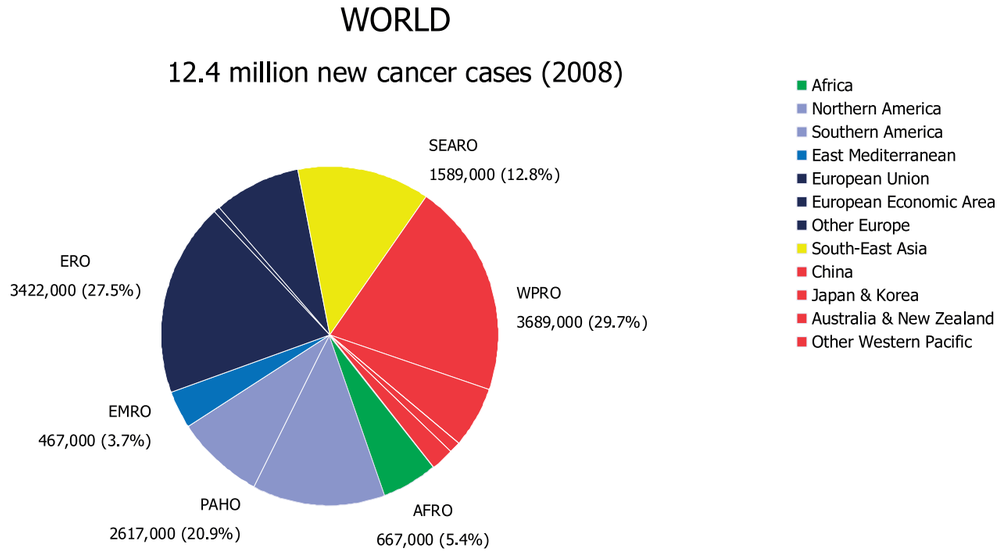


Fig. 1.1.9 *Distribution of Global Cancer burden by World Health Organization Region (2008)*

an estimated 19 years for the proportion of the population to double from 7% (2000) to 14% (2019)(Figure 1.1.11).

In China, due to vast improvements in health over the past five decades, life expectancy at birth has increased by two thirds, from 40.8 to 71.5 years, between 1955 and 2005. The percentage of elderly people (over 65) in China is projected to triple from 8 percent to 24 percent between 2006 and 2050. Because chronic health problems become more common in old age, China's population aging has led to increases in the country's prevalence of chronic disease and disability [37,38].

The third element that can lead to an increase in the cancer burden, even when the population size remains constant and the age distribution remains unchanged, is an underlying increase in the incidence rates. In France, cancer incidence rates increased by 1.3% per annum between 1978 and 2000 [19,21]. In the Indian cancer registries, between 1983 and 1997, the incidence rate increased at an annual rate of 0.5% per annum. In China (Qidong), between 1973 and 1997, the incidence rate increased at an annual 1.4% per annum. In Latin American registries between 1985 and 1997 the incidence rate increased at an annual rate of 1.0% per annum [39-46].

The growth and ageing of the world's population and the continual increase in the underlying incidence rates in low- and middle-income countries will contribute to increases in the global cancer burden. The global cancer burden under a range of scenarios of percentage increases is presented in Table 1.1.3. It is clear that population growth and ageing contribute much more to the future cancer burden than an underlying increase in the incidence rates (Table 1.1.3). Under the zero increase in cancer incidence scenario, the global burden will increase from 10.9 million in 2002 to nearly 20 million in 2030. Similar figures and conclusions are available for mortality data (Table 1.1.4).

By extrapolation of these data, taking into account demographic changes and factoring in a yearly increase in cancer incidence of 1%, it could be expected that by 2030 there will be approximately 26.4 million incident cases of cancer and 17.0 million cancer deaths a year (Table 1.1.4). The extrapolations made are likely to produce conservative estimates of the cancer burden

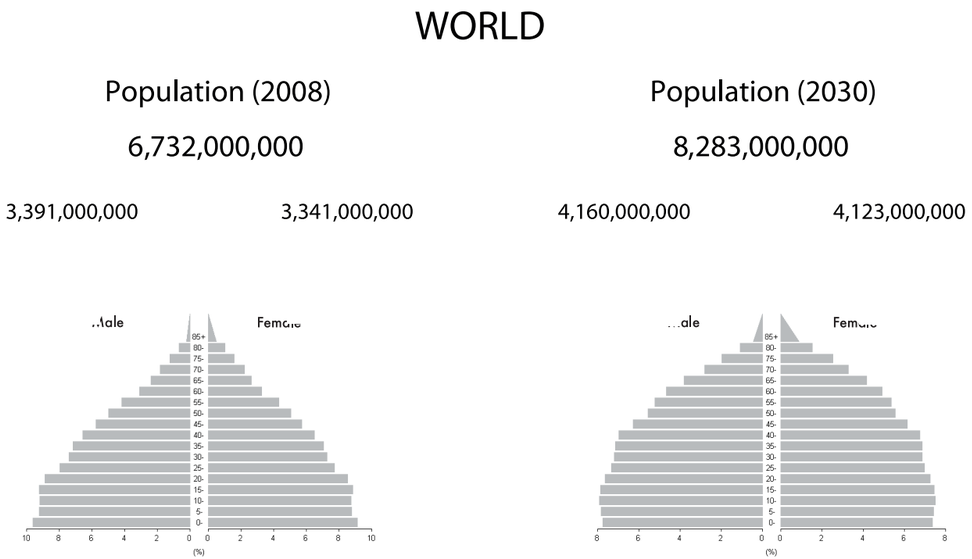


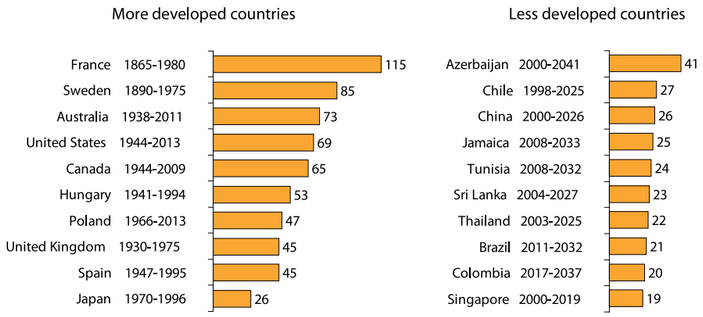
Fig. 1.1.10 *Estimates of global population by gender and age, 2000 and 2030*

when the 1% annual increase in incidence rates is assumed.

Action Required. At present, the most common forms of cancer differ between high-resource countries and those of low and middle resource. In high-resource countries, cancers of the lung, breast, prostate and colorectum dominate; a third of cancers are caused by tobacco use and 10% by chronic infection. In countries of low and middle resources, cancers of the stomach, liver, oral cavity and pharynx and cervix dominate; a quarter of these seem to be caused by chronic infection, although the proportion of cancer caused by tobacco is growing. However, the pattern is changing rapidly, with large increases in many parts of the world where lung, breast and colorectal cancer have been historically uncommon.

Priority setting for cancer control and cancer services in any region needs to be based on knowledge of the cancer burden and the local mix of cancer types which predominate. Unfortunately, neither the number of new cases of cancer nor the number of deaths caused by cancer is available from many parts of the world, and only estimates can be made based on the partial incidence and mortality data available. Such estimates are a first crucial step in providing insight into the cancer burden in all regions of the world, thereby allowing a process of priority identification and priority setting to be engaged.

Currently about half the world's population is covered by death registration schemes with a medically certified cause of death. This analysis has been restricted to data from such schemes to allow comparability in the methods of estimation and the sources used. However, there are a number of ongoing schemes in different regions of the world that give insights into causes of death in a larger proportion of the world population [47]. For example, in India



* Dates show the span of years when percent of population age 65 or older rose (or is projected to rise) from 7 percent to 14 percent.

Fig. 1.1.11 *Number of years for percentage of population age 65 or older to rise from 7% to 14%*

there is a sample registration system and an urban system of medically certified causes of death. In China, there is a Disease Surveillance Points system in place and an urban death registration scheme [37,38].

However, the estimates made here, for all their imperfections, reflect the cancer burden in different parts of the world and serve as a basis for establishing priorities in cancer control activities. Their first impact is to establish clearly that cancer is a worldwide problem.

Although data were sparse when IARC was founded in 1965 [48], cancer was then widely considered to be a disease of developed, high-income countries [39]. The situation has changed dramatically with at least half of the global cancer burden found in low-resource and medium-resource countries. In 2008, five cancers in every ten occurred in residents of four WHO Regions that are mainly constituted of low-resource and medium-resource countries: the African Region (AFRO)(5.4%), the Eastern Mediterranean Region (EMRO)(3.7%), the South East Asia Region (SEARO)(12.8%) and the Western Pacific Region (WPRO)(29.7%) (Figure 1.1.9).

The continued growth and ageing of the world's population will greatly affect the future cancer burden. Given these demographic changes (Figure 1.1.10), and factoring in an annual increase in cancer incidence and mortality of 1%, by 2030 it could be expected that there will be 26.4 million incident cases of cancer and 17.0 million cancer deaths annually (Tables 1.1.3 and 1.1.4). An annual increase of 1% per annum in the incidence rate seems reasonable, and may well be conservative.

These estimates made herein correspond closely with those made by other groups [34, 49-52] (Table 1.1.5). For example, the estimates of the global cancer deaths made by the American Cancer Society [32] for 2007 are 7.6 million, and the calculation presented herein estimates the same number of cases in 2008. The World Health Organization [52] has made an estimate of 11.5 million deaths in 2030, comparable to our estimate of 12.9 million under the hypothesis of no increase in cancer death rates. Although there are clear indications that the incidence rate of cancer is rising in many parts of the world, the assumption of the same percentage increase in death rate could be questioned. For example, if the overall increase in incidence is driven by forms of cancer for which the case fatality rate is low, then the mortality rate may not rise so quickly. On the other hand, if the increase in incidence is driven by forms of cancer for which fatality is high, then the increase in mortality may be greater than that in incidence. Assuming the same change in mortality rates as incidence is in many respects the optimal course, although the estimates of the burden of cancer deaths may be less reliable than those of the global burden.

The growth and ageing of the population of countries of low or middle income, together with westernisation of lifestyle and the rapid growth of tobacco smoking, are contributing to dramatic changes on the burden of cancer. Changes in lifestyle habits (including adoption of a more sedentary lifestyle, weight gain and obesity) and sociological changes (notably increasing age at first birth and decreasing parity in women) are leading to large increases in breast and colorectal cancer in particular. Indeed, in view of the substantial delay—about 40 years—between changes in smoking prevalence in populations being reflected in changes in disease rates, the peak of the tobacco-smoking related cancer epidemic in countries of low and middle income has probably yet to materialise.

The cancer burden will increase in each of the WHO Regions. In the African region (AFRO), the burden will increase from 700 000 in 2008 to 1 200 000 cases in 2030 if there is no increase in the incidence rate or 1 600 000 if there is a 1% annual increase in incidence factored in (Table 1.1.6). In the Western Pacific Region (WPRO), the burden will increase from 3 700 000 in 2008 to 6 100 000 cases in 2030 if there is no increase in the incidence

rate, or 8 100 000 if there is a 1% annual increase in incidence (Table 1.1.6). Similar estimates are presented for mortality data (Table 1.1.7).

Evidently, the greatest effect of this increase will fall on low-resource and medium-resource countries where, in 2001, almost half of the disease burden was already from non-communicable disease [53]. Low-resource and medium-resource countries are, arguably, harder hit by cancer than the high-resource countries. The effects will be considerable in terms of the treatment needs and the costs of treatment, especially in low- and medium-resource countries still faced with the burden of infectious disease and a low budget for health. Cancer treatment facilities are not universally available, and life-extending treatment is often unavailable, generally for economic reasons. The increasing burden of cancer and other chronic diseases could thus cause devastating damage to entire families in several circumstances, including when the head of household and the only source of income for a frequently extended family succumbs to cancer, or when death of the mother results in girls stopping their education to look after the household.

Necessity and Prospects for Cancer Control. Epidemiology provides compelling evidence that a large proportion of human cancer may be avoidable. Different populations throughout the world experience different levels of different forms of cancer, and these levels change with time. Groups of migrants acquire the cancer pattern of their new home, sometimes within decades (as demonstrated by migrants to Australia) [54]. From evidence such as this the environmental theory of carcinogenesis has developed [20,55], and it is widely held that upwards of 80%, and perhaps 90%, of human cancer may be attributable to environmental factors, defining "environment" in its broadest sense to include a wide range of (sometimes poorly defined) lifestyle aspects, including dietary, social and cultural practices.

Annual Percentage Change	Men	Women	Both sexes
-1.50(%):	7.183	5.893	13.076
-1.25(%):	7.712	.326	14.038
-1.00(%):	8.277	6.791	15.068
-0.75(%):	8.883	7.287	16.171
-0.50(%):	9.531	7.819	17.351
-0.25(%):	10.225	8.388	18.614
0.00(%):	10.968	8.997	19.965
0.25(%):	11.762	9.649	21.411
0.50(%):	12.611	10.346	22.957
0.75(%):	13.520	11.091	24.611
1.00(%):	14.491	11.888	26.380
1.25(%):	15.530	12.740	28.270
1.50(%):	16.640	13.651	30.291

Table 1.1.3 *Number of new cancer cases (millions) expected globally in 2030 (based on 2002 rates and annual percentage changes)*
For comparison purposes, there were 10.9 million cancer cases in 2002

Annual Percentage Change	Men	Women	Both sexes
-1.50(%):	4.837	3.605	8.442
-1.25(%):	5.193	3.870	9.063
-1.00(%):	5.574	4.154	9.728
-0.75(%):	5.982	4.458	10.440
-0.50(%):	6.419	4.783	11.202
-0.25(%):	6.886	5.131	12.017
0.00(%):	7.386	5.504	12.890
0.25(%):	7.921	5.902	13.823
0.50(%):	8.493	6.329	14.821
0.75(%):	9.104	6.785	15.889
1.00(%):	9.759	7.272	17.031
1.25(%):	10.458	7.794	18.252
1.50(%):	11.206	8.351	19.556

Table 1.1.4 *Number of cancer deaths (millions) expected globally in 2030, (based on 2002 rates and annual percentage changes).*
For comparison purposes, there were 6.7 million cancer deaths in 2002

Source	Year estimated	Deaths (millions)	Incidence (millions)	Notes
American Cancer Society [32]	2007	7.6	12.0	a
IARC	2008	7.6	12.4	
World Health Organization	2005	7.6	none	a
U.I.C.C [52]	2002	6.7	10.9	
Globocan 2002 [31]	2002	6.7	10.9	
Institute of Medicine [49]	2001	7.0	none	
Mathers and Loncar [50]	2030	11.5	none	
IARC	2030	12.9	20.0	b
IARC	2030	17.0	26.4	c

Table 1.1.5 *Various estimates of the global cancer burden*

a, Estimates based on Globocan [31];
b, Assumes no change in underlying rate;
c, assumes a 1% per annum increase in incidence.

Region	2008	2030[a]	2030[b]
AFRO	0.7	1.2	1.6
EURO	3.4	4.1	5.5
EMRO	0.5	0.9	1.2
PAHO	2.6	4.8	6.4
SEARO	1.6	2.8	3.7
WPRO	3.7	6.1	8.1
WORLD	12.4	20.0	26.4

Table 1.1.6 *Estimated (2008) and projected numbers (millions) of cancer cases*
a, No temporal change in incidence rates during the period;
b, under scenario of 1% per annum increase in incidence rates.

Region	2008	2030[a]	2030[b]
AFRO	0.5	0.9	1.3
ERO	1.8	2.6	3.4
EMRO	0.3	0.6	0.9
PAHO	1.3	2.3	3.1
SEARO	1.1	1.9	2.6
WPRO	2.6	4.4	5.9
WORLD	7.6	2.9	17.0

Table 1.1.7 *Estimated (2008) and projected numbers (millions) of cancer deaths*
a, No temporal change in incidence rates during the period;
b, under scenario of 1% per annum increase in incidence rates.

In theory, therefore, the large majority of human cancer diagnosed each year may be avoidable, but avoidable causes of many common cancers have not yet been clearly identified. A prerequisite of cancer prevention lies in identifying the determinants of cancer risk. Cancer control embraces a number of important elements with the aim of reducing the incidence of cancer and, failing primary prevention, reducing mortality either by finding disease at an earlier and more 'curable' stage or by improving survival stage-for-stage through improvements in therapy. There are a number of disciplines involved within this embrace, including epidemiology, clinical science, behavioural science and health education. It is a complex and at times uncoordinated package, and many details will be presented in individual sections below.

Cancer would chiefly be an economic problem if it were not for the fact that half of the people who develop cancer die from their disease. Thus the concept of Cancer Control has been developed to attack the cancer problem at various points:

(i) Primary Prevention

The most obvious ways to prevent people dying from cancer are either to find cures for the different forms of the disease or to find ways to stop the development of clinical cancer in the first instance. At present, cancer prevention involves determining the causes of cancer (risk determinants) among those factors shown to be associated with the development of the disease by epidemiological studies (risk factors). Avoiding a changing exposure to risk determinants would result in a reduction in cancer risk.

The evidence that cancer is preventable is compelling. Different populations around the world experience different levels of different forms of cancer [56], and these levels change with time in an orderly and predictable manner [57]. Groups of migrants quickly leave behind the cancer levels of their original home and acquire the cancer pattern of their new residence sometimes within one generation [54, 58]. Thus those Japanese who left Japan for California left behind the high levels of gastric cancer in their homeland and exchanged it for the high levels of breast and colorectal cancer present among inhabitants of their new home. Furthermore, groups whose lifestyle habits differentiate themselves from other members of the same community frequently have different cancer risks (c.f. Seventh Day Adventists and Mormons [59]. Although all of the avoidable causes of cancer have not yet been clearly identified (e.g. in France, one third of cancer deaths can be explained by known risk factors [22]), it is thought that risk determinants exist for about one half of cancers. Thus, primary prevention in the context of cancer is an important area of public health.

The American Cancer Society has established a goal of reducing cancer mortality in the United States by 25% and cancer incidence by 50%by 2015. There has been significant progress in recent years in addressing the cancer problem. Cancer death rates have decreased by 18.4% among men and 10.5% among women since the early 1990s.

The *Annual Report to the Nation on the Status of Cancer, 1975-2005, Featuring Trends in Lung Cancer, Tobacco Use and Tobacco Control* is a joint report of the American Cancer Society, the US Centers for Disease Control and Prevention (CDC), the National Cancer Institute (NCI), and the North American Association of Central Cancer Registries (NAACR) [Jemal et al. *Journal of the National Cancer Institute* 2008; 100: 1672-1694].

The cancer death rate in the United States continues to go down and now cancer incidence–the rate at which new cancers are diagnosed also–appears to be dropping. Cancer death rates for both sexes combined declined about 1.8% per year from 2002 through 2005, almost double the 1.1% per year decrease seen from 1993 through 2002. For the first time in the 10-year history of the report, incidence rates for all cancers combined decreased, falling by 0.8% per year from 1999 to 2005.

Cancer death rates in the United States declined for 10 of the 15 most common causes of cancer death among both men and women, but increased for a few individual cancers, such as esophageal and bladder cancers among men, pancreatic cancers in women, and for cancers of the liver in both.

The decline in cancer incidence was largely due to declines in the most common cancers: lung, colorectal and prostate cancer for men and breast and colorectal cancer for women. Lung cancer death rates in women leveled off from 2003 through 2005, but incidence rates are still rising, though more slowly than they have risen in the past. Lung cancer death rates have been decreasing in men since the 1990s.

There are still significant differences in lung cancer deaths in different parts of the United States. In California, for instance, the lung cancer death rate dropped by about 2.8% per year among men between 1996 and 2005. That decline is more than double that seen in some Midwestern and Southern states, and may be due in part to California's strong tobacco control policies.

(ii) Secondary Prevention

It is very frequently the case that the probability of successful treatment of cancer is increased, sometimes very substantially, if the cancer can be diagnosed at an early stage. Awareness of the significance of signs and symptoms is important, but all too often cancers that exhibit symptoms are at an advanced stage. *Screening* is a term frequently applied to the situation where tests are used to indicate whether a (generally asymptomatic) individual has a high or low chance of having a cancer. Detecting cancers at an early, asymptomatic stage could lead to decreases in the mortality rate for certain cancers.

(iii) Tertiary Prevention. An obvious way to prevent cancer death is to cure those cancers which develop. However, there have been few major breakthroughs in cancer treatment in the sense of turning a fatal tumour into a curable one. Notably successes have been in testicular teratoma [60], Hodgkin disease [61], children's leukaemia, Wilm's tumour and choriocarcinoma. Progress in survival of the major cancers has been very much less than hoped. Adjuvant chemotherapy and tamoxifen have improved survival in breast cancer [62], adjuvant chemotherapy has also contributed to improvements in prognosis of ovarian cancer and colorectal cancer [63], and there has been additional progress that could be attributed specifically to certain treatments.

General progress in medical science has led to modern anaesthesia making more patients candidates for surgery, and the surgery itself safer; better control of infection and bacterial diseases; better imaging, which has improved tumour localisation and staging; and better devices being available to deliver the appropriate doses of radiation and drugs. Thus, more patients can get better and more appropriate therapy and hence have a better prognosis.

The quality of life issue has not been neglected, with breast conservation therapy now almost supplanting traditional, radical mastectomy in the majority of women; as well as more plastic breast reconstruction, less amputation of limbs for bone and soft-tissue sarcomas, and better colostomies being some important advances. Although increased attention has been given to issues of palliative, supportive and terminal care, there is still much work to be done (see Chapter 1.8).

Achieving cancer control: The example of the European Union

Turning theoretical knowledge of cancer risk factors into screening efficacy is a challenge. In the European Union, the High-level Cancer Experts Committee set a target in 1985 of reducing the number of deaths expected in the year 2000 by 15%, i.e. from 1 000 000 to 850 000 according to their calculations. Against this background of cancer as an important public health problem that is one of the commonest causes of premature and avoidable death in Europe, the *European Code Against Cancer* was introduced to be a series of recommendations that if followed could lead in many instances to a reduction in cancer incidence and also to reductions in cancer mortality. The recommendations were all evidence-based and were practicable to apply.

The *European Code Against Cancer* was originally drawn up and subsequently endorsed by the European Commission High-level Cancer Experts Committee in 1987. In 1994, the European Commission invited the European School of Oncology to assemble a group of international experts to examine and consider revision of the scientific aspects of the recommendations given in the current Code. This exercise took place and a new version was adopted by the Cancer Experts Committee at its meeting of November 1994 [64]. A further revision took place in 2003, producing the third version of the Code [65].

Any recommendation made to reduce cancer occurrence should not be one that could lead to an increased risk of other diseases. The recommendations which comprise the revised *European Code Against Cancer* should, if followed, also lead to improvements in other aspects of general health (Table 1.1.8). It is also important to recognise from the outset that each individual has choices to make about their lifestyle, some of which could lead to a reduction in their risk of developing cancer. These choices, and the rationale underlying their recommendation, are presented below.

The Code initially contained ten points [64] but was increased to eleven points for the third version [65]. If followed, this would lead to reductions in cancer incidence and/or mortality. The first point in the Code is the most important, while the others are not necessarily in order of importance in terms of how many cases or deaths could be prevented.

1. *Do not smoke; if you smoke, stop doing so. If you fail to stop, do not smoke in the presence of non-smokers.*

It is estimated that 25–30% of all cancers in developed countries are tobacco-related. From the results of studies conducted in Europe, Japan and North America, between 87 and 91% of lung cancers in men, and between 57 and 86% of lung cancers in women, are attributable to cigarette smoking. For both sexes combined the proportion of cancers arising in the oesophagus, larynx and oral cavity attributable to the effect of tobacco, either acting singly or jointly with the consumption of alcohol are between 43 and 60%. A large proportion of cancers of the bladder and pancreas and a proportion of cancers of the kidney, stomach, cervix and nose and myeloid leukaemia are also causally related to tobacco consumption. Because of the length of the latency period, tobacco-related cancers observed today are related to the cigarette smoking patterns over several previous decades. On stopping smoking, the increase in risk of cancer induced by smoking rapidly ceases. Benefit is evident within 5 years and is progressively more marked with the passage of time.

Smoking also causes many other diseases, most notably chronic obstructive pulmonary disease (commonly called chronic bronchitis) and an increased risk of both heart disease and

stroke. The death rate of long-term cigarette smokers in middle age (from 35 to 69 years of age) is three times that of life-long non-smokers, and approximately half of regular cigarette smokers who started smoking early in life, eventually die because of their habit. Half the deaths take place in middle age, when smokers lose approximately 20–25 years of life expectancy compared to non-smokers; the rest occur later in life when the loss of expectation of life is 7–8 years. There is now, however, clear evidence that stopping smoking before developing cancer or some other serious disease avoids most of the later risk of death from tobacco, even if cessation of smoking occurs in middle age. While the rate at which young people start to smoke will be a major determinant of ill-health and mortality in the second half of this century, it is the extent to which current smokers give up the habit that will determine mortality in the next few decades and which requires the urgent attention of public health authorities.

Tobacco smoke released to the environment by smokers, commonly referred to as environmental tobacco smoke (ETS) and which may be said to give rise to enforced "passive smoking", has several deleterious effects on people who inhale it. It causes a small increase in the risk of lung cancer and also some increase in the risk of heart disease and respiratory disease and is particularly harmful to small children. Smoking during pregnancy increases the risk of stillbirth, diminishes the infant's birth weight, and impairs the child's subsequent mental and physical development, while smoking by either parent after the child's birth increases the child's risk of respiratory tract infection, severe asthma and sudden death.

Although the greatest hazard is caused by cigarette smoking, cigars can cause similar hazards if their smoke is inhaled, and both cigar and pipe smoke cause comparable hazards of cancers of the oral cavity, pharynx, extrinsic larynx and oesophagus.

Worldwide, it is estimated that smoking killed four million people each year in the 1990s and that altogether some 60 million deaths were caused by tobacco in the second half of the 20th century. In most countries, the worst consequences of the tobacco epidemic are yet to emerge, particularly among women in developed countries and in the populations of developing countries

This first point of the European Code Against Cancer is refers to the most important cause of cancer [65] and should be viewed as containing three distinct messages:

Many aspects of general health can be improved and many cancer deaths prevented, if we adopt healthier lifestyles:	
1.	Do not smoke; if you smoke, stop doing so. If you fail to stop, do not smoke in the presence of non-smokers.
2.	Avoid Obesity.
3.	Undertake some brisk, physical activity every day.
4.	Eat a variety of vegetables and fruits every day: eat at least five portions daily. Limit your intake of foods containing fats from animal sources.
5.	If you drink alcohol, whether beer, wine or spirits, moderate your consumption to two drinks per day if you are a man or one drink per day if you are a woman.
6.	Care must be taken to avoid excessive sun exposure. It is specifically important to protect children and adolescents. For individuals who have a tendency to burn in the sun active protective measures must be taken throughout life
7.	Comply strictly with regulations aimed at preventing occupational or environmental exposure to known cancer-causing substances. Follow advice of National Radiation Protection Offices.
There are Public Health programmes which could prevent cancers developing or increase the probability that a cancer may be cured:	
8.	Women from 25 years of age should participate in cervical screening. This should be within programmes with quality control procedures in compliance with "EU Guidelines for Quality Assurance in Cervical Screening".
9.	Women from 50 years of age should participate in breast screening. This should be within programmes with quality control procedures in compliance with "EU Guidelines for Quality Assurance in Mammography Screening".
10.	Men and women from 50 years of age should participate in colorectal screening. This should be within programmes with built-in quality control procedures.
11.	Participate in vaccination programmes against Hepatitis B Virus infection.

Table 1.1.8 *European Code Against Cancer (Third version)[65]*

Do not smoke. Smoking is the largest single cause of premature death.

Smokers: stop as quickly as possible. In terms of health improvement, stopping smoking before having cancer or some other serious disease avoids most of the later excess risk of death from tobacco even if smoking is stopped in middle age.

Do not smoke in the presence of non-smokers. The health consequences of your smoking may affect the health of those around you.

2. *Avoid obesity.*

3. *Undertake some brisk, physical activity every day.*

Obesity is an established and major cause of morbidity and mortality. It is the largest risk factor for chronic disease in Western countries after smoking, increasing in particular the risk for diabetes, cardiovascular disease and cancer. Most countries in Europe have seen the prevalence of obesity (defined as a body mass index of ≥30 kg/m^2) rapidly increase over the years.

Many studies have examined the relationship between physical activity and the risk of developing cancer. The protective effect of physical activity on cancer risk improves with increasing levels of activity–the more the better–though such a recommendation should be moderated in individuals with cardiovascular disease. Regular physical activity that involves some exertion may be needed to maintain a healthy body weight, particularly for people with sedentary lifestyles. This could involve half an hour per day three times per week. More vigorous activity several times per week may give some additional benefits regarding cancer prevention.

4. *Increase your daily intake and variety of vegetables and fruits: eat at least five servings daily. Limit intake of foods containing fats from animal sources.*

Diet and nutritional factors commenced to be the focus of serious attention in the aetiology of cancer from the 1940s onwards. Initially dealing with the effects of feeding specific diets to animals receiving chemical carcinogens, research turned to the potential of associations with human cancer risk. Initially this was conducted through international comparisons of estimated national per capita food intake data with cancer mortality rates. It was consistently found that there were very strong correlations in these data, particularly with dietary fat intake and breast cancer. As dietary assessment methods became better, and certain methodological difficulties were identified and overcome, the science of nutritional epidemiology emerged.

5. *If you drink alcohol, whether beer, wine or spirits, moderate your consumption to two drinks per day if you are a man or one drink per day if you are a woman.*

There is wide variability among European Union countries in terms of *per capita* average alcohol consumption and preferred type of alcoholic beverage. Although three groups of countries are traditionally identified according to the prevalent drinking culture (wine drinking in the South, beer drinking in the Central Europe and spirit drinking in the North), there is considerable variability within such groups and within countries, and new patterns are evolving rapidly (e.g. increasing consumption of wine in Northern countries; increasing prevalence of binge drinking, in particular among women).

There is convincing epidemiological evidence that the consumption of alcoholic beverages increases the risk of cancers of the oral cavity, pharynx and larynx and of squamous-cell carcinoma of the oesophagus. Risk of breast cancer and colon cancer is also increased by alcohol consumption. The risks tend to increase with the amount of ethanol drunk, in the absence of any clearly defined threshold below which no effect is evident.

6. *Care must be taken to avoid excessive sun exposure. It is specifically important to protect children and adolescents. For individuals who have a tendency to burn in the sun active protective measures must be taken throughout life.*

Skin cancer is predominantly, but not exclusively, a disease of white-skinned people. Its incidence, furthermore, is greatest where fair-skinned peoples live at increased exposure to ultraviolet light, such as in Australia. The main environmental cause of skin cancers is sun exposure, and the ultraviolet light is deemed to represent the component of the solar spectrum involved in skin cancer occurrence. Exposure to artificial sources of sunlight, such as from sunbeds or sunlamps, is also known to increase risk of melanoma, with the effect particularly prominent if exposure starts as a teen or young adult.

7. *Apply strictly regulations aimed at preventing any exposure to known cancer-causing substances. Follow all health and safety instructions on substances which may cause cancer. Follow advice of national radiation protection offices.*

The prevention of exposure to occupational and environmental carcinogens has followed the identification of a substantial number of natural and man-made carcinogens, and has led to significant reductions in cancer occurrence. The message in this item of the code solicits responsible behaviour for individuals in three respects: (1) from those who have to provide timely and clear instructions, primarily legislators and regulators who should adapt scientific consensus evaluations into European Union law, and control compliance with these regulations; (2) from those who should follow these instructions and comply with the laws to protect the health of others, for instance managers, hygienists and doctors in industry; (3) from every citizen who in order to protect their own health and the health of others, ought to pay heed to the presence of carcinogenic pollutants and follow instructions and regulations aimed at mitigating or preventing exposure to carcinogens. The control of the prevalence and level of exposure to occupational and environmental carcinogens through general preventive measures has historically played a more important

role in preventing cancers than individual measures of protection.

Apart from individual lifestyle choices, there are public health programmes that could prevent cancers developing or increase the probability that a cancer may be cured.

Early detection is an important factor in reducing the death rate from cancer, whether it is achieved by personal actions or through participation in early detection programmes. Awareness of different visual body signs or symptoms that could easily be observed by anyone and that are possibly related to cancer is important. It is unequivocally established that cancer survival is better for early, localised disease than for the later stage, advanced form of the disease. Thus the earlier in the process that a cancer can be diagnosed and treated then the better this is for the patient. Much effort has gone into cancer screening and the development of methods for finding cancers at an earlier stage in their development and increasing prospects for cure. It is possible to make recommendations based on the available evidence.

8. *Women from 25 years of age should participate in cervical screening. This should be within programmes with quality control procedures in compliance with EU guidelines for quality assurance in cervical screening.*

The effectiveness of screening for cervical cancer has never been demonstrated in a randomised trial. There is, however, sufficient non-experimental evidence showing the efficacy of screening using a cervical smear (Pap) test performed every 3–5 years. The effects are somewhat smaller at a population level. In some of the Nordic countries, the reduction was about 80% in women in the age groups exposed most intensively to screening. In the mid-1980s, after several years of organised screening, the overall incidence was 5–15 per 100 000 woman-years.

Cervix cancer screening should be offered to all women over 25 years. There is limited evidence of benefit of screening in women over 60 though the likely yield of screening is low in women over age 60, since the incidence of high-grade cervical lesions declines after middle age. Screening this age group is associated with potential harm from false-positive results and subsequent invasive procedures. Stopping screening in older women is probably appropriate among women who have had 3 or more consecutive previous (recent) normal Pap smear results. Yield is also low after hysterectomy, and there is scant evidence to suggest that screening produces improved health outcomes.

9. *Women from 50 years of age should participate in breast screening. This should be within programmes with quality control procedures in compliance with "EU guidelines for quality assurance in mammography screening".*

There is considerable evidence that breast cancer screening with mammography is effective at reducing mortality from breast cancer. A well-organised programme with a good compliance should lead to a reduction in breast cancer mortality of at least 20% in women aged over 50. The value of screening women under 50 years is uncertain. No trials having large enough statistical power to analyse these women separately have been completed. What recommendations should be made for mammographic screening of women aged 40–49 is an important question that cannot now be answered; over 40% of the years of life lost due to breast cancer diagnosed before the age of 80 years are attributable to cases presenting symptomatically at ages 35–49 years, frequently an age of considerable social responsibility.

Mammographic screening is only one step in the total management of the woman with breast cancer. As has been shown from long-term established programmes in the United Kingdom, Sweden, Finland and the Netherlands, recognition of the importance of the multidisciplinary team in the assessment of mammographic abnormalities had spread into the symptomatic sector, leading to the development of integrated multidisciplinary breast care centres. Staffed by dedicated surgeons, radiologists and pathologists working alongside breast care nurses, counselling and other support personnel, these centres offer the necessary care for women with breast cancer.

10. *Men and women from 50 years of age should participate in colorectal screening. This should be within programmes with built-in quality control procedures.*

The identification of a well-determined pre-malignant lesion, the adenomatous polyp, together with the good survival associated with early disease, make colorectal cancer an ideal candidate for screening. In the past quarter century, progress has been made in our ability to screen patients for colorectal cancer or its precursor state, using advances in imaging and diagnostic technology. Faecal occult blood guaiac test cards were first employed in the 1960s, the flexible sigmoidoscope was introduced in the mid-1970s to replace the rigid sigmoidoscope which had been first introduced in 1870, and colonoscopy has been available since 1970.

Despite the evidence showing that screening is worthwhile, most citizens of developed countries have not been screened for colorectal cancer by any means. While this situation persists the chance is being missed to prevent about one quarter of the colorectal cancer deaths that occur each year in the European Union.

11. *Participate in vaccination programmes against Hepatitis B infection.*

Chronic infection with hepatitis B virus (HBV) and hepatitis C virus (HCV) accounts for the majority of liver cancer cases in Europe. In a large case-series of liver cancer from six European Liver Centres, only 29% of liver cancer patients had no marker of either HBV or HCV infection.

An effective vaccine against HBV has been available for 20 years now. Several countries in the European Union (e.g. Denmark, Finland, Ireland, the Netherlands, Sweden and the United Kingdom) do not perform routine vaccination against HBV in children, on account of the low prevalence of HBV infection in the general population (http://www.who.int/), whereas other countries (e.g. Belgium, France, Germany) report coverage below 50%. There is scope for reconsidering national policies regarding universal vaccination against HBV, since selective vaccination of high-risk groups rarely works and travelling and migration facilitate the mixing of high- and low-risk populations. Although infection with HBV in young adulthood (typically through sexual intercourse or contaminated needles) carries a much lower risk of chronic hepatitis and liver cancer than does infection at birth or during childhood, it frequently induces acute hepatitis.

Impact of cancer control activities: The example of Europe

During the lifespan of the 'Europe Against Cancer' program, cancer mortality in the (then-15) Member States of the European Union (EU) had started to decline; the estimated number of deaths in 2000 was 940 510, which was 9.0% fewer than the 1 033 083 deaths expected on the basis of application of the age-specific mortality rates from the mid-1980s to the 2000 population [66,67]. When all the mortality data for 2000 were eventually available (and only Belgium is still an estimate, with 1997 being the most recent year for which data are available), there were 935 219 cancer deaths in the EU, which is 9.5% fewer than expected. These declines have subsequently been confirmed [68,69].

Bosetti et al. [69] present confirmation that these downward trends are continuing in the enlarged Member States of the EU (26 Member States, since Cyprus did not have data available). It is wonderfully reassuring to gaze at the downward trends in mortality rates in almost all forms of cancer. Now there can be more emphasis placed on the cancer sites where the mortality rates are rising. Notable among these are liver and pancreas cancer in both men and women, and the dramatic increases taking place in lung cancer in women. These continual upward trends are now more prominent when mortality rates from all other forms of cancer are in decline [69].

This decline was previously predicted by Quinn et al. [70], who made statistical forecasts of the trends in the EU-15 until 2020. While rates of most cancers were predicted to fall, in some countries rates in men were set to stabilise. While this was good news, it was tinged with the sad realisation that the stable rate achieved among men would be twice as high in Hungary as it would be in Sweden [70].

Cancer control is necessary and possible

There is strong evidence that cancer is, and will be for the immediate future, a major public health problem. The majority of human cancers may be avoidable, and for several of them avoidable causes have already been identified. In global terms, the greatest impact would be from the control of tobacco smoking and the control of breast cancer. While tobacco control could be achieved using a series of government and societal actions [29], prospects for the prevention of breast cancer, for example, are more remote.

Failing primary prevention, screening for breast, cervix and colorectal cancer could have a significant effect on reducing mortality from these common diseases. Screening for other forms of cancer will emerge as public health strategies once there has been proper evaluation; the current situation with prostate cancer is salutary in this respect.

With the expansion in the absolute numbers of cases of cancer set to continue into the next century, the role of prevention in cancer control strategies will increase in importance, as will the central role of epidemiology. This latter will also have to change: arguably the time has come to de-emphasise the chase for risk factors and to re-focus on the implementation of current knowledge in populations where many thousands, if not millions, of frequently premature deaths could be avoided.

A major challenge for many countries is finding sufficient funds to develop the capacity to treat the large numbers of cancers that will be diagnosed in the coming years. Effective prevention will reduce the risk of cancer and effective screening will allow many others to be successfully treated for their disease. Prevention actions can be implemented today to reduce the burden of major cancer killers: e.g. tobacco control against lung cancer and other forms of cancer [27, 28] and vaccination against cancers of the cervix and liver. Cancer control in developing nations must serve to de-stigmatise cancer and raise governmental and public awareness and dispel the myth equating cancer diagnosis with death.

Radiotherapy is an essential component of the treatment of cancer, and whether used for cure or palliation, radiotherapy has been shown to be cost effective. In high-income countries, over half of new cases receive one course of radiotherapy and up to one quarter of cancer patients may receive a second course. In low and middle-resource countries the need for radiotherapy is much greater due to late-stage presentations and the types of cancer that predominate. Breast and cervical cancers, the two leading female cancers globally, are highly treatable when detected early, and radiotherapy plays a major role in treatment protocols. Cervical cancer is the commonest form of cancer in women in Africa, and radiotherapy is an undeniable necessity. Simultaneously, it is essential to alter the 70%:30% balance of palliation over cure that exists at present [71].

Most low- and middle-resource countries have limited access to radiotherapy, although over 30 African and Asian countries have no services at all. In Africa the actual supply of radiotherapy is 20% of needs, while in the Asia-Pacific Region, with over 3 million new cases of cancer each year and the need for 4000 radiotherapy machines, only 1200 or so machines exist [72]. Total global shortages in low- and middle-resource countries are over 7000 radiotherapy machines, and it is clear that accessible, affordable, and suitable radiotherapy technologies are needed.

The *Programme of Action on Cancer Therapy* (PACT), established by the International Atomic Energy Agency (IAEA) and partners, aims principally to ensure effective and sustainable transfer of radiation technology to underserved regions of the world where need exists and to integrate radiotherapy into the broader public health priorities on cancer as part of *National Cancer Strategies*. In addition, PACT has the potential to serve as a focus to establish a series of evidence-based, appropriate actions to reduce cancer incidence and cancer mortality and increase the amount of effective palliation that can be delivered. The international cancer control community requires a focus [26], which PACT could provide.

The Millennium Development Goals (MDGs) (United Nations, 2005) have galvanised unprecedented efforts to meet the needs of the world's poorest communities. Achieving the MDGs has become a competitive challenge for many countries and will be of immense value to populations world-wide. Cancer prevention and control must acquire the same focus as provided by the MDGs [26,73]. In many parts of the world, the absence of a specific MDG on cancer (or indeed chronic disease) has led to cancer control taking on something of a lesser role in terms of allocated priority. There needs to be greater incentive developed for low-resource and medium-resource countries to prioritise cancer and other chronic diseases. A similar argument has been made regarding cardiovascular disease [74], and there is a wider recognition that this is necessary [75,76].

Although increasingly many medium-resource countries assign high priority in their national health strategies to chronic diseases including cancer, the donor community and most bilateral development agencies do not as yet consider cancer control a high priority. If cancer is not given higher priority through focused global efforts, health-care systems in low-resource and middle-resource countries will encounter even further problems as the number of cancer cases increases. More and more people will die prematurely and needlessly from cancer, with devastating social and economic consequences for households, communities and countries alike. Cancer could become a major impediment to socioeconomic development in low resource and economically emerging nations.

Current Opportunity

The timing is now right to address this growing cancer burden, part of the neglected epidemic of chronic disease and a neglected development goal [26,74,76]. The WHO Resolution on Cancer Control (WHA58.22) [77] provides a strong impetus for countries to develop programmes aimed at the reduction of cancer incidence and mortality. Although this is a strong incentive, there is an overwhelming and urgent need for leadership and coordination in this area. Compared to other global health communities, the global cancer control community is diffuse and often ineffective.

This has important implications for public health as well as other elements of health services around the world. There will be a need for more medical, nursing and related staff to treat these patients, there will need to be more hospitals and treatment facilities available, and this will all be a major expense as well as a major logistical problem for the near future. The implications for planning are that cancer control activities will need to increase to help reduce the mortality burden that is otherwise likely to materialise.

Priorities must be realistic and achievable, and include a focus on low-resource and medium-resource countries and the identification, delivery and assessment of effective cancer control measures. Depending on resources and competing health priorities, all steps must be taken to prevent those cancers which are preventable; to treat those cancers which are treatable; to cure those cancers which are curable; and to provide palliation and supportive care to patients throughout their cancer trajectory.

In the chapters that follow in this volume, current knowledge of cancer causes and prevention prospects will be outlined to serve as a basis for cancer control planning and prioritisation in regions at different resource settings.

CANCER CONTROL IN MEDIUM-INCOME COUNTRIES: THE CASE OF HUNGARY

Hungary, situated in central Europe, has an estimated 2008 population of 10.1 million, two thirds of whom live in urban areas. There are 3.3 doctors and 7.9 hospital beds per 1000 population; 7.9% of Gross Domestic Product (GDP) is spent on healthcare.

National Institute of Oncology

With a single regulation in 1952, the Ministry of Health created the National Institute of Oncology on the former territory of the Siesta sanatorium, thus creating the centre of Hungarian oncology and significantly affecting the whole of the Hungarian fight against cancer. According to the functions set down in its charter, the National Institute of Oncology became the epidemiological, organisational, methodological, treatment, research, and training centre for Hungarian oncology, and it remains so today. After the National Institute of Oncology moved to its new location, the 300 beds initially available at the Institute slowly increased to 348. Although this number has not changed significantly since then, the structure of the clinical departments underwent changes on several occasions in response to the challenges of the times.

At the time, the clinical department of the National Institute of Oncology consisted of seven clinical inpatient departments: Surgery (61 beds), Gynaecology (65 beds), Urology (49 beds), two Departments of Radiology (57 beds and 68 beds), Internal Medicine, and Temporary Post-treatment Care. The Institute also included X-ray diagnostics, a central medical laboratory, outpatient care, a pathological and histological laboratory, a radiation physics and isotope laboratory, a pharmacy, and the methodological-organisational-statistical department, managing the nationwide network of oncology care centres. The Oncopathological Research Institute (OPI) has been carrying out its diagnostic and experimental activities within five departments (Pathology, Experimental Morphology, Experimental Pharmacology, Cellular Biology, and Biochemistry) in the same complex since 1954, and has always maintained strong organisational connections with the National Institute of Oncology.

In 1956, Prof Dr Tibor Venkey was named Director-General. The chemotherapy and diagnostic internal medicine department was formed in the first half of 1953; in 1955, the Onco-dermatology Department was created. In 1958, the Isotope Department was launched; last, in 1959, the Department of Laryngology became a separate organisational unit. At the end of 1955 a separate outpatient care department was formed with the appointment of seven outpatient care consultants, easing the burden on the physicians in the clinical departments. (In 1958, the Institute was equipped with a cobalt gun, which entailed the reorganisation of the department of radiotherapy.)

Between 1959 and 1970, Dr János Vikol was the Director-General of the Institute. He played a vital role in involving the Institute in the cancer control programmes of the World Health Organization (WHO), thereby laying the foundations for the exceptional international performance of the Institute. In 1966, Dr Vikol was put in charge of the Cancer Control Section of the WHO, which involved frequent visits abroad; therefore the Institute was managed by Dr Iván Rodé as temporary Director in 1968. Under Dr Rodé's leadership, the scope of radiotherapy further expanded. In 1970 was installed a 25 MeV circular accelerator (betatron), unique at that time, allowing tumours located deep within the body to be successfully treated due to its high energy and accurate dose counts.

In 1971, Prof Dr Sándor Eckhardt was appointed superintendent, leading to a number of changes in the operation of the institute. The structure of the institute has mirrored the development in the field of cancer, allowing for the approximation of the European standards with regard to tumour treatment and research. The international recognition and integration of the National Institute of Oncology was significantly improved by the election of Prof Eckhardt as the president of UICC.

Professor Eckhardt also further strengthened the Oncology Committees according to tumour localisation. Until 1970, the physicians of the institute had held joint meetings to discuss the controversial cases and make diagnostic and therapeutic decisions. Since the number of patients consulted was continuously growing, it seemed necessary to establish expert committees for gynaecological tumours, abdominal and accessory cavity tumours, haemoblastoses, breast tumours, skin melanoma, and head-neck tumours (1970). Institute members held clinico-pathological conferences on a monthly basis, where, apart from the autopsy results, they evaluated the results of the more interesting biopsies, along with the clinical history of the patients.

In 1971 the Department of Internal Medicine, which had previously had 24 beds and one outpatient office, was expanded to 60 beds and two outpatient offices. In addition to these, an immunology laboratory was added in 1974 for the examination of the immunological changes sometimes concomitant with malignancies. By 1976 the Department had 65 inpatient beds and 14 physicians, and the Internal Medicine outpatient centre examined, treated and checked more than 6000 patients.

The management of the Institute has been carried out by a Board of Directors since 1987. This relative organisational, material and intellectual freedom proved inspirational for research, resulting in considerable development over the subsequent decade.

In 1992, Prof Dr Miklós Kásler became the superintendent of the National Institute of Oncology, and restructured the Institute with three centres in line with the three distinct activities at the Institute: the Centre for Clinical Oncology, the Centre for Pathology and the Centre of Research. In 2002, the Director General established a management structure more suited to constantly changing financial conditions and to the European norms. As a result of the international activities of Prof Kásler, Hungary participated in the development of the European Code against Cancer (2004) and the National Cancer Control Programme meetings organised by the UICC and WHO. Prof Kásler headed the Educational Team of the Organization of European Cancer Institutes; he is presently assisting the international integration of the National Institute of Oncology as a member of the steering committee of the European Alliance against Cancer. The development (1993) and expansion (1997, 2005) of the Hungarian National Cancer Control Programme are both linked with the name of Miklós Kásler. He was appointed president of the National Programme against Cancer Council in February 2005. In this role, Dr Kásler commenced the European harmonisation of the Hungarian oncology care system.

The main feature of the Institute of Oncology is its capability to provide patients with complex clinical onco-therapeutic treatment (surgery, chemotherapy, and radiation therapy). The personal conditions paired with the state-of-the-art tumour diagnostics (CT, MRI, imaging, laboratory, pathological) equipment provide high-quality diagnostic and monitoring capabilities with the help of a highly trained expert team well-versed in imaging, laboratory, and pathological diagnostics.

Cancer in Hungary

Hungary's cancer mortality statistics have long been dramatically elevated. At present, there are about 300 000 cancer patients, and 33 530 people died of malignant diseases in 2003. Cancer is the second most frequent cause of death in Hungary, following cardiovascular disease. Cancer occurs so frequently that the prevention, up-to-date treatment, and control of cancer have become major public health challenges. At present in Hungary there are 601 specialists in medical oncology and 120 radiotherapists, some of whom have medical oncology as a second specialisation.

The first National Cancer Control Programme (NCPP) was established in 1993, and evolving cancer patterns and trends in Hungary have provided the basis for evaluating priorities for cancer control. These priorities include:

1. Primary prevention: Health education, oncology-related programmes on TV, development of new education programmes for the medical and paramedical staff;
2. Secondary prevention: Improvement of screening for breast, colorectal, cervix and head and neck tumours, and promotion of research related to early detection;
3. Treatment: Establishment of treatment protocols;
4. Establishment of a National Cancer Registry (fulfilled 1999); and
5. Rehabilitation.

Evolution of the Hungarian National Cancer Registry

The Országos Rákregiszter GRID (ORG) project was established to develop the next generation of the National Cancer Registry (NCR) for Hungary. The NCR started operation in 1999, and its central mission is the collection, management and analysis of medical data on people who have been diagnosed with malignant or neoplastic disease.

The ORG project is a consortium of the Department of Distributed Systems (DSD) of SZTAKI, Arvato Systems Hungary Inc. and the National Institute of Oncology. It has been responsible for building new online infrastructure to collect and validate medical data, which will greatly improve the quality of NCR data on cancer and thus provide a much stronger statistical base for decision-makers and medical researchers. One of the other important objectives of the ORG project is to broaden the range of data collected, including relevant healthcare, environmental, political, demographical and economic data associated with a given geographical territory in addition to the standard cancer-specific medical and demographic data.

The ORG Cancer Registry finished its test phase in 2007, and the old and the new systems are running in parallel in order to eliminate any remaining errors in the system, train personnel, and prepare for the final switch from the old system to the new one.

Sources

Additional information on the National Cancer Control Programme can be accessed at: http://www.eum.hu/index.php?akt_menu=2652&archiv=1
Additional information on the National Cancer registry can be accessed at: http://dsd.sztaki.hu/projects/org/en/

CANCER CONTROL IN MEDIUM-INCOME COUNTRIES: THE CASE OF TURKEY

Cancer control practices in Turkey started in 1947 when the Turkish Cancer Research and Control Institution was established. The Ahmet Andicen Oncology Hospital was started in Ankara in 1955, and the Department of Cancer Control in Primary Health Services was established in 1962, becoming the Department of Cancer Control in the Ministry of Health in 1970. The Department is responsible for the regulation of preventive services and treatment cervices in relation to cancer control, and for implementing, executing and inspecting cancer treatment resources. In 1970, the week of 1-7 April was designated as National Cancer Week, and this continues to this day.

In 2008, the estimated population of Turkey was 73.2 million. There are 1.4 doctors per 1000 population and 2.6 hospital beds per 1000 population. An estimated 7.7% of Gross Domestic Product (GDP) was spent on healthcare in 2008. There are an estimated 150 000 new cases of cancer in Turkey each year. In men, the commonest cancers are those of the trachea, bronchus and lung (33%); stomach (9%); urinary bladder (9%); colon and rectum (8%); prostate (6%) and larynx (6%). In women, the commonest cancers are those of the breast (24%); colon and rectum (9%); stomach (7%); ovary (6%); trachea, bronchus and lung (6%); leukaemia (5%); and cervix (5%) and corpus (5%).

Cancer treatment facilities. Cancer treatment in Turkey is available in public hospitals, university hospitals and in private institutions. The majority of oncologists generally work in large centres having high standards. There are three oncology institutes in Turkey (Oncology Institute of Hacettepe University, Oncology Institute of Istanbul University and the Oncology Institute in Dokuz Eylul University) and 44 centres for cancer diagnosis and treatment.

At the beginning of 2007, there were 170 specialists in medical oncology in Turkey; this is less than optimum and recognised as one of the key bottlenecks in the development of cancer treatment services. Certain steps that will go into effect in the near future have been taken to address this situation. However, a serious impediment remains the high costs of many chemotherapeutic drugs which could overwhelm the health budget of the country.

"Interpreting Cancer Control as simply Treatment Services is a problem all over the world. Awareness that cancer is a preventable and controllable disease has been recognised only very recently." (A Murat Tuncer, 2008).

Turkey has an active programme in radiation oncology, with approximately 300 active radiation oncologists and an increasing number of radiation oncologists in training. However, lack of a domestic radiotherapy equipment manufacturer has a led to a number of problems frequently entailing long delays between launching a bid and having the new, modern equipment installed and working. There also remains a shortage of medical physicists.

Oncology nursing is recognised, and there have been training courses in the country since 1987 with the (Turkish) Association for Oncology Nursing having been established in 1989. There are currently over 500 oncology nurses in Turkey.

Cancer prevention and early diagnosis. A project for the creation of cancer registries was established in 1992. Today, the main priority in the cancer control plan, which is now accepted as national policy, is the collection of reliable and accurate data on cancer incidence. In 2006, priority was given to create and develop cancer registries in Ankara, Antalya, Samsun, Erzurum, Trabzon, Izmir, Edirne and Eskisehir. In addition, steps are being taken to establish a Cancer Early Diagnosis and Screening Centre (KETEM) in every city (by the end of 2008 there will be 83 such centres). This KETEM project was initiated jointly by the European Union and the Turkish Ministry of Health in 1996 and was launched in 2004. Moreover, population-based screening programmes for cervix and breast cancer, designed according to established EU criteria for quality control, are rapidly gaining ground throughout the country.

Tobacco is recognised as the major cause of cancer in Turkey, and a *Law on Tobacco Control and Preventing the Damages of Tobacco Products* (law 5727 of 3rd January 2008) has been passed. This law bans smoking in bars, restaurants and public places. It represents an important investment for the future of cancer control in Turkey.

A detailed description of the current situation in Turkey can be found in the following publication:

Cancer Control in Turkey. Editor: Prof Dr A Murat Tuncer. Department of Cancer Control, Turkish Republic Ministry of Health, Ankara, 2008

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1.2 Cancer Nomenclature

Neoplasia (Greek for "new growth") is the abnormal and uncontrolled proliferation of cells in a tissue or organ. Most neoplasms proliferate to form distinct masses (tumours). Malignant neoplasms show a great degree of anaplasia and have the properties of invading neighbouring structures and an ability to spread through the lymphatic system and bloodstream to other organs. The term cancer is largely synonymous with neoplasm and is used as a general term for many diseases that are characterised by uncontrolled, abnormal growth of cells. Most frequent are carcinomas, malignant tumours that arise from epithelial cells in skin, the gastrointestinal tract and other internal organs. Sarcomas are derived from soft tissues (muscle, blood vessels, adipose tissue) and bone. Gliomas result from the transformation of glial cells in the central nervous system.

The WHO and IARC contribute significantly to cancer control worldwide by providing reliable cancer statistics that are a basis for the identification of cancer risks, time trends in cancer incidence and public health resource allocation. The basis of this must be a statistical classification of disease and pathology.

WHO Classification of Tumours

Cancer is typically diagnosed by pathologists on histological sections routinely stained with hematoxylin and eosin (H&E) as well as by immunohistochemistry. More recently, tumours have also been characterised by their genetic profiles, which complement histopathology and are increasingly used to predict prognosis and response to therapy.

To ensure an international standard for histopathological classification, the WHO publishes the book series WHO Classification of Tumours (WHO Blue Books). Since its initiation in 1957, the objectives of the WHO Classification have remained the same, i.e. to establish a classification and grading of human tumours that is accepted and used worldwide. IARC has been publishing the Blue Book series since 2000. Reflecting the recent rapid progress in genetics and our understanding of molecular mechanisms of cancer development, the 3rd edition (2000–2005) contains not only the histopathological classification, but includes genetics, genetic susceptibility, and concise sections on epidemiology, clinical signs and symptoms, imaging, prognosis and predictive factors. Publication of the 4th edition began in 2007, the first volume dealing with tumours of the central nervous system (Figures 1.2.1 and 1.2.2) [1].

Inclusion of new entities is a very important function of the WHO Classification. Entities are characterised by distinctive morphology, location, age distribution and biological behaviour, and not simply by an unusual histopathological pattern, whereas histological variants are defined as being reliably identified histologically and having some relevance for clinical outcome, but are still part of a previously defined entity. Once an entity or new variant is included in the WHO Classification, a morphology code of the International Classification of Diseases for Oncology (ICD-O) is assigned, which is used by cancer registries worldwide and forms the basis for the generation of histopathologically stratified data on cancer incidence. The cancer registry data provide essential data for the IARC book series *Cancer Incidence in Five Continents* (Figure 1.2.3) [2].

Tumour Grade and Stage

In the clinical setting, tumour grade and tumour stage are important additional factors that influence the choice of treatment, and allow a prediction of prognosis. Histological grade combines histological parameters, in particular the degree of dysplasia, that reflect the aggressiveness of a tumour. Grade is rated numerically (e.g. grade 1–4) or descriptively ("high-grade" or "low-grade"). The higher the numeric grade, the less differentiated the tumour cells are; a low-grade cancer is usually well-differentiated. The TNM classification system, developed and maintained by the International Union Against Cancer (UICC) is the most widely used tool for classifying the extent of cancer spread. This classification is based on the extent of the primary tumour (T), the absence or presence of regional lymph node metastasis (N), and the absence or presence of distant metastasis (M) [3].

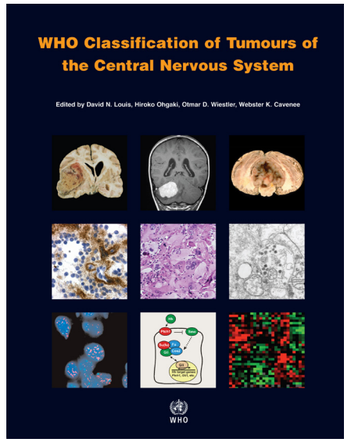

Fig. 1.2.1

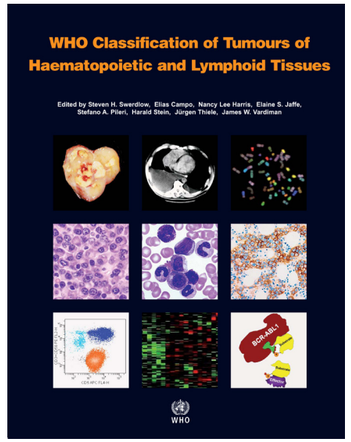

Fig. 1.2.2

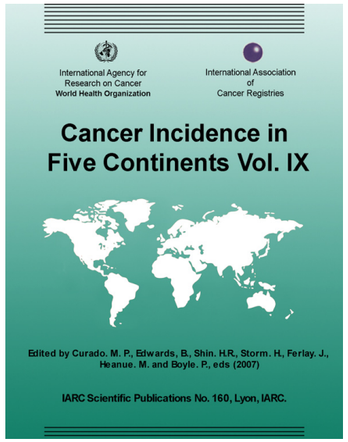

Fig. 1.2.3

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1.3 Worldwide Cancer Burden

Summary

- In 2008, there were 12.4 million new cancer cases and 7.6 million cancer deaths worldwide
- Lung cancer burden, in terms of incidence and mortality, is among the highest in the world
- More than half of cancer cases and 60% of deaths occur in the less-developed countries
- There are striking variations of cancer patterns by site from region to region
- Future cancer burden will be influenced by trends in the elderly population of both the less-developed and more-developed areas
- The role of prevention in cancer control programmes (tobacco control, vaccination, screening) will increase in the coming decades

Estimating the burden of cancer in terms of incidence (number of new cases occurring) and mortality (number of deaths) is necessary to establish priorities for cancer control. Overall in 2008, based on the most recently available international data [1,2,3], there were an estimated 12.4 million new cases and 7.6 million deaths. The most common cancers in the world in term of incidence were lung (1.52 million cases), breast (1.29 million) and colorectal (1.15 million). Because of its poor prognosis, lung cancer was also the most common cause of death (1.31 million), followed by stomach cancer (780 000 deaths) and liver cancer (699 000 deaths).

Figure 1.3.1 shows the magnitude of the most common cancers in terms of incidence and mortality, for men and women in the more-developed (Europe, North America, Australia/New Zealand and Japan) and the less-developed countries of the world. Overall, 53% of the total number of new cancer cases and 60% of the total number of deaths occur in the less-developed countries. In men, prostate cancer is now the most common form of cancer diagnosed in the more-developed regions recently (643 000 cases, 20.2% of the total of new cases), but only sixth in the less-developed countries (197 000 cases, 5.6%), whereas lung cancer ranks first (538 000 cases, 15.3%). In women breast cancer is by far the most frequent cancer worldwide, with an estimated 715 000 new cases diagnosed in the more developed regions (26.5% of the total) and 577 000 in less developed countries (18.8%).

Mortality reflects the fatality of the different cancers, and in men lung cancer remains the most common cause of death, with an estimated 455 000 deaths in the more developed regions (27% of the total number of deaths), and 475 000 in less developed countries (18.2%). Breast, lung and colorectal cancers represent 42.5% of the total deaths in women in more developed countries, while cancer of the uterine cervix ranks first in less developed countries, with an estimated 275 000 cancer deaths (13.9% of the total), followed by breast cancer (252 000 deaths, 12.7%) and stomach cancer (189 000 deaths, 9.6%). Figure 1.3.2 summarises these results and illustrates the striking variations among regions (as classified by the WHO) in the patterns of cancer occurence. Figure 1.3.3 shows the cancer incidence by site with the 20 registries with the highest and lowest rates in the Cancer Incidence in Five Continents Volume IX [4].

In 2008, the world population was estimated at around 6.7 billion, and it will reach about 8.3 billion by 2030 [5]. A 38% increase in the population of the less-developed countries is expected between 2008 and 2030, while the population growth of the more developed areas will be limited to 4%. Cancer affects mainly older age groups, and within the same period, the proportion of people over age 65 is projected to increase from 5.3% to 9.8% and from 14.6% to 22.6% in less developed and more developed areas respectively. We have already noted that there are slightly more cancer cases and deaths occurring in less-developed than in more developed countries, and since the biggest changes in the world's demography will take place in the developing areas, the future cancer burden will be more evident in these countries, and will be influenced by the elderly populations of both the more developed and less developed areas [6]. Table 1.3.1 shows the predicted number of new cases and deaths from cancer, based on demographic change and time trends. Without a change in current rates, cancer could kill more than 13 million people by 2030; with a 1% annual increase in the rate that number would be more than 17 million.

The role of prevention in cancer control programmes will increase in the coming decades: control of tobacco use, vaccination for human papillomavirus (HPV) and hepatitis B virus (HBV), and screening for breast and colorectal cancer and in less developed countries for cervical cancer remain significant challenges. If widely implemented, these measures could have a great impact in reducing the global burden of cancer.

Region	2008		2030[1]		2030[2]	
	Cases	Deaths	Cases	Deaths	Cases	Deaths
World	12.4	7.6	20.0	12.9	26.4	17.0
Africa (AFRO)	0.7	0.5	1.2	0.9	1.6	1.3
Europe (ERO)	3.4	1.8	4.1	2.6	5.5	3.4
East Mediterranean (EMRO)	0.5	0.3	0.9	0.6	1.2	0.9
Pan-America (PAHO)	2.6	1.3	4.8	2.3	6.4	3.1
South-East Asia (SEARO)	1.6	1.1	2.8	1.9	3.7	2.6
Western Pacific (WPRO)	3.7	2.6	6.1	4.4	8.1	5.9

Table 1.3.1 *Estimated (2008) and projected numbers (millions) of cancer cases and deaths, all cancers, both sexes, by development status or WHO region*
[1] no change in current rates
[2] with 1% annual increase in rates

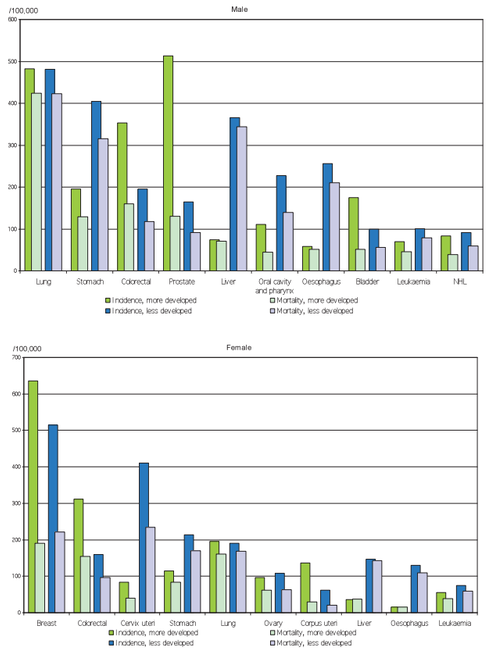

Fig. 1.3.1 *The incidence and mortality of the most common cancers in males and females in more-developed and less-developed countries*

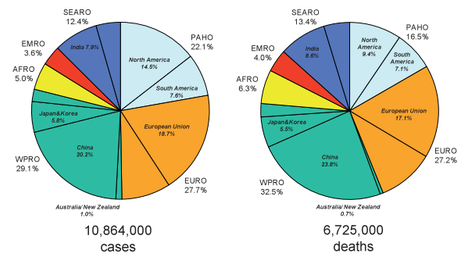

Fig. 1.3.2 *Incidence and mortality in the six WHO world areas.*
AFRO: Africa; EMRO: East Mediterranean; EURO: Europe; PAHO: PanAmerican; SEARO: South-East Asia; WPRO: Western Pacific

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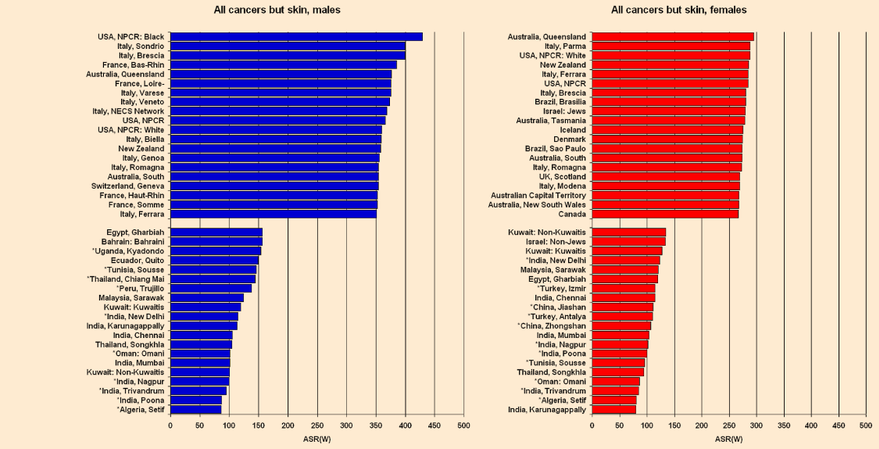
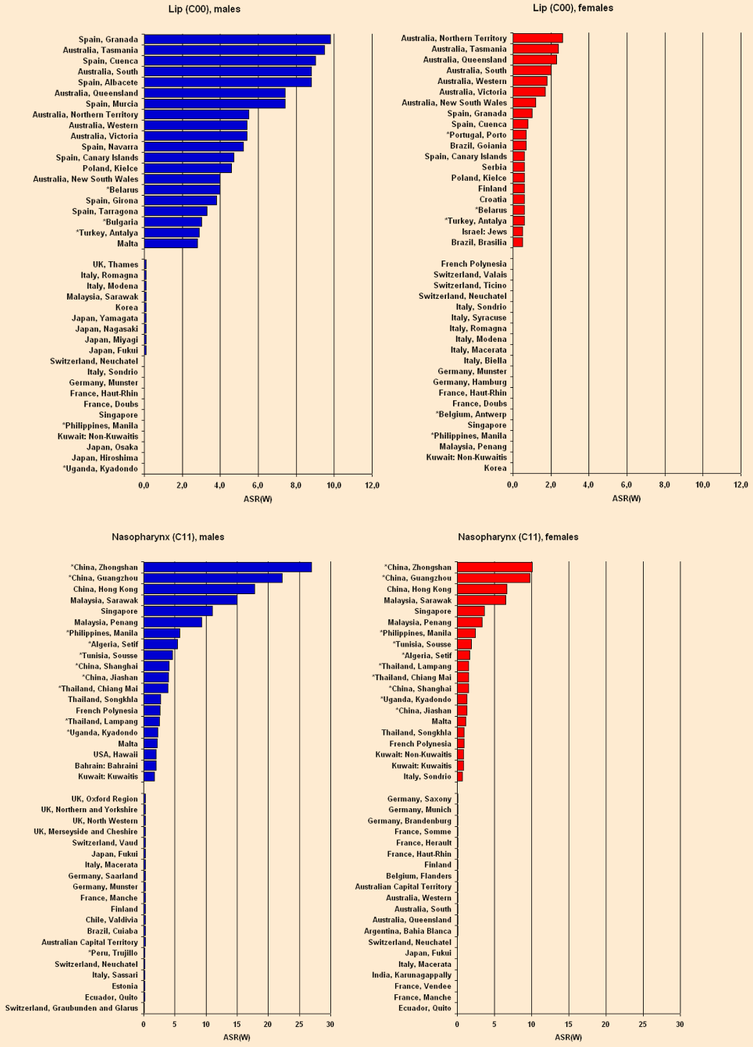


Fig. 1.3.3 *Cancer Incidence by site with the 20 registries with the highest and lowest rates*



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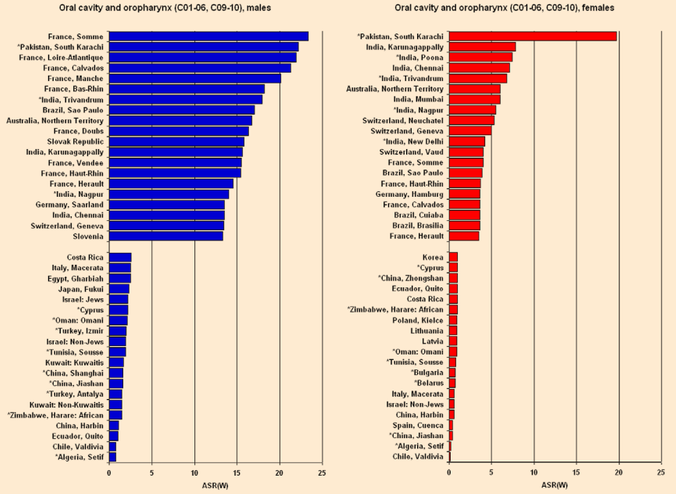

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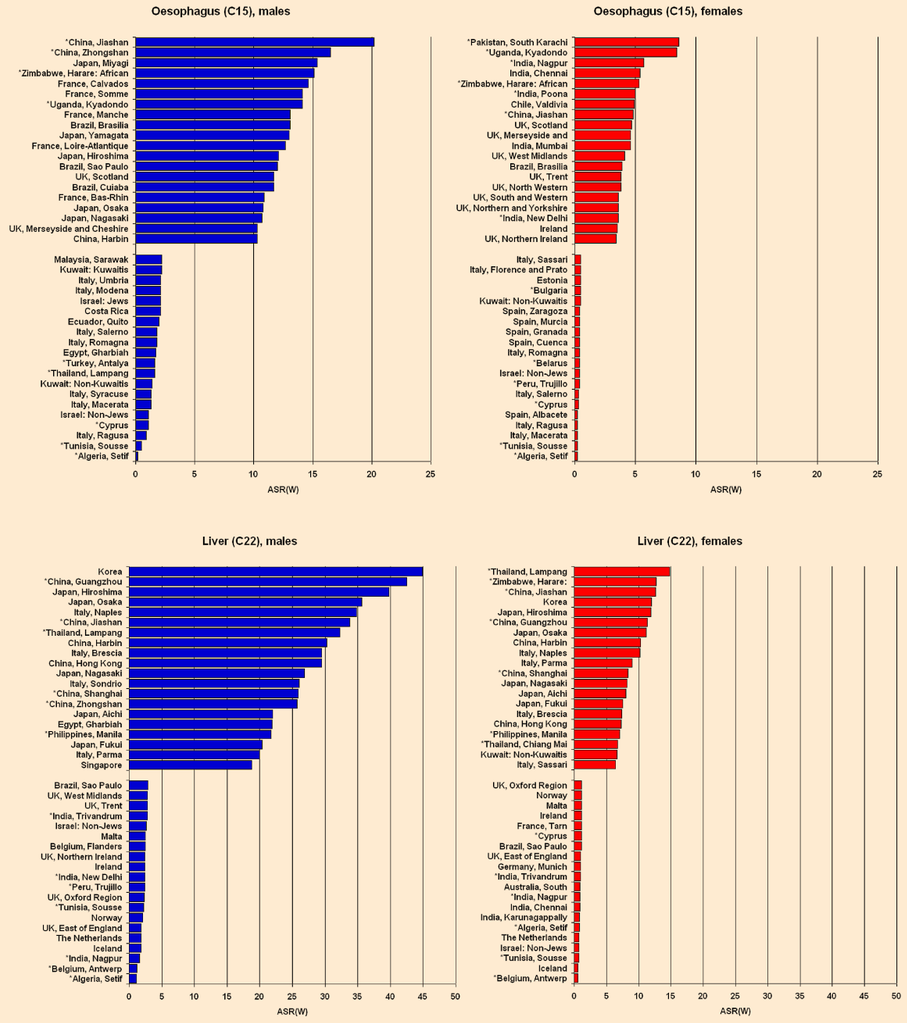

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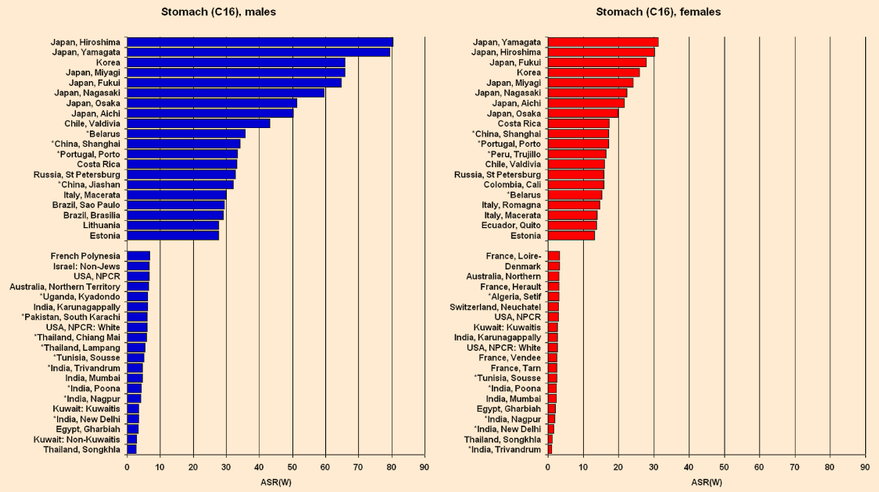

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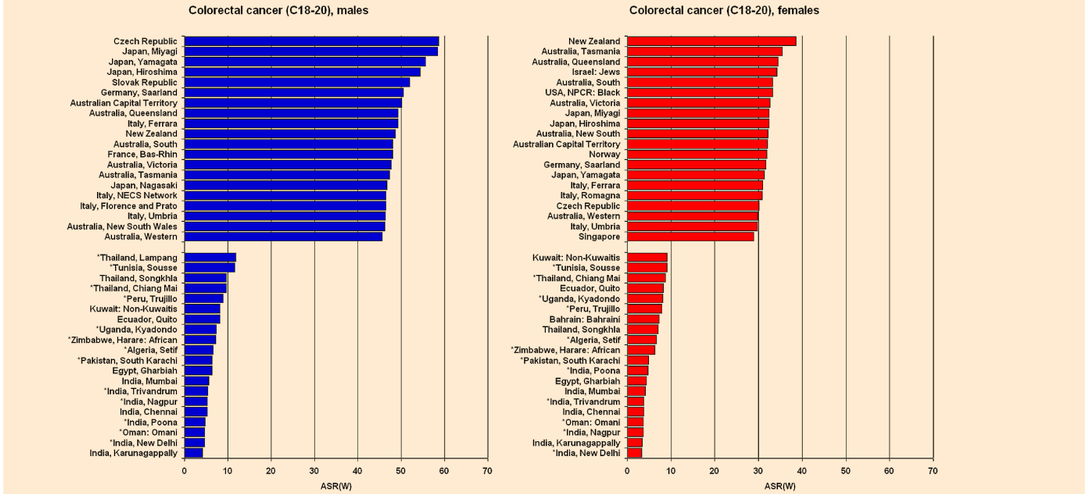

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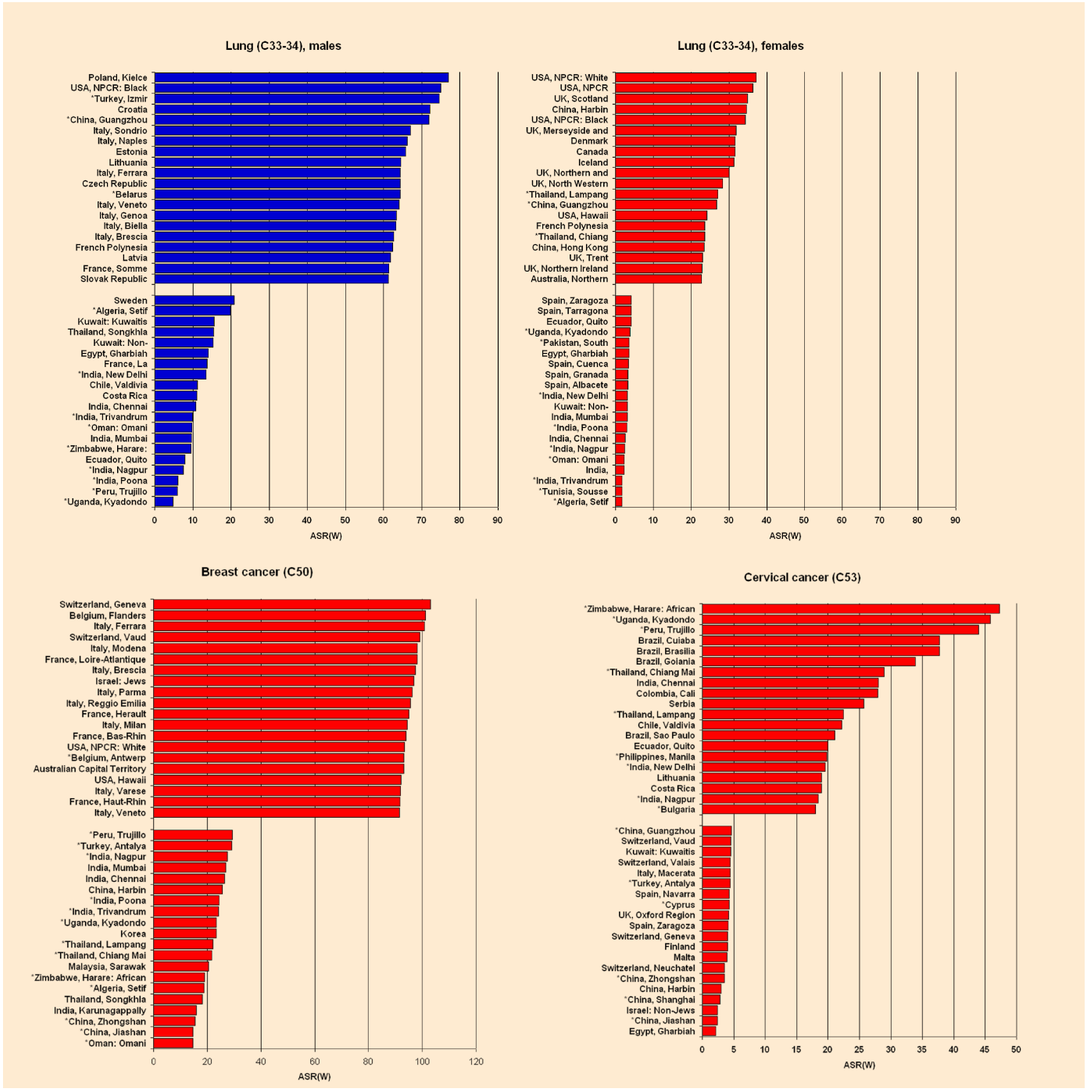

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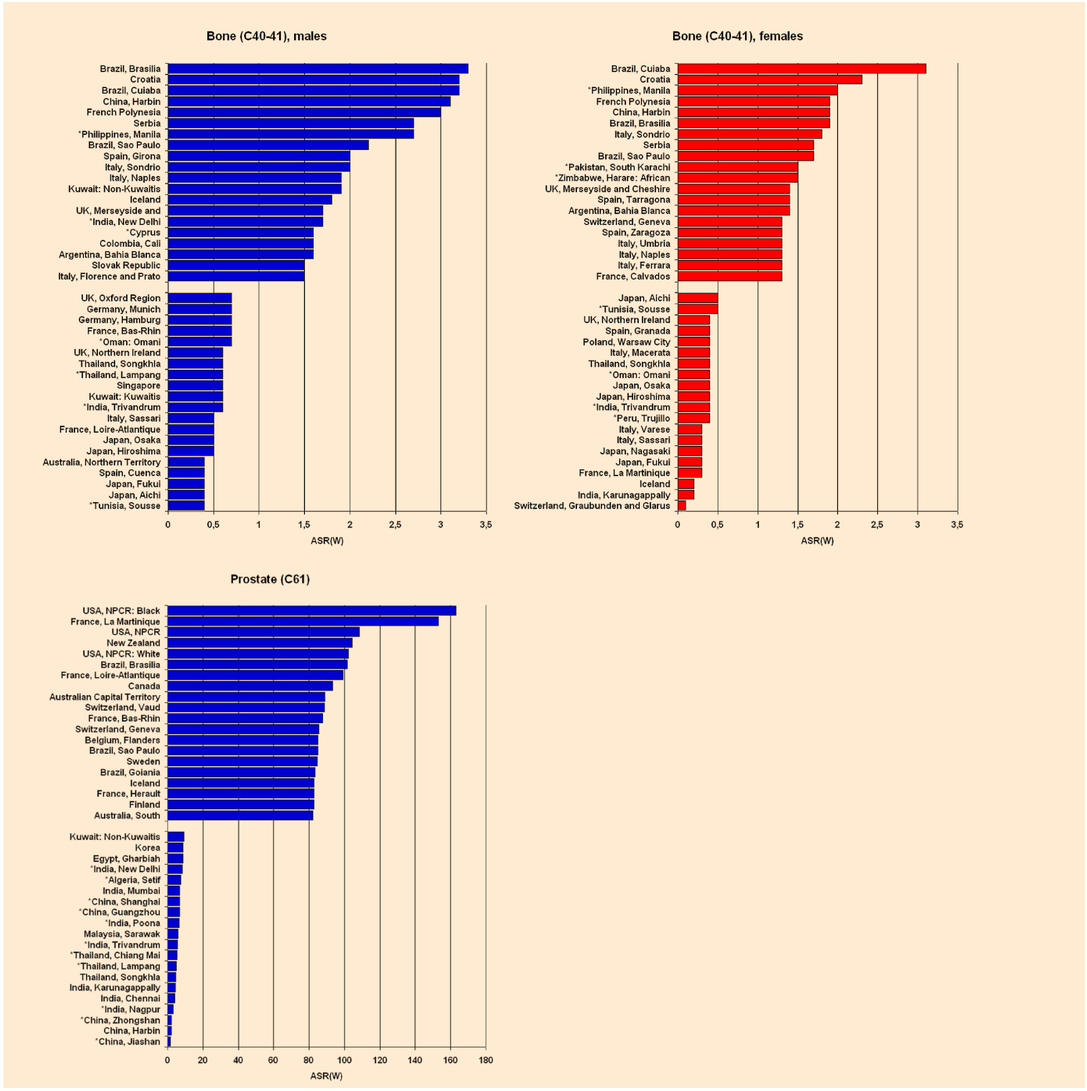

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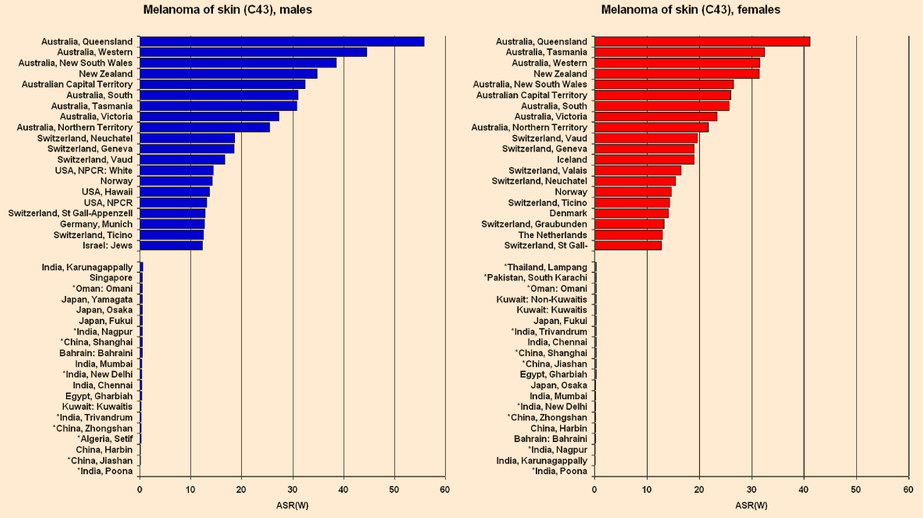

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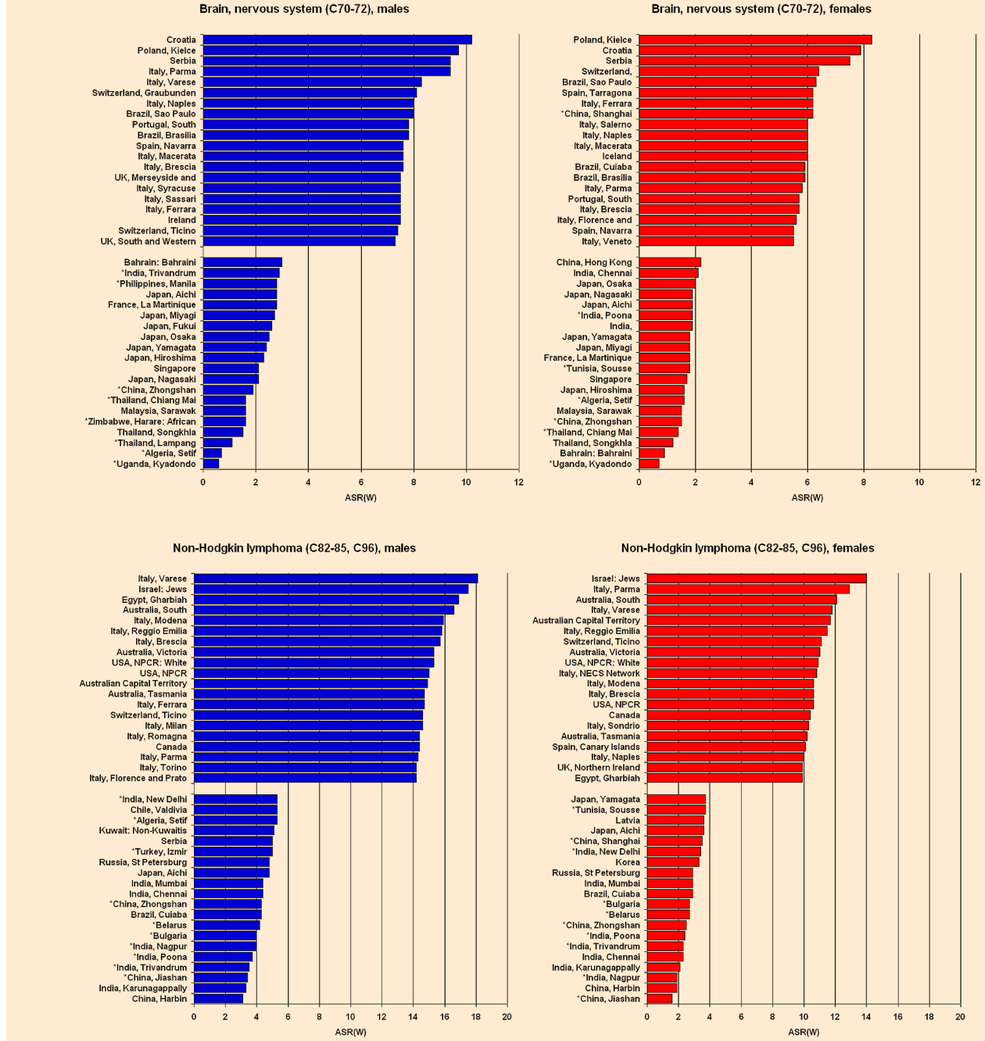

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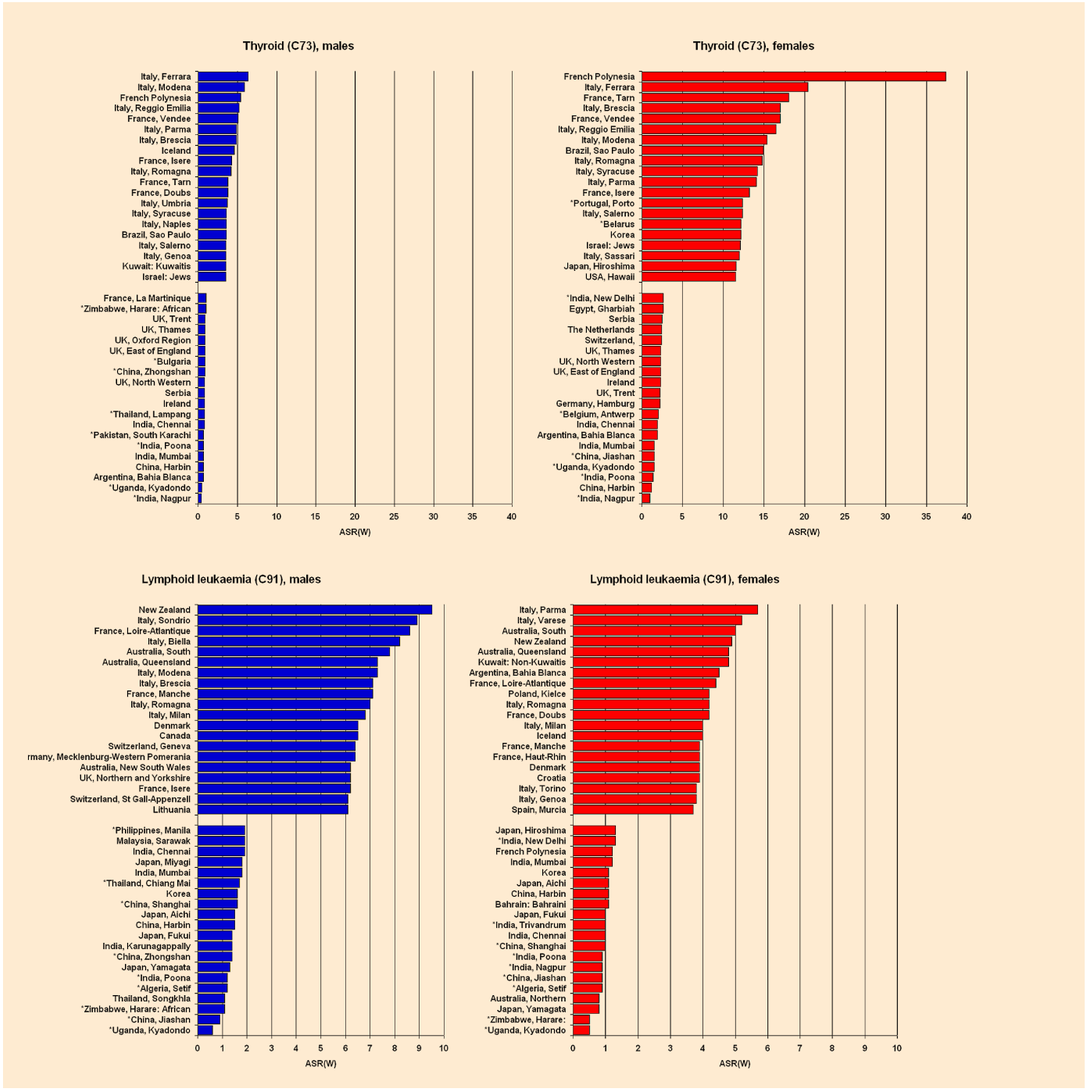

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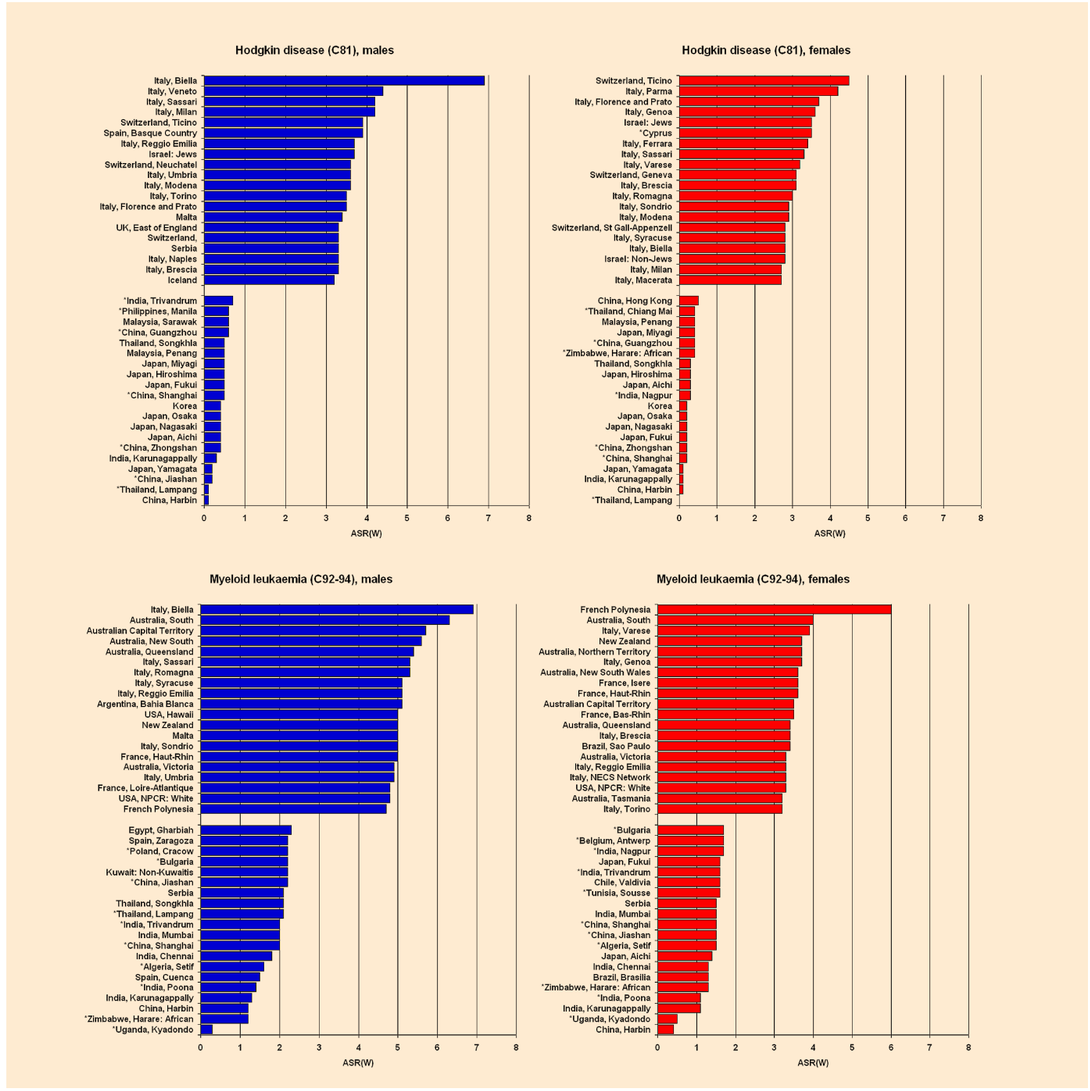

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1.4 Cancer Control in Low-Resource Environments

The burden of cancer in low-resource environments is growing, and threatens to exact a heavy toll in morbidity, mortality and economic cost in these countries in the next 20 years. The expected public health dimensions of the cancer pandemic in low-resource countries demand a widespread effective international response. The good news is that the majority of cancers in low-resource environments are preventable, and the efficacy of treatment can be improved with early detection. Currently there is enough knowledge to implement sound, evidence-based practices in cancer prevention, screening/early detection, treatment and palliation. The information at hand could prevent up to one third of new cancers and increase survival for another one third of cancers detected at an early stage. To achieve this, knowledge must be translated into action.

In the developed countries, great strides have been made over the past half century in translating knowledge into action but the same is not true in low-resource environments where cancer is generally low or absent on the health agenda. This is very unfortunate because the number of new cases of cancer in the world is predicted to increase to more than 27 million by 2030, with deaths increasing to 17 million; much of the burden of cancer incidence, morbidity and mortality will occur in low-resource countries.

However, despite the seemingly bleak outlook for cancer incidence in low-resource environments, there are many reasons for optimism. First, cancer is potentially the most preventable of the chronic illnesses [1]. Existing knowledge is sufficient to prevent at least one third of the 12 million cancer cases that occur annually. In addition, we already have the knowledge and tools needed to aggressively curb the cancer burden due to infections in low-resource environments. With the appropriate low-technology tools and resources for the application of these tools, an additional third of expected new cases can be prevented. For those with early stage cancer, there are effective strategies that can increase survival. For those with advanced and disseminated cancer, understanding of palliative care could also alleviate a great deal of suffering and improve the quality of life of cancer patients and their families.

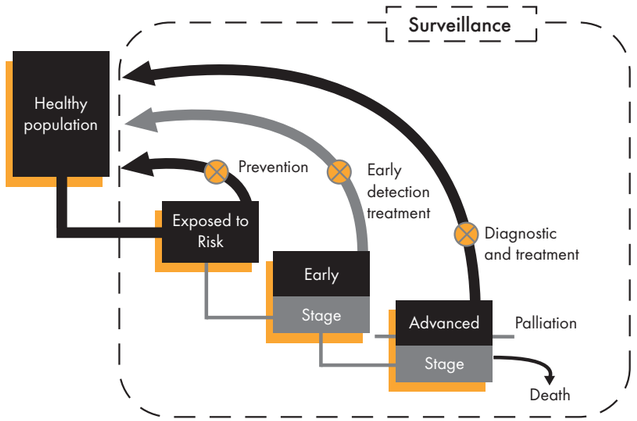

Fig. 1.4.1 *WHO's comprehensive approach to cancer control*

In most low-resource countries prevention remains suboptimal, but there are promising approaches such as the use of visual inspection methods with acetic acid (VIA) and the availability of a vaccine to prevent cervical cancer caused by human papilloma virus [2].

The WHO, in response to the looming pandemic, has intensified its fight against worldwide cancer with many promising avenues for sustainable change. In 2005, the World Health Assembly of the WHO (WHA 58) marked the urgency of global cancer incidence by the adoption of a sweeping resolution on cancer prevention and control [3]. This resolution provides the foundation for what is envisaged as a global strategy to accelerate the translation of knowledge into effective and efficient public health measures for cancer.

In low-resource environments, there is no doubt that this will be an enormous endeavour, requiring comprehensive policies and strategies to mobilise resources in prevention, early detection, diagnosis, treatment, rehabilitation and palliation [4]. These strategies will require substantial economic and human resources (as well as political will) that are non-existent at the moment. Importantly, in low-resource environments the success of cancer control will depend on the formation of equitable and enduring partnerships and the use of interventions that are culturally appropriate, economically feasible and evidence-based. Even in low-resource environments there is a large variation among countries in their ability to implement cancer control programmes; a unified cancer control strategy must consider the major differences in the implementation of cancer control activities.

The role of WHO in a unified cancer control strategy

To appreciate the role of WHO in a unified cancer control strategy, countries must look at the WHO's comprehensive approach to cancer control. This approach comprises 5 focus areas (Figure 1.4.1).

1. Surveillance

Ongoing surveillance is essential to: (1) identify the need for intervention according to the current and future cancer burden; (2) provide the evidentiary basis to formulate research plans and priorities; and (3) monitor the outcomes of preventive interventions, cancer treatment and palliation [5].

2. Primary Prevention

There are 3 step-wise interventional categories in the implementation of cancer control programmes. First is primary prevention, which means the elimination or reduction of exposure to recognised risk factors in susceptible populations. This approach potentially offers the most valuable method to improve public health, and is by far the most cost-effective and enduring intervention for reducing the cancer burden. Examples include curtailing the use of tobacco, controlling overweight and sedentary behaviour, reducing occupational exposures to carcinogenic chemicals or pollutants and diminishing the spread of cancer-associated infections such as hepatitis B virus (HBV) and human papilloma virus (HPV).

3. Secondary Prevention

The next component of WHO strategy is secondary prevention, or early detection, which entails timely diagnosis in symptomatic individuals and screening in at-risk asymptomatic persons.

Education to increase awareness of cancer signs and symptoms is an important part of this strategy. Early detection of cancer increases the chance that treatment is curative, especially for cancers of the cervix, breast, mouth, larynx, colon, rectum, testes and skin. For many of these cancers, individuals can be taught to recognise early warnings, such as a lump or lesion.

4. Diagnosis and Treatment

Diagnosis requires clinical assessment through use of modalities such as endoscopy, cytology, imaging, and histopathology. Appropriate services to combat cancer and return the patient to normal health include surgery, radiotherapy, chemotherapy or a combination of these.

Optimal treatment can improve cancer survival significantly. Unfortunately, diagnosis of cancer in low-resource environments is too frequently made in advanced stages [1].

5. Palliative care

WHO defines palliative care as an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and assessment and treatment of pain and other problems, physical, psychosocial and spiritual.

Palliative care:

- provides relief from pain and other distressing symptoms;
- affirms life and regards dying as a normal process;
- intends neither to hasten or postpone death;
- integrates the psychological and spiritual aspects of patient care;
- offers a support system to help patients live as actively as possible until death;
- offers a support system to help the family cope during the patients illness and in their own bereavement;
- uses a team approach to address the needs of patients and their families, including bereavement counselling if indicated;
- enhances quality of life, and may also positively influence the course of illness; and
- applies early in the course of illness, in conjunction with other therapies that are intended to prolong life, such as chemotherapy or radiation therapy, and includes those investigations needed to better understand and manage distressing clinical complications.

Surgical and radiological palliation and pain management are essential parts of the spectrum of cancer control and should be given high priority in every country. This is especially true in low-resource countries where late stage presentation is the rule, and the majority of cancer patients will remain uncured in the coming decades [5,6].

WHO initiatives toward a unified cancer control strategy

Over the years the WHO, in addition to producing publications on cancer control, has put forth several initiatives that can be considered milestones in the effort to put knowledge into action. These include a major international treaty on tobacco, global strategies on diet and physical activity, planning and implementing cervical cancer prevention and control programmes and several guidelines on national cancer control programmes.

1. Tobacco Treaty – The Framework Convention on Tobacco Control (WHO FCTC)

Tobacco consumption in low-resource environments is increasing. The devastation that will be caused by the increase in tobacco consumption is enormous. If no interventions are put in place, this will place a mammoth burden on healthcare systems in low-resource environments.

Tobacco is the single greatest preventable cause of cancer in the world, causing 80–90% of all lung cancers and 30% of all cancers in the developing countries. Under the current patterns of use, world tobacco-related deaths will continue to rise on a trajectory that will reach 500 million by 2050 [7]. Interventions that decrease the number of new smokers by half would lower that mortality to 340 million. While smoking rates have fallen in developed countries, tobacco multinationals have concerted their efforts toward promotion of new

markets in Asia, Central and Eastern Europe, and Latin America.

2. Global Strategy on diet and physical exercise

Most of the world's cancer burden is attributable to a few preventable risk factors. Diet is one of the modifiable risk factors for cancer that deserves worldwide attention and merits alliances comparable to those of the WHO FCTC. The WHO's Global Strategy on Diet and Physical Activity was adopted in 2004. The guiding principles of the resolution are four-fold: (1) improving the evidence for policy and guiding interventions according to the relationships between diet, activity, and disease; (2) advocating policy change; (3) increasing stakeholder involvement in implementation of a global strategy; and (4) formation of a strategic framework for action. Low-resource countries should adopt national food policies and develop ethical principles for marketing to children because these problems, while once considered problems of high-income nations, are now beginning to affect developing countries. This reflects a significant change in dietary habits and physical activity levels worldwide as a result of industrialisation, urbanisation, economic development and increasing food market globalisation. In addition, many countries still consume an excess of highly salted foods. A healthy diet of fresh fruit and vegetables can reduce risk for many cancers.

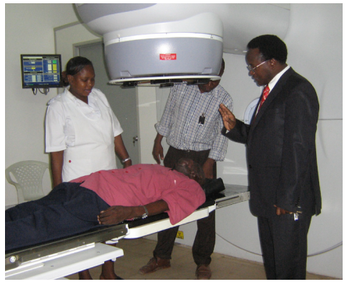

Fig. 1.4.2 *Professor Twalib N'goma in the Radiotherapy Department at the Ocean Road Cancer Institute in Dar es Salaam, Tanzania*

3. Comprehensive Cervical Cancer Control: A Guide for Essential Practice

Cervical cancer is one of the most important health problems for adult women in developing countries [8]. Cervical cancer is the second most common cancer among women worldwide.

There are 409 000 new cases diagnosed annually and 234 000 deaths in the developing world from cervical cancer [9]. The substantial burden of disease, together with the proven impact of effective screening and early treatment programmes, makes this an essential area for action [10].

Several notable resources from WHO have assisted in guiding the development and implementation of cervical cancer control programmes. An expert consultation initiated by WHO in 2001 resulted in the report *Cervical Cancer Screening in Developing Countries* [11]. This report documents guidelines on the importance of a position on cytology screening in middle-income countries with specific recommendations for improving efficacy and effectiveness of programmes in this type of setting. Additionally, it spurred development of a status report on use of visual examination with acetic acid and HPV screening for cervical cancer. The report analyzes level of evidence of their efficacy and effectiveness in different resource settings and highlights research issues that still need to be addressed for adequate policy development [11]. Guidance for the implementation of these policies is found in *Planning and Implementing Cervical Cancer Prevention and Control Programs: A Manual for Managers,* [12] which was developed to help management teams plan, implement, and monitor cervical cancer prevention and control services. This manual contributes to global efforts to improve women's health by promoting appropriate, affordable, and effective service delivery mechanisms for cervical cancer prevention and control. Detailed information on guidelines for clinical practice are available in the WHO publication *Comprehensive Cervical Cancer Control: A Guide for Essential Practice* [13].

Barriers to WHO initiatives in low-resource countries

1. Lack of recognition of cancer as a major public health issue

Cancer is often not a stated priority for health care expenditure in developing countries. Because infectious diseases typically dominate the healthcare agendas of such countries, cancer control efforts generally fall behind other priorities of the national health authorities. Due to low cancer awareness, although the majority of cancers are curable if detected and treated in the early stages, this is not the case in developing countries, because about 80% of all patients with cancer have advanced-stage disease at initial presentation.

Another factor is the lack of population-based data on cancer incidence and mortality. This problem aggravates the degree to which cancer is underappreciated as a significant healthcare challenge. The lack of local data and tendency to use data generated from western settings contributes to the low priority accorded to cancer, because ministries of health would that they do not have compelling evidence-based guidance on how cancer in their countries can best be addressed. Furthermore, because of differences in social and cultural factors, lifestyles, and available technology among other factors ,findings from studies performed in populations from developed countries may not have much relevance or applicability in developing countries. Another point is that although it is true that cancer has a low priority on the formal health care agenda of developing countries, resources nonetheless are spent on cancer when patients require care for advanced-stage disease. Such unplanned use of resources may not only be associated with poorer outcomes, but may also be more costly than planned, systematic use.

The good news is that since cancer is becoming an increasing public health problem as infectious diseases become better controlled and the population ages in developing countries, the WHO passed an important and sweeping cancer prevention and control resolution (WHA 58) that creates a mandate for member countries to address cancer care, including prevention, early detection, diagnosis, treatment and palliation of symptoms of cancer around the globe. This call for countries to address cancer control is a novel opportunity for ministers to act to address cancer in general as a core national health care issue with the expectation that assistance will be forthcoming.

2. Health care personnel and infrastructure shortages

Recruitment, training and retention of health care professionals constitute a very difficult problem in developing countries. Physicians, nurses and allied healthcare personnel are few in number and often most lacking in regions of greatest health care need. Funds are insufficient to fully equip hospitals and provide competitive salaries for appropriately trained health personnel. Developing countries are often unable to provide their professionals with an opportunity for career development and adequate remuneration. They lack the infrastructure required for professionals to carry out their work, leading to frustration and disenchantment with the system. Collectively, these factors make it difficult to attract new professionals and to retain those who have already been trained. Different developing countries will require different solutions for the same cancer problem, depending on their resources, their populations, the prevalence of disease and other factors. Thus, performing a situational analysis in developing countries is necessary before introducing cancer interventions. Situational analyses will allow researchers and health care ministries to identify ways in which the existing health care system can be used to improve cancer care in their countries.

3. Research viewed as a luxury in low-resource countries

There is an unfounded notion that research is a luxury in low-resource countries. This is not true. There are three categories of research (basic, epidemiological, interventional) that can be undertaken in developing countries. Currently most research in low-resource countries is epidemiological; some interventional research is starting while public health research is lacking. Health systems research assesses availability of manpower, training, and core equipment; the distribution and support of facilities; and the availability of funding for consumable supplies should be highly recommended in low-resource countries. It is also relevant to perform needs assessments in the general community and in the medical community, including asking the public and healthcare professionals, respectively, what their needs are and what problems they face. This type of research is efficient and allows the tailoring of programmes to a specific healthcare setting. Regarding the establishment of regional or national research programmes in low-resource countries to facilitate basic research, there is no doubt that the need exists and will grow over time with economic development. Basic research laboratories should be established, whether newly created or as an expansion of activities in existing institutions, because basic and clinical research provides for protocol-driven care in which intervention suitable to the population and resource level can be tested and adopted.

4. Loss of healthcare professionals by migration

In addition to the inherent manpower shortage, there is a problem of healthcare professionals migrating from rural to urban areas, transitioning from public to private health sectors, and emigrating from poorer to richer countries. The loss of trained health care professionals to other countries is often called the "brain drain", as professionals are actively pulled away by wealthy countries offering better opportunities. This loss could also be termed "brain flight" in that professionals are sometimes fleeing from a system that cannot offer them a viable career commensurate with their training and potential for professional growth. Thus, both low- and high-resource countries play a role in this migration phenomenon.

5. Social and cultural barriers to cancer care

In some low-resource countries non-economic barriers impede early detection and effective management of cancer. These include a host of cultural and ethnic beliefs and taboos, which can vary between different regions of the same country, religions and cultures. Failure to recognise these internal obstacles can doom the success of any cancer care programme, even when adequate resources are provided. If patients lack trust in their health care system, believe that cancer cannot be cured, or face discrimination or loss within their community by virtue of having a cancer diagnosis, they will predictably fail to use cancer services, no matter how accessible and affordable they may be. Patients will commonly turn to alternative health care strategies and traditional healers, believing them to have equal or superior ability to address difficult health problems. If cancer patients avoid seeking care until their disease is undeniably extensive, they create a self-fulfilling prophecy by virtue of the fact that the disease is truly incurable at that point. Moreover, advanced cancer requires aggressive treatment that results in side effects further adding to the fears and barriers that keep patients from seeking care. In the worst-case scenario, the public comes to believe that the treatment, rather than the cancer, causes death. These beliefs, which are difficult to overcome once established in the social network, can undermine, if not shut, down any ministry efforts toward early detection programs. Because the social stigmata of cancer can be so powerful, social barriers must be fully understood before any improved strategy is implemented in low-resource countries.

Experience from Tanzania shows that it may not be enough to simply establish a system and expect the public to use it. It may also be necessary to provide the public with the rationale for why they would want to use the system, especially in societies where there are substantial barriers to seeking care for cancer, such as lack of awareness, fatalism, stigma and fear. Societal barriers can be overcome by educating the public

and including a message of empowerment for patients to take charge of their own health.

Several parties can help overcome social barriers to cancer care. A potentially very effective way of promoting public participation is by involving the public itself or trusted community religious leaders to give the public a sense of ownership.

6. Poor resource allocation in cancer services in low-resource countries

Setting priorities for health care in general, and cancer care specifically for, is particularly difficult in limited-resource environments in light of the meagre resources set aside for health services. By creating evidence-based guidelines that stratify health care interventions into specific levels and through programmatic proposals based on cost-neutral implementation strategies, ministries of health can be offered realistic options for planning the delivery of cancer services within their public health system.

7. Lack of collaboration with other sectors and organisations

Improving a healthcare system so that it can deliver better cancer care can be accomplished if multiple sectors and organisations act in collaboration. A good example is that of the IAEA/PACT programme. The Programme of Action for Cancer Therapy (PACT) was created within the International Atomic Energy Agency (IAEA) in 2004 to build on the Agency's experience in radiation medicine and technology, with a mission of enabling developing countries to introduce, expand or improve their cancer care capacity and services in a sustainable manner. PACT does this by integrating radiotherapy into a comprehensive cancer control programme that maximises therapeutic effectiveness and impact. PACT integrates and aligns cancer prevention, screening and early detection, treatment and palliative care activities. Based on the WHO guidelines, PACT also addresses other challenges, such as long-term support for the continuing education and training of cancer care professionals in developing countries.

8. Limited use of information technology and other creative approaches

Overcoming cancer care constraints and obstacles in low-resource countries requires novel thinking and creative approaches. This is important because low-resource countries have limited availability of trained human resources and adequate facilities for prompt cancer diagnosis. The use of commonly available communication technology to transmit images to facilities in developed countries, i.e. diagnosis using telemedicine, would be very helpful in low-resource countries.

Conclusion

Low-resource countries face numerous challenges in designing and implementing programmes to improve cancer care. Although financial constraints are one obvious barrier to improving cancer outcomes, low-resource countries face a variety of other barriers, such as lack of scientific and epidemiological information to guide resource planning, shortage of trained professionals to provide necessary clinical care, competing health care crises, political insecurity or wars, or combinations thereof that divert attention from long-term healthcare issues, and social/cultural factors that obstruct the timely and effective delivery of care.

In particular, efforts aimed at early cancer detection are impeded by public misconceptions about cancer that make patients reluctant or unwilling to seek care when they notice early symptoms.

The World Health Organization has provided the framework for cancer control and improving outcomes for patients with cancer in low-resource countries and has also stressed the importance of alliances and working together with other organizations working in the cancer field. The International Atomic Energy Agency has established a Programme of Action for Cancer Therapy (PACT) and so far has six PACT model demonstration sites project in Tanzania, Sri Lanka, Vietnam, Albania, Nicaragua and Yemen.

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1.5 Principles of Cancer Therapy: Medical Oncology

Summary

> There are 20–30 cytotoxic drugs commonly used in the treatment of malignant disease

> These drugs are often administered in combination, using multiple mechanisms to induce cancer cell death

> Cytotoxic drugs can be associated with a range of side effects (neutropenia, oral ulceration, diarrhoea, hair loss, and nerve and kidney damage)

> Chemotherapy has significantly improved survival of breast, colorectal, testicular and ovarian cancer, sarcoma and a range of haematological malignancies

> Molecular biological insights have given us a range of new targets based on growth factors and their receptors which have already begun to yield new drugs

One of the most striking innovations in cancer therapy over the past decade has been the widespread realisation that cancer care is better delivered by a consultant team made up of the requisite disciplines, cooperating to construct a joint treatment plan. Improvements in the quality and standard of pathology services, driven by an internationally-agreed reporting format, which describes all the relevant morphological prognostic features coupled to high-fidelity imaging modalities (computed tomography, magnetic resonance imaging and positron emission tomography scanners), provide an ever-refined platform upon which to judge the stage of the cancer and offer the most rational treatment option. In the UK, all new cancer patients have their case presented and discussed in the multidisciplinary forum (MDT), a formal meeting subject to peer review, which minutes and implements all treatment decisions made [1]. The advantages of the MDT include the following:

- Improvements in the consistency and quality of clinical decision-making
- Creation of a forum that promulgates clinical trial recruitment
- A focus for audit, cancer registration and population studies
- A vehicle through which the latest trial results can be incorporated into current care
- A mechanism for delivering service improvement around patient access, waiting times, etc.
- An educational opportunity for students and postgraduate trainees

The therapeutic mainstays of cancer remain surgery, radiotherapy and chemotherapy, the relative contribution of each being mandated by the natural history of the specific tumour.

Principles of chemotherapy

The process of metastasis often puts the cancer beyond the potential for surgical extirpation or local ablation by radiotherapy, defining the need for a truly systemic drug based approach to cancer treatment. The history of antineoplastic drug treatment can be usefully, if rather falsely, divided into two discrete phases: drug-development pathways based on enlightened empiricism and more recently, rational drug design linked to a clear mechanism of action.

The early tumour model systems, predominantly murine cell lines which could be cultivated in vitro and in vivo, which were used to screen large chemical libraries for evidence of anti-cancer activity, had a high proliferation rate, short doubling times and a large proportion of cycling cells. This predisposed the screens to selecting inhibitors of DNA synthesis and these features led to the early taxonomies describing broad classes of cytotoxic drugs [2].

Antimetabolites are chemicals which by virtue of structural similarity to an existing metabolite, vital for the cancer cell's economy, can interfere with its utilisation, deplete its intracellular stores and promote cell death. One of the earliest examples of this class is methotrexate, an inhibitor of the enzyme dihydrofolate reductase (DHFR) which reduces dihydro to tetrahydrofolate a cofactor required for methyl transfer, e.g. in synthesis of the DNA building block thymidine (Figure 1.5.1).

The pyrimidine anti-metabolites include 5-fluorouracil, which is metabolised by cancer cells to 5-flurodeoxyuridine monophosphate, which inhibits the enzyme thymidylate synthase [3], a key component of the DNA synthetic pathway, and cytosine arabinoside and gemcitabine, which deplete intracellular pools of deoxycytidine. Similarly, the purine antimetabolites, thioguanine and mercaptopurine inhibit enzymes involved in synthesis of guanine and tend to be used in haematological malignancies.

DNA adductors. These drugs are activated to more chemically reactive species that can bind to DNA, distorting it by forming monofunctional adducts that interfere with DNA synthesis or bifunctional crosslinks that bind the two strands of the double helix together, preventing access of the various polymerases required to reduplicate DNA. This class encompasses the alkylating agents (cyclophosphamide nitrosoureas), platinum analogues (cisplatin, Carboplatin and Oxaliplatin) and mitomycin C.

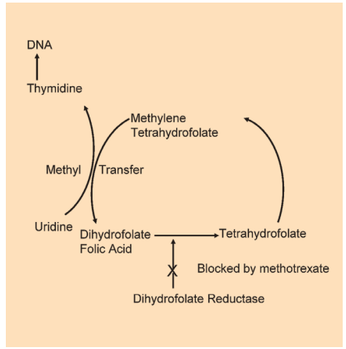

Fig. 1.5.1 *Mechanism of action of methotrexate*

Mitotic inhibitors. After the cell has doubled the amount of its DNA during the S-phase of the cell cycle, it eventually enters mitosis, when the chromosomes are pulled apart so that each daughter cell receives a full chromosomal complement. There is a complex cellular "winch", the mitotic spindle, that requires the cooperation of many proteins, chiefly tubulin, to correctly align and separate these newly synthesised chromosomes. Several anticancer agents interfere with this carefully choreographed process, by either preventing construction of the tubulin scaffold necessary for mitotic separation or indeed from inhibiting its dissolution. These are the taxanes (taxol and taxotere), the vinca alkaloids (vincristine and vinblastine) and the emerging class of epothilones.

Prevention of DNA unwinding. Doxorubicin [4] (an anti-tumour antibiotic) and etoposide (both of which are topoisomerase II inhibitors) and irinotecan and topotecan (topoisomerase I inhibitors) bind to and inhibit the enzymes responsible for the complex unwinding of the double helix required for DNA synthesis, pushing the cancer cells into an apoptotic death.

Hormone receptor antagonists

The growth and proliferation of breast and prostate cancers can be driven by their respective classes of steroid hormones estrogens and androgens by binding to their cognate receptors. One of the great therapeutic successes in cancer treatment was the development of tamoxifen, an estrogen receptor (ER) antagonist that is well tolerated and effective in patients with ER-positive breast cancer. More recent drugs like arimedex reduce production of estrogen at multiple sites within the body and have been shown to be effective breast cancer treatments, whilst androgen receptor blockers like flutamide have a useful role in the management of prostate cancer. Similarly, luteinising hormone releasing hormone (LHRH) agonists can be used to prevent the release of LHRH, by the pituitary gland, reduce production of testosterone and deprive prostate cancer cells of the androgen they need to drive proliferation.

Chemotherapy toxicity

Although these agents have disparate mechanisms of action, they tend to be more selectively cytotoxic to rapidly proliferating cell compartments, causing a number of common toxicities (e.g. bone marrow suppression leading to neutropenia, anaemia and thrombocytopenia; hair follicle cell damage leading to alopecia; induction of apoptosis (programmed cell death) of gastrointestinal crypt cells leading to diarrhoea and oral ulceration [mucositis]). There are specific toxicities associated with individual drug classes; e.g. the anthracyclines can cause cumulative damage to the heart; several drugs (cisplatin, taxanes, vinca alkaloids) damage peripheral nerves leading to sensori-motor neuropathy; cisplatin can cause renal damage; bleomycin, methotrexate and cyclophosphamide can cause pulmonary fibrosis. Thus these are potentially toxic drugs which must be prescribed by clinicians who have been sufficiently well trained in their delivery. The narrow safety margin for conventional cytotoxic drugs is magnified by the fact that most cancer patients are elderly, may suffer from co-morbidity that could sensitise them to the side effects of chemotherapy (e.g. a diabetic patient with poor renal function would need dose reductions in cytotoxic drugs like capecitabine) or may be receiving other drugs that could interact with chemotherapy and worsen toxicity (e.g. aspirin and methotrexate). Rather than Descartes' famous dictum "Cogito ergo sum", the medical oncologist, highly trained to deliver these complex agents, could have his or her professional standing described as "veneno ergo sum".

Combination therapy

The majority of cytotoxic drugs are given in combination, doublets or triplets (two or three different drugs combined) based on the notion that it is likely to induce greater degrees of cell kill by using drugs with a different mechanism of action and hopefully non-overlapping toxicity. The idea would be to use both drugs at their optimal individual doses, but in clinical practice, it is more likely that the drugs need to be dose-reduced in order to be accommodated in a multi-drug regime. Clinical trials have also explored alternating treatment between different chemotherapy regimes in order to try to prevent the outgrowth of resistant disease (with some success in breast cancer), and other studies have explored the duration of treatment, finding for example for patients with advanced colorectal cancer that there is improved quality of life for patients who have "chemotherapy holidays" of 2–3 months compared to continuous chemotherapy until the cancer progresses, without having a negative impact on the length of time patients survive [5].

Markers of effectiveness

It is interesting to consider how the effectiveness of anticancer agents is assessed. Clearly, the long-term aim is to increase overall survival for cancer patients, but in clinical trials it has proven necessary to develop a number of markers of efficacy like response rate—using modern imaging techniques like CT, PET and MRI scans to measure tumour volume prior to and at intervals during treatment to monitor tumour shrinkage or growth—and related markers like the duration of the response or the length of progression-free survival. These are useful to measure in clinical trials of new agents, as progression-free survival often correlates with overall survival, but mean that the clinical investigators do not have to wait as long to pronounce a drug effective or ineffective. Of course, as with all drug therapy, there needs to be a balance between the potential benefits (buying an extra couple of months of life) and detriments of toxicity and reduced quality of life whilst on chemotherapy, especially for those patients at the end of life. There have been steady advances in the treatment of cancer with chemotherapy and there are now tumour classes which can be cured, even when presenting at an advanced stage [6] e.g. testicular and germ cell ovarian cancers, some pediatric cancers, lymphomas and leukaemias.. The majority of common solid cancers (Table.1.5.1) can be palliated with chemotherapy, associated with significant prolongation of survival, but not cure e.g. the average survival

for cancer patients with advanced colorectal cancer without treatment is approximately six months, but rises to 20–24 months for patients who receive sequential chemotherapy [7]. Adjuvant therapy (six months of chemotherapy following surgical resection of the primary cancer) has increased the cure rate for both breast and colorectal cancer by around 10% [8]. Thus a history of steady progress rather than of the "breakthroughs" which we see so heavily promulgated in the media, but which are now reflected, for breast and bowel cancer, in improvements in population-based national cancer survival statistics.

Novel agents

The past decade has seen a remarkable increase in the translation of basic scientific knowledge into novel treatments, particularly in the field of growth factor signalling [9]. This is an evolving and increasingly complex area of science but the broad principles can be illustrated with the simple schematic in Figure 1.5.2.

A peptide growth factor, e.g. Epidermal Growth Factor (EGF), binds to its cell membrane receptor, changing the conformation of the receptor which allows it phosphorylate (tyrosine kinase activity) a host of intracellular proteins, which in turn activate ras, one of the key drivers of proliferation, which activates a cascade of kinases including B-raf, mek and erk, which signal into the nucleus, instructing the cancer cell to proliferate. Each of the proteins mentioned in this hugely simplified signal transduction pathway is a target for therapeutic intervention, blocking the pathway at a control point, reducing the rate of proliferation of the tumour cells and increasing the possibility of apoptotic cell death.

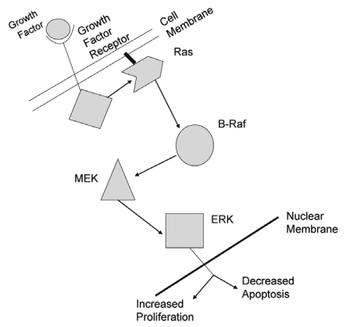

Fig. 1.5.2 *Growth factor – receptor signal transduction cascades offer multiple potential targets for anticancer drug development*

The EGF receptor is a validated target, with a number of licensed agents that disrupt its activity (e.g. the monoclonal antibody cetuximab binds to and inhibits the external surface of the receptor, preventing EGF from engaging its own receptor; lapatinib acts within the cell, inhibiting the tyrosine kinase function of the receptor, preventing onward passage of the signal following EGF binding and receptor activation) already firmly established in the clinic for the treatment of breast and colorectal cancer. The other downstream effectors (B-raf, mek and erk) are all druggable targets that have novel inhibitors in early phase clinical trials.

Inhibition of angiogenesis

Micrometastases can grow to a size of 1–2 mm in diameter, but to advance further, require establishment of their own blood supply. The tumours signal their lack of oxygen by releasing vascular endothelial growth factor (VEGF) which stimulates the growth and invasion of new blood vessels into the tumour nodule, greatly accelerating its proliferative capacity (Figure 1.5.3). The most successful means of blocking angiogenesis has come from the development of the monoclonal antibody bevacizumab, which binds to and inactivates VEGF. This antibody has been assessed in a number of large, well-designed clinical trials and prolongs survival (2–4 months) in patients with advanced colorectal, breast and lung cancer [10]. The antibody is well tolerated (it causes hypertension, proteinuria and rarely, thrombosis) but

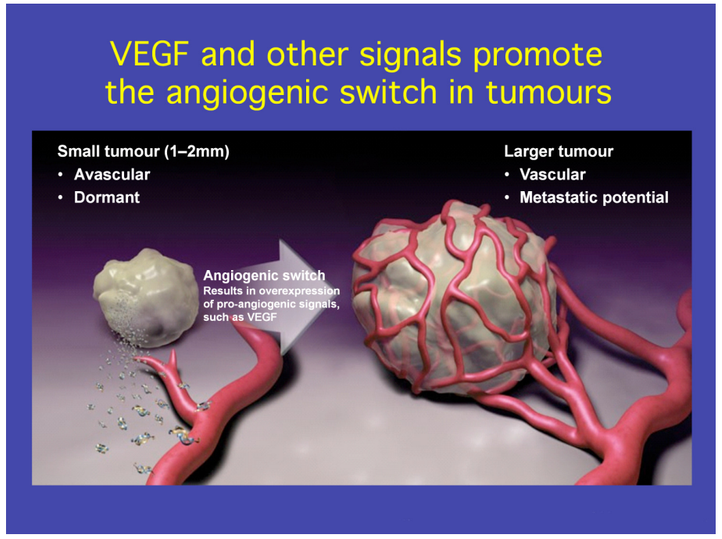

Fig. 1.5.3 *Angiogenesis. Adapted from Bergers G et al (2002) Nature Reviews: Cancer 3(6): 401-410*

expensive, costing up to $100 000 per year for individual patients, putting it currently beyond the cost-effectiveness model employed by the UK's National Institute for Clinical Excellence.

These innovative cancer medicines pose an enormous challenge to the oncology community given the profusion of new targets, novel agents and the potential they have to be combined with conventional chemotherapy and with other transduction inhibitors. It will require a huge number of empirical clinical trials, or a change in trial paradigm in which we try to select patients with tumour-associated biomarkers which would predict a higher-than-average likelihood of response. If we can use tumour biology to identify markers of chemosensitivity, then these can be used to enrich the population of patients we treat, then we should be able to refine and speed up recruitment to clinical trials. We are entering a period when sophisticated molecular tools—e.g. RNA signatures, specific DNA mutations, and patterns of phosphorylation of specific proteins—will give us the technical capacity to deliver on the potential of personalised medicine, saving patients from the needless toxicity of inactive drugs, and allow healthcare systems the possibility of targeting expensive new cancer drugs to the subpopulation of patients who will benefit most [11].

Medical oncology in the developing world

As has been emphasised elsewhere (Chapter 1.1), the increasing incidence of cancer in the developing world presents an extraordinary challenge to the healthcare systems of these emergent nations. Whilst realising that there are many competing priorities (cancer screening early detection and prevention, palliative care etc.), this does not detract from the requirement

Category	Tumour type
1	Childhood cancer; leukaemia; lymphoma; testicular cancer (teratoma and seminoma); germ cell tumours of ovary; choriocarcinoma
2	Early breast and colorectal cancer; sarcoma
3	Advanced breast, colorectal, lung, gastric, ovarian, hepatocellular, pancreatic and renal cancer, myeloma
4	Breast and rectal cancer; sarcoma
5	Melanoma; brain tumours

Table 1.5.1 *Chemotherapy efficacy in different cancer types by category*
Category 1: Tumours for which there is evidence that the use of a single or a combination of drugs used alone or with other therapeutic modalities will result in cure as defined by a normal lifespan in some and prolongation of survival in most patients.
Category 2: Tumours where the average survival is prolonged when chemotherapy is used as an adjuvant to local surgery or radiotherapy in the early stages of disease.
Category 3: Tumours where there is evidence that a single drug or a combination will produce clinically useful responses in more than 20% of patients. Prolongation of survival occurs in most responding patients but may be of short duration.
Category 4: Tumours where local control may be improved by using chemotherapy before, during or after surgery and radiotherapy.
Category 5: Tumours for which there are currently no effective drugs. Objective responses occur in less than 20% of patients and there is no evidence of survival benefit in randomised controlled trials when compared to best supportive care.

Alkylating drugs	Cytotoxic antibiotics	Antimetabolites and related therapy	Vinca alkaloids and etoposide	Other antineoplastic drugs
Cyclophosphamide	Bleomycin	Cytarabine	Vinblastine and vincristine	Asparaginase
Chlorambucil	Doxorubicin	Fluorouracil	Etoposide	Cisplatin
	Dactinomycin	Mercaptopurine		Dacarbazine
	Daunorubicin	Methotrexate		Procarbazine
		Calcium folinate		

Table 1.5.2 *WHO drug list*

to treat patients who present with established cancer. These nations suffer from a relative paucity of treatment facilities, few accredited oncologists and limited access to the appropriate drugs, coupled to the fact that patients tend to present with advanced disease. Given the background of intercurrent illness (infection, AIDS) and malnutrition, dose adaptation from conventional cytotoxic drug regimes is often required. There is a large survival gap comparing outcomes between high-resource and low-resource nations, especially when comparing the potentially chemocurable cancers. Survival rates for childhood cancers can be more than twenty times better in developed healthcare systems. As previously described, research has yielded steady improvements in outcome from novel agents, but at a hugely increased cost. This must be set against a context of the per-capita total healthcare expenditure of approximately $8 per annum in Kenya [12]. It would seem rational to create a priorities list of essential anticancer drugs, striking a balance between efficacy, tolerability and cost. The WHO has published a cancer formulary, identifying drugs that are generic, relatively cheap and moderately effective. As national cancer plans are developed by individual countries, priority should be given to those tumours which may be curable, perhaps focusing on paediatric cancers and on prevalent tumours where chemotherapy can offer useful palliation and prolongation of life, e.g. breast and cervical cancer, by far the two most common cancers of women in Africa, accounting for about 60% of disease burden.

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CANCER INSTITUTE PROFILE:
Cancer Australia

Cancer Australia is a national agency established by the Australian Government in 2006 to help reduce the impact of cancer on all Australians. Cancer Australia also aims to lessen differences in outcomes for people with cancer whose survival rates or cancer experiences are poorer, including Australia's indigenous people, people living in rural and regional areas and people from culturally and linguistically diverse backgrounds. It works directly, and in partnership with consumers, health professionals, cancer organisations, researchers and governments, to improve cancer outcomes.

Cancer Australia's initial priorities are to:

- enhance support and information for people affected by cancer,
- increase coordination and funding of cancer research and support clinical trials,
- improve cancer services and the availability and use of cancer data,
- support professional development of the cancer care workforce,
- review national cancer control and cancer research activity and identify action to improve cancer outcomes in Australia, and
- establish and manage the National Centre for Gynaecological Cancers.

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1.6 Basics of Cancer Surgery

History

The first reported use of surgery to treat cancer was in ancient Egypt circa 1600 BCE, though Hippocrates (400 BCE) later advised against it, and his advice influenced the attitude of the Christian church throughout the Middle Ages. Since then, surgery has become a potent tool in the management of cancer. Epochal events in the surgical management of cancers include the development of surgical methods for primary treatment of cancers of the larynx, oesophagus and stomach by Albert Theodore Billroth, breast by William Stewart Halstead, thyroid by Emil Theodore Kocher and prostate by Charles Huggins [1]. In contrast with those early days, surgery is now used within the context of multidisciplinary management of cancer patients, where it plays a role as one of the components of modern cancer management.

Surgery for cancer screening and prevention

Surgery has a well-defined role in the prevention of cancers. Apart from clinical conditions that are treatable by surgery, which can undergo malignant transformation if left untreated for a long time (for example scar carcinomas associated with burns, chronic skin ulcers and chronic infections like pulmonary tuberculosis), surgery can be used for the treatment of precancerous lesions or for removal of normal organs which are at an elevated risk of developing cancers.

Fig. 1.6.1 *Professor Clément Adebamowo, Professor of Surgery at the University of Ibadan, Nigeria*

Well-identified precancerous lesions where surgical intervention is beneficial include Medullary Thyroid Carcinoma (MTC) when it occurs as part of Multiple Endocrine Neoplasia Syndrome (MENS) Types 2A and 2B. MENS arises as a result of autosomal dominant germline mutations in *RET* proto-oncogene, and all carriers of the mutations develop MTC. To prevent MTC, prophylactic total thyroidectomy is done before 5 years of age in MENS 2A and during the first year of life in MENS 2B [2]. Germline mutations in BRCA1 and BRCA2, present in between 1 in 150 to 1 in 800 North Americans, is associated with about an 80% lifetime risk of breast cancer and between 23–54% lifetime risk of ovarian cancer. Prophylactic mastectomy and surgical oophorectomy are among established methods of reducing this risk [3]. Several high-penetrance genetic risk factors for colorectal cancer have been identified, and their presence is an indication for increased frequency of screening and in some cases prophylactic resection of the colon and rectum [4,5]. Surgical intervention in intraepithelial neoplasms (IEN) involving organs such as the oral cavity, urinary bladder, breast, uterine cervix and oesophagus also lead to substantial reduction in invasive cancer risk [6].

Surgeons have access to other individuals at high risk for malignancies. With the marked improvements in outcome for treatment of cancers, there is an increasing number of cancer survivors who are at elevated risk of developing new cancers in residual tissues, as a result of genetic predispositions or due to mutagenic effects of chemotherapeutic or radiotherapeutic treatments [7]. Other high-risk populations that may be seen with precancerous lesions and opportunities for cancer prevention include people with albinism, who are at risk for a range of skin lesions including cancer [8].

Apart from these active surgical interventions, surgeons also have an important role to play in referring patients for genetic counselling and testing, and counselling patients on smoking, weight control, healthy diet, physical activity and other behavioural risk factors [9]. Given the high prevalence of obesity worldwide [10], the role of high dietary calorie intake in cancer etiology [11] and the increasing role of bariatric surgery in weight management, surgical management of obesity [12] may soon become an important cancer prevention intervention.

Surgery for cancer diagnosis

The role of the surgeon in cancer diagnosis is very important because this is often the first step for many patients, and the choices made by the surgeon may have significant and far-reaching effects on the treatment and outcome for the individual patient. Careful history-taking and clinical examination remains the bedrock upon which a sound diagnosis is based. This includes evaluation of the presence of risk factors, clinical stage of disease, presence of co-morbid factors, family history of cancer, psycho-social status of the patient and the patient's expectation from treatment. Clinical interaction also provides an opportunity for the clinician to educate the patient about the disease and treatment options, ascertain the patient's treatment preferences and let the patient know follow-up requirements. It is often the surgeon's duty to obtain a tissue sample for diagnosis. In order to do this and obtain tissue that will help the pathologist contribute to the management of the patient, the surgeon must select the appropriate biopsy method, decide on need for ancillary imaging facilities, ensure that the tissue is properly fixed and gets to the pathologist on time, and that the results are obtained promptly from the pathologist. The work of communicating with the patient about the illness starts with the clinical evaluation and continues with explanation of the tissue diagnosis and need for additional tests as may be required.

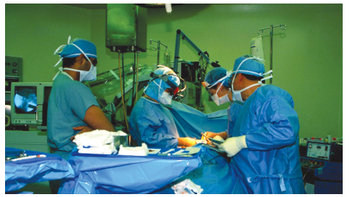

Fig. 1.6.2 *A surgical intervention*

Surgery for cancer staging

Surgery plays an important role in the clinical staging of cancer. Staging is important in order to objectively document the extent of disease, choose appropriate treatment for stage, follow-up the patient's response to treatment, prognosticate, enhance ability to compare treatment outcomes across health systems and facilitate research. The most widely used staging system is the TNM system, but a few other cancers like lymphomas use a different classification system that reflects the natural history of those diseases and guides planning of their treatment [13].

Surgery for cancer treatment

Modern cancer treatment involves a multidisciplinary approach that includes other treatment options and is based on knowledge of the molecular biology of cancer. Optimisation of cancer treatment depends on careful orchestration of the different treatment modalities in order to provide patients with maximal benefit. In deploying surgery for the treatment of cancer, the surgeon must make a careful preoperative evaluation of the patient, weigh the risks and benefits of surgery, identify and correct underlying health problems and take account of co-morbid factors. The choice of surgical intervention depends on the nature and stage of disease. Standard indications exist for choosing limb- or body part-preserving surgeries over more extirpative procedures. The trend is towards use of less mutilating procedures except where indicated. Surgical intervention may also be needed to provide vascular access for chemotherapy [14], for cytoreductive surgery as an adjunct to other treatments [15], for the treatment of complications of cancer treatment and for the treatment of metastases.

Surgery for rehabilitation

After primary treatment for cancer, surgery plays a role in the rehabilitation of patients. Cosmetic surgery to fashion body parts, enhance form, function or cosmesis is important and is an integral part of surgical interventions designed to improve the quality of life. Other surgical interventions for improvement in quality of life include bypass surgery in hollow viscus obstruction even when the primary tumour is inoperable or not surgically curable, surgical creation and care of ostomies, provision of psychological support and other interventions designed to maintain and improve quality of life.

Surgery for palliative care

Surgical palliation is designed to relieve symptoms for patients beyond cure when non-surgical measures are not feasible, not effective or not expedient. It encompasses all treatment options that are designed to enhance quality of life rather than eliminating disease [16]. The provision of comfort and control of cancer-related symptoms can optimise the remaining life of a patient, increase functioning and enable self-care [16]. Active surgical procedures designed for palliative care include nerve plexus blocks, epidural and pudendal blocks for the management of pain, enteral and parenteral nutrition, wound or ulcer care, intubation for bypass of hollow viscus obstruction, tracheostomy for airways obstruction, management of renal failure and management of rectal or urinary incontinence.

Surgery for cancer emergencies

Certain presentations of cancers require emergency intervention in order to save the life of the patient, relieve pain or prevent organ deterioration and failure. Examples of such situations include perforation of hollow viscera which may occur on account of progression of cancer or as a complication of chemotherapeutic treatment, for example, in gastrointestinal lymphoma. Cancers can also perforate and cause acute peritonitis or chronic abscesses. Major haemorrhage may arise from cancers and this can be due to growth of cancers into and erosion of major vascular structures; capillary haemorrhage from ulcerated cancer, and tumour rupture [17]. Other oncological emergencies include progressive spinal cord compression after corticosteroids and radiation therapy; relief of respiratory distress secondary to pleural effusion and surgical extirpation of localised carcinoids.

Factors that influence outcome of treatment

Outcome of surgical treatment depends on healthcare personnel (including surgeons) related factors, patient-related factors and healthcare environment and infrastructure-related factors. Health care personnel-related factors include surgical skills, volume of surgery, specialisation, adequacy of support staff, etc., which all have a direct influence on outcome of surgical intervention. Patient-related factors include the patient's psycho-social state; diligence in following complex treatment plans; compliance with follow-up regime and symptom surveillance for early detection of complications, recurrence and metastasis; nutrition and physical activity; post-operative emotional state; and co-morbidities. Infrastructure-related factors that can also influence the outcome of surgical treatment of cancers include the adequacy and level of sophistication of treatment resources and outreach to the individual patient.

Future of surgery in cancer management

Despite advances in other treatment modalities, surgery will continue to play an important role in the multidisciplinary treatment of cancer. Further clarification of the genetic risk

of cancer and identification of populations at risk may increase the role of surgery in prevention. Future advances include expanded use of laparoscopic and other minimally invasive techniques, robotic surgery, image-guided interventions and telemedicine. In developing countries, surgical services, though grossly inadequate, remain the most widely used treatment for solid tumours [18]. Efforts at improving availability and consideration of alternative models for delivery of surgical treatment for cancer patients are needed [19].

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CANCER INSTITUTE PROFILE: National Cancer Center of Korea (NCC)

Founded as a government-funded institution in 2001, the National Cancer Center of Korea (NCC) strives to reduce cancer incidence and mortality in Korea through research, patient care, support for the national cancer control programs, and education and training for cancer specialists. NCC is composed of three main components: Research Institute (RI), Affiliated Hospital (Hospital) and National Cancer Control Research Institute (NCCRI).

The RI conducts its own research and supports the Korean cancer community's research activities through its intramural and extramural programs focused on translational research.

The hospital has 6 organ-specific centres. Staffed by medical, surgical, radiation oncologists and oncology nurses, each centre always provides patients with quality cancer care services.

NCCRI plays a think-tank role, assisting the government in formulating, implementing and evaluating the government's cancer control programmes.

Currently, more than 1000 employees, including 250 medical doctors and researchers, are involved in the NCC's activities.

website: www.ncc.re.kr/index.jsp

1.7 Radiotherapy

Summary

> Radiotherapy has been developing as a clinically essential part of the armamentarium against cancer since the last decade of the nineteenth century, when Röntgen invented a means of generating X-rays

> A little over 50% of all patients who develop cancer will require radiotherapy at some time during their illness. This percentage will vary from one tumour type to another

> The basic essentials then of a modern radiotherapy department would be sufficient linear accelerators to deliver the treatment capacity requirements for the region served. However, radiotherapy is one of the least expensive cancer treatments per patient and one of the most effective in terms of cure and overall survival

> Radiotherapy has seen a technology avalanche in the last twenty years that has offered the same level of exciting prospects that the quantum leap from kilovoltage to megavoltage equipment encouraged sixty years ago

> Radiotherapy is part of the multimodality and multidisciplinary management of patients with cancer. It is essential for good cancer care: chemotherapy and surgery cannot effectively replace it. Where it is not available 50% of cancer patients are being denied appropriate care.

Radiotherapy has been developing as a clinically essential part of the armamentarium against cancer since the last decade of the nineteenth century, when Röntgen invented a means of generating X-rays. The scientific basis has been explored and explained through radiobiology and its associated sciences. The clinical foundation of radiotherapy has expanded through high-quality clinical trials. The economic and social justification for radiotherapy is defined by numerous cancer service and public health reviews.

A little over 50% of all patients who develop cancer will require radiotherapy at some time during their illness [1]. This percentage will vary from one tumour type to another. About 70–83% of breast cancer patients would be expected to undergo radiotherapy [2] while only 1% of patients with colonic cancer will require such intervention [2]. Service needs depend, therefore, on the disease profile in a community. It is also affected by the extent of disease at presentation. Where the disease burden is such that the norm at presentation is more locally advanced disease, indications for a given treatment intent and duration will differ from situations where early presentation, for example through screening, is more common.

Radiotherapy may be applied with different intents which vary with the disease type and its extent. Palliative radiotherapy, delivered often in a few (one to five or ten) radiation exposures (or fractions) and using simple, often single-field techniques, will be offered to improve quality of life and reduce symptoms in advanced or metastatic disease. It is particularly effective in the palliation of bone metastases pain, dyspnoea from obstructive lung tumours, dysphagia from obstructive oesophageal cancer, bleeding from advanced pelvic malignancies, headache and symptoms of raised intracranial pressure from brain secondaries, superior vena caval obstruction and early presentation of malignant spinal cord compression.

Radical and generally high-dose radiotherapy may be required either as sole treatment or as an adjunct to surgery (usually post-operative) for early-stage malignancies. Typically such courses of treatment last several weeks with radiotherapy delivered daily and using multi-field complex techniques.

Such adjuvant treatments are routinely used in breast cancer after breast-conserving surgery or in selected patients after mastectomy to reduce local recurrence risk by two thirds, with the prospect of reducing breast cancer mortality by one sixth and improving overall survival. Radical radiotherapy alone may be delivered for early laryngeal cancer with the intent to cure while preserving function and the voice.

Essential components of a radiotherapy service

While radiotherapy has been prescribed since the early days of the X-ray era in medicine, the first major developments leading to improved effectiveness and reduced morbidity were introduced in the 1950s. The introduction then of machines capable of delivering high-energy–megavoltage–X-rays (rather than kilovoltage beams) or gamma-rays, the former from linear accelerators and the latter from equipment such as the cobalt therapy machine utilising high activity radioactive sources, was critical to the further development of modern radiotherapy. High-energy ionising radiation beams spare the surface tissue, thereby removing one limitation to delivering an adequate radiation dose deep in the body at a tumour: the skin surface was no longer the area of maximum dose and the acute radiation skin reaction no longer limited the patient's tolerance.

With mega-voltage machines, radiation beams were delivered from equipment that no longer required leaded cones to direct and confine the beam. Treatment machines could, therefore, be mounted on 360° gantries allowing treatment utilising multiple beams, each of which could be shaped into rectangular fields from a small size (about 4x4cm) up to very large sizes. Rectangular beams could be shaped by the placement of custom-made lead blocks into the beam. More normal tissue could, thereby, be spared.

Such principles remain the basis of modern radiotherapy while the technological improvements in equipment in the last two decades have refined the processes and significantly increased the possibilities. Now beams can be made smaller by utilising special beam modifiers that allow stereotactic beam arrangements in, for example, the brain. Beam shapes can be varied using multi-leaf collimators consisting no longer of two sets of thick steel shutters set at right angles (to give rectangular shapes) but of, for example, 120 single sliding steel "leaves", each 0.5cm thick and capable of independent placement in the beam.

Beam energies can be varied to give different degrees of dose penetration. While X-rays and (less so) gamma-rays are still used, high-energy electrons can also be delivered to treat more superficial tumours of variable depth while sparing deeper tissues.

This sophistication of treatment delivery has required a similar improvement in systems to keep patients immobilised for the few minutes of treatment and to image the treatment areas before treatment is embarked upon, before individual treatment exposures are delivered and after radiation exposure. In the latter half of the twentieth century, much of the planning of an individual patient's treatment depended on clinical skills, palpation, direct visualisation and plain, often orthogonal, X-ray films. From the 1970s, image intensifiers mounted on gantries of the same specification and accuracy as a linear accelerator–radiotherapy simulators–provided more accurate treatment field placement. In recent years, with the introduction of digital imaging processes and cross-sectional imaging, these simulators have developed basic CT capability to further improve treatment field planning.

More recently still, CT scanners have been used to provide cross-sectional images that can be incorporated into the computers used to determine radiation dose distribution from optimal field arrangements. Now it is commonplace to have specific CT scanners designed for radiotherapy field simulation–CT simulators–in radiation oncology departments, dedicated to radiotherapy planning and often replacing simulators.

The basic essentials then of a modern radiotherapy department would be sufficient linear accelerators to deliver the treatment capacity requirements for the region served. Where electrical supply is more erratic and unreliable, an adequate option is a cobalt therapy megavoltage unit. The linear accelerators must be of a specification to deliver safe treatments efficiently. Multi-leaf collimation, while highly desirable for field shaping, is not absolutely essential but more efficient and safer for use than customised blocks.

In addition, an accurate imaging process–a diagnostic level CT scanner or a CT specified simulator or CT-simulator–is required. A computerised planning system provides the other essential component.

These demand an initial high capital outlay. However, radiotherapy is one of the least expensive cancer treatments per patient [3] and one of the most effective in terms of cure and overall survival. It accounts in the UK for less than 10% of the cancer budget, while chemotherapy will cost more than 15% and surgery more than 30%, as does emergency unscheduled care for cancer patients [4].

Apart from equipment needs, any radiotherapy department requires a multi-professional team of oncologists, physicists, dosimetrists, radiation therapy technicians or radiographers, nurses and clerical and administrative staff. A comprehensive cancer care service also needs allied health staff in psychology, speech and language therapy, nutrition, occupational therapy and physiotherapy. Each group requires adequate prequalification training and subsequent and on-going professional development.

Quality and safety

Improvements in radiotherapy technology and equipment have facilitated improvements in care and generally resulted in a reduction in radiation-induced morbidity. Radiotherapy can be offered to more patients with a broader range of performance status for not just a wider range of tumours but also a broader spectrum of stage. While some innovations were developed to improve safety, such as the automatic and digital transfer of radiation beam data from computer planning systems to the record and verification systems that manage and control the treatment units, others have demanded increased quality checks.

An essential component for any radiotherapy centre is, therefore, a robust multi-professional quality and safety protocol and review process as described in the recent multi-professional report *Towards Safer Radiotherapy* [5].

Recent radiotherapy developments

Radiobiologically it has been understood for over fifty years that hypoxic cells are more resistant to X-, gamma- and beta-(electron) rays. Various approaches have been investigated to overcome this problem. To date irradiation in hyperbaric oxygen, concurrent treatment with hypoxic cell sensitisers and the use of high

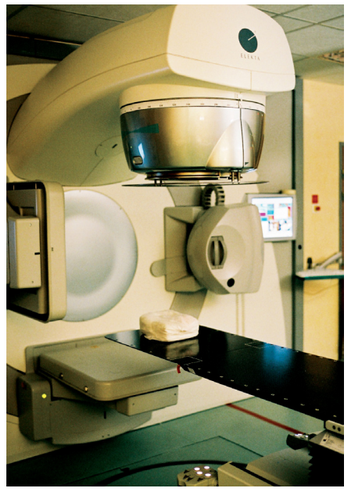

Fig. 1.7.1 *Radiotherapy is part of the multimodal and multidisciplinary management of patients with cancer*

linear energy transfer (LET) radiation such as neutron therapy have either proved ineffective, too toxic or logistically too complex.

The effect of radiation may be increased by the use of concomitant chemotherapy as used increasingly in oesophageal, head and neck, cervix and rectal cancers. Concomitant radiation and targeted therapies–such as cetuximab in head and neck cancer–is also being used in selected patients.

Altered fractionation of radiotherapy has been explored for a number of tumours. In head and neck cancer, twice-daily treatment has been found more effective than daily treatment. For non-small cell lung cancer Continuous Hyperfractionated Accelerated RadioTherapy (CHART) given in three fractions per day over twelve consecutive days (no weekend break) has been shown to be superior to single daily (Mon–Fri) treatments over six weeks. Acute toxicity with these combinations and other alterations from standard therapy may be more severe.

Stereotacticly aimed and delivered small beams have been used for both malignant and benign intracranial lesions for many years. Arterio-venous malformations may be thrombosed with single high-dose treatments, known as stereotactic radio*surgery*. If a fractionated course is given it is stereotactic radio*therapy*.

These stereotactic techniques are being explored in extracranial sites such as head and neck and also lung (for small peripheral lesions) and intra-abdominally for liver metastases. These require significant modification of a linear accelerator and special immobilisation techniques. It is also essential where organ and hence tumour movement is marked with respiratory movements to deliver the radiation beam only in specific parts of the respiratory cycle. Respiratory gating is now available as an add-on to modern linear accelerators. Systems to confirm tumour position radiologically before and during treatment are also essential, and modern linear accelerators can be equipped with on-board kilovoltage or cone-beam CT imaging devices.

In addition there are megavoltage treatment units with built in CT scanner capability (Tomotherapy™) or which have high precision stereotactic treatment capability (Cyberknife™).

In the last decade the value of heavy particle irradiation with protons or heavy ions has been investigated following the development of particle generators delivering manipulateable and often multiple beams. These therapies have a proven role in the management of some orbital tumours and, for example, base of skull sarcomas. Due to very high cost few such installations exist, but as the cost is falling and as the clinical role is becoming further defined, national services are being proposed.

Overview

Radiotherapy has seen a technology avalanche in the last twenty years that has offered the same level of exciting prospects that the quantum leap from kilovoltage to megavoltage equipment encouraged sixty years ago.

Equipment costs have risen, as has demand on staff and the need for improved quality assurance and safety. However, as the range of treatments has correspondingly increased, toxicity has decreased. Thus, what were common side effects, such as 3–4% incidence of acute pneumonitis and unacceptable levels of radionecrotic fractures of rib and even the low but dreadful incidence of radiation-induced brachial plexopathy from breast radiotherapy technique and noted too often until the 1980s, are now rarities.

While the cost of radiotherapy has slowly risen over the last twenty years, those costs remain lower per episode of care than for other modalities, the mean cost for "standard treatment" delivering 21 fractions being estimated at €3239 across three European and one Canadian studies [3].

However, while radiotherapy technology has changed beyond recognition and hence requires a greater initial capital outlay, high quality radiotherapy demands no more than a functioning megavoltage unit–cobalt or linear accelerator–with facilities for adequate beam shaping, a process to image the area of interest to determine field placement, a basic planning computer system and, of course, trained and dedicated medical, physics and technology staff committed to safety. High quality but basic and hence low-cost equipment is now being produced by major equipment manufacturers for lower-resource nations. These developments may allow the introduction of low-cost sustainable radiotherapy services where none or few exist currently.

Radiotherapy is part of the multimodality and multidisciplinary management of patients with cancer. It is essential for good cancer care: chemotherapy and surgery cannot effectively replace it. Where it is not available 50% of cancer patients are being denied appropriate care.

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1.8 Principles of Supportive and Palliative Care

Summary

> Every cancer service requires an active and resourced Supportive and Palliative Care Service (spanning university teaching hospitals to community care) that is engaged in a timely way for patients and their families

> Supportive and Palliative Care Services should be developed in parallel with cancer services (in high-resource and low-resource countries)

> Opioids, together with other key medications for symptom control, need to be more systematically available around the world

> People with advanced cancer should have access to supportive and palliative care services long before their terminal phase. 'Terminal care' represents a small fraction of the illness trajectory for which supportive and palliative cancer care services should be available

'If you treat the disease, it is win or lose. If you treat the person you will always win.'

Patch Adams

Impact of cancer around the world

Cancer continues to be a major cause of human suffering everywhere. The diagnosis of cancer is strongly associated with premature death in the mind of the community. Despite continuing significant advances in understanding modifiable risk factors, prevention programmes, early detection of some cancers or pre-cancerous conditions and rapid advances in the treatment of many previously universally fatal cancers, for many people around the world, cancer will cause premature death. For others, active cancer will be present at the time of their death although not directly causing it, and for a third group of people, cancer will have been diagnosed and treated at some earlier time in life sometimes with long-term consequences.

Premature death from cancer affects all age groups. Very poor five-year survival persists for many cancers, including lung and unknown primary, even in high-resource countries.

In low-resource countries, cancers associated with infectious diseases (cervical cancer, hepatocellular carcinomas, nasopharyngeal carcinoma) continue to cause premature mortality that has significant consequences for families and the communities in which they live. The increasing contribution to premature death because of lifestyle factors such as tobacco use has not peaked in many countries.

In parallel with therapies designed to improve cure or survival rates is a process of optimising a person's function while having therapy and subsequently in line with the resources available [1]. Such care needs to be planned in a national framework that reflects the resources, practices and beliefs of the country [2]. Wherever people are in their disease trajectory, there is a need to address symptom control. This happens in tandem with disease modifying therapy [3].

Like any area of clinical practice, much of the work of palliative and supportive care needs to be achieved by a wide range of health professionals. For a number of people, involvement of health professionals with specific training in supportive and palliative care is needed to meet the complexity of their needs, take forward an agenda of research to refine clinical practice and service provision, and educate existing practitioners (for whom supportive and palliative care was not part of their training) and those still in training.

Definitions

There are three populations covered in these definitions. *Supportive care* sits in parallel with therapy to modify the course of cancer irrespective of the possible outcomes (cure, living with cancer in the long term or premature death because of cancer) and includes symptom control, psychosocial support and rehabilitation.

A sub-set of supportive care is *palliative care,* where it is anticipated that life will be shortened as a result of cancer. Having disease-modifying therapy is still open to patients in this context, but with advanced disease, cancer should be considered a systemic disease, with systemic problems mostly causing death.

A subset of palliative care is *terminal care* – the last few hours or days of life as the person's body closes down. This final common pathway for many people is an almost seamless extension of their inexorable systemic decline: increasing fatigue, weight loss and anorexia. Care in this setting should reflect goals that are entirely built around the comfort of the dying person, as at this time nothing can change the course of the disease.

Given these three definitions, it can be seen that the skill base of supportive care and palliative care draws from the same body of specialist knowledge.

Every health professional should be able to provide care and support to people with cancer, and to have a working understanding of symptom control, psychosocial care and how to optimise a person's function. Such processes need to take account of the physical, social, emotional, existential, sexual and financial issues involved. Most of the issues encountered in people with advanced cancer span several such domains, and the solutions therefore are also likely to span several domains.

There are a group of people with cancer whose needs are more complex, and their care demands the involvement of healthcare professionals whose substantive work is in supportive and palliative care. Specialised supportive and palliative care services are configured within the broader provision of health around the world in different ways.

The definition of *comprehensive cancer care* cannot be derived in isolation of the contribution of supportive and palliative services. To exclude supportive and palliative care from comprehensive cancer care limits the definition to trying to modify the clinical course of the cancer, not of treating the patient. Disease-modifying treatment is only one aspect of any cancer care plan. How can one possibly have a comprehensive cancer centre without supportive and palliative care? By doing this, one is making no provision for the one in two people who will die prematurely because of their cancer.

Specialized supportive and palliative care services are a catalyst for research (improving care and improving models of health service provision) and educational programmes (for existing practitioners who may not have been exposed to supportive and palliative care as they trained, for the next generation of health practitioners for inclusion in their curricula, and for the community more broadly in expectations for good palliative care).

The threshold for the involvement of a broader team of health professionals is based on the needs of the person with cancer, their family and other caregivers and the needs and skills of the health care professionals serving them. Referral is *not* defined by prognosis, but ensuring that needs have been systematically evaluated and, where possible, addressed. Such a model also acknowledges that many people do not need to access specialist services: the current care of family and health professionals is meeting their needs.

Informed decisions include all the reasonable options, including not having any therapy aimed at changing the course of the disease at any given time. For most of the palliative care phase, there will be decisions that need to reflect the patient's input. These decisions will arise because the course of the illness (either as a direct result of the cancer, the treatment of cancer or inter-current co-morbid disease) can potentially be modified. Equally, there comes a time when changes in the course of the illness are no longer possible.

Why do we need specifically identified supportive and palliative care services? Its breadth includes the direct effects of the cancer and the short- and long-term effects of its treatment, co-morbid illnesses that can be affected by the systemic challenge to the body of cancer. Alongside the physical effects are the psychological and existential effects of a diagnosis synonymous with death around the world. Even for those people with a cancer that will cause no further problems in the person's lifespan, there is still the real challenge to one's mortality.

Every health professional can contribute to improving care across the whole trajectory of cancer. Prolonged doctor-patient or nurse-patient relationships may *lessen* the likelihood of discussing highly relevant but sensitive topics as patients try and protect their health practitioners [4]. The practitioner who claims 'to do my own palliative care' may be compromising discussions about key issues to people as death approaches.

Measures of supportive and palliative care

Across the whole course of cancer, in parallel with disease control, there needs to be agreement on the metrics to measure the impact of supportive and palliative care. This allows assimilation of supportive and palliative care into a comprehensive cancer care.

How does the impact of cancer define the needs for palliative and supportive care around the world? The metrics for measuring cancer translate directly to measuring the needs for supportive and palliative care: incidence defines the population who need supportive care; prevalence defines the population at risk of ongoing problems as a result of cancer or its treatment; mortality rates define the population who need to be assessed for referral to specialist palliative care services and life years lost define, in part, bereavement support needed.

Although often framed around quality of life, or more specifically health-related quality of life, the goals of care are to optimise function and comfort in domains that cover the full spectrum of human endeavour (physical, social, sexual (including change in body image as the result of the cancer or its treatment), financial, existential, and emotional aspects of a person's life). This does not limit involvement of supportive and palliative care services to uncontrolled physical symptoms, although that is most often the catalyst to referral [5]. It means that each domain needs comprehensive assessment in order to ensure that, wherever possible, unmet needs are addressed. Such attention to detail requires specific resources, skills and continuing professional development.

Outcomes from supportive and palliative care need to be measured across time, not limited to only the terminal phase of care. This includes outcomes for the person with cancer [6] and their caregivers, while in the role and after they have relinquished the role. Caregiver outcomes can be seen to relate to metrics associated with widely reported health outcomes – survival, impaired health states, health service utilisation, mental health and physical functioning.

The evidence base for supportive and palliative care

What is the evidence base of net benefit (benefit and burden) from the specific involvement of specialist supportive and palliative care services for people with more complex needs from cancer? There are four levels at which such a conversation could occur:

– The person with cancer;
– Family caregivers;
– Health service providers; and
– Whole populations.

No single systematic review has brought together the many aspects of care across time covered by supportive and palliative care services. The net impact of supportive and palliative care services is a cumulative effect from each aspect of assessment and care.

At a community level, end-of-life care is valued consistently as an integral part of quality health care [7]. Such care demands adequate resources, a trained workforce and application of the increasing evidence base in practice [8].

What are the issues that are important for people with advanced cancer? Issues as time becomes finite include excellent symptom control, planning for future care, resolving problematic relationships, having a legacy (the things by which we will be remembered and valued) and being able to finalise one's personal affairs [9]. The ability to be cared for in the environment of choice may include one's home or, at times by choice, an inpatient setting [10].

Benefits from specialised palliative care service involvement for patients with advanced cancer that have been identified include:

- the "quality of dying" and comfort in the last two weeks of life; [11,12]
- pain assessment; [13]
- management of people dying in nursing homes; [14]
- symptomatic management in people admitted to hospital; [15]
- met needs; [16] and
- satisfaction with care [17-19].

For caregivers, data from around the world support that specialised palliative care service involvement has been shown to:

- improve satisfaction with care; [16,18]
- be associated with fewer identified unmet needs for day-to-day caregivers; [20,21]
- improve adjustment when caregivers relinquish the role [20].
- help reduce caregiver anxiety [19]; and
- be associated with improved caregiver survival having relinquished the role [22].

For health funders, the involvement of specialised palliative care services for appropriate patients leads to:

- reduced inpatient bed days [17,23];
- reduce number of hospital admissions [24];
- decreased costs when compared to conventional care [17,25]; and
- potentially influence the likelihood that place of death is that of the patient's choosing [26].

Importantly, there is often a perception that referral to a hospice/palliative care service will compromise care in a way that may shorten prognosis. Although this could not be tested with randomised controlled trials, it is noteworthy that in at least one large population-based study, prognosis was longer for each of the 16 diagnoses that were studied, 12 of which were advanced cancers [27].

Systematic reviews of the impact of specialised palliative care services suggest benefit in a number of domains [28-30]: pain and symptom control [31]; satisfaction with services, reduced hospital bed days and overall costs [32] and potential benefits for caregivers [33]. It has been more difficult to access people who have not accessed services, [34-36] explore the wide regional variation in referral and access patterns [37], or account for the variations in time from referral to death in different health systems but similar burdens of cancer [28,38-40].

Delivering supportive and palliative care services around the world

What are the supportive and palliative care services offered around the world? There is wide variation in the availability and structure of services around the world. These reflect:

- local philosophy relating to health service resource distribution;
- funding models within health systems (user pays versus universal health care);
- service development philosophies (supportive and palliative care services will be developed when all other oncology services are fully established compared with parallel growth of both);
- the availability of trained staff;
- the overall competing demands for health resources (or in many cases for any resources);
- communities' beliefs and values surrounding the infirm and dying; and
- the background disciplines (anaesthetics, psychiatry, surgery, oncology, family medicine, other branches of internal medicine) of people providing specialised supportive and palliative care.

Despite these wide variations, there is evidence of strong growth of supportive and palliative care services around the world, of the qualified staff to provide care and further develop services and of increasing infrastructure in research and education [41-44].

There are data to demonstrate that a start has been made in developing services in every region of the world. The capacity building to provide comprehensive supportive and palliative care around the world includes:

- providing the skills for all health professionals to optimise care for people wherever they are in the cancer trajectory (living with cancer, having survived cancer with no known disease, or facing premature death because of cancer);
- employing core staff who will take responsibility for providing care for people with more complex needs, service planning, seeking funding, research and education; and
- making available key medications, including opioids for pain.

In high-resource countries, there are still cancer centres and services that refuse to invest in either the staff to provide supportive and palliative care, nor the inpatient beds for acute symptom assessment units. Without these resources, cancer services cannot claim to be comprehensive. These centres often have limited links to the community care needed by people as they become more frail.

In resource-challenged countries, issues include workforce, competing demands for scarce health resources and the predictable supply of medications used in symptom control, especially opioids for analgesia [45,46]. The continuing struggle to provide predictable access to therapeutic opioids is an indictment of health and regulatory systems around the world that needs urgent and effective action [47].

In recognition of the need for models of sustainable practice, the World Health Organization has collaborating centres in places such as Jordan and Spain [48,49].

Fig. 1.8.1 *Supportive and palliative care services should be developed in parallel with cancer services*

The Future

As mapped by the World Health Organization, there is much that needs to be done in every country around the globe to improve access to specialist supportive and palliative care at every level of the health system from university teaching hospitals (which should all have acute inpatient symptom assessment units) to community-based care, continued development of the clinical workforce at all levels and in all disciplines, improved infrastructure (most notably equitable access to opioid analgesia) and community care that can support people who want their care to be at home [2]. This is a challenging agenda, but much has been achieved since the publication of the first IARC World Cancer Report in 2003 [50].

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1.9 Psycho-Oncology

Summary

> Psycho-oncology addresses the psycho-pathological and psychosocial impact of cancer on patients and their relatives

> This discipline is integrated into oncology supportive care and fosters a global approach to the care of cancer patients

> Across countries, up to 50% of cancer patients have been reported with psychological distress, with rates depending on medical, individual, interpersonal or social factors

> Lack of attention to cancer patients' psychosocial needs or deficiencies in physician-cancer patient communication may exacerbate cancer patients' psychological distress

> Psycho-oncology offers evidence-based psycho-social interventions targeted at patients, families or their social milieu, or focusing on caregivers and healthcare professionals to address psychosocial concerns, foster adaptation to the disease and treatment course, and therefore improve healthcare outcomes

Psycho-oncology is a subspecialty of oncology that has developed rapidly over the past 30 years with the recognition of the psychosocial impact of cancer and its treatment and the need to foster global, holistic care of the person confronted with this disease. Global care refers to the consideration of the multidimensional aspects of health, i.e. the physical health, mental health, social well-being and role functioning. Human aspects of care have been underscored in the face of increasing emphasis on bio-technological aspects of medicine, especially in Western countries.

The global care approach is particularly relevant in the field of cancer. Cancer and its associated conditions may significantly damage patients' quality of life. Complementary to therapy for cancer, the care provided in oncology must include the management of disease symptoms, treatment side effects and sequelae, as well as psychosocial distress and needs that arise in that context.

A dimension of quality of life is psychological well-being, which may be considerably affected by the diagnosis of cancer and the therapeutic process. Patients as well as their family members are confronted with a number of distressing emotions and experiences, including fear of death and uncertainty about the nature, evolution and prognosis of the disease. Individuals affected by cancer have to face a reduced ability to control their life, increased dependency on others, and disequilibrium in familial, professional and social life. Untreated psychological conditions may further damage quality of life as well as increase medical costs by longer hospital stays or higher rates of utilisation of primary care medical services [1,2].

Psycho-oncology addresses the psychosocial needs of patients and their family members across the continuum of care, from prevention and early detection through treatment and survivorship to palliative and end-of-life care [3]. Psychosocial interventions in oncology include the facilitation of patients' and families' coping, relief of psychological distress and also address the wellbeing of oncology professionals. The psycho-oncology discipline also strives to contribute to World Health Organization efforts in cancer prevention and engaging community-based interventions to enhance health promotion (e.g. smoking cessation, sun protection, physical activity and healthy diet endorsement, early detection of cancer).

The psycho-oncology field promotes a multidisciplinary co-ordinated approach in the psychosocial care of cancer patients. As a component of supportive care, psycho-oncology concerns a number of health professions such as psychiatry, psychology, social work, nursing, integrative medicine, allied health practitioners or spiritual/religious counsellors, who work in close collaboration with other supportive care professionals. Activities of psycho-oncology professionals are integrated into supportive care services that provide treatment to prevent, control or relieve complications and side effects of cancer treatment (e.g. pain, anaemia, fatigue, infections, nausea and emesis) in order to improve the patient's comfort and quality of life.

Although psycho-oncology has become an important part of cancer care in many countries, at present it has only been fully integrated in a few countries [4]. This is highlighted by the numerous unmet care needs in cancer patients, not only while under treatment across the entire spectrum of psychological needs, health system inadequacies, need for information, physical and daily living, patient care and support, and sexuality [5] but also in the survivorship phase, with regard to emotional, physical, treatment-related and home care, and social (insurance, employment) domains of life [6] The use of mental health services is significantly higher in cancer survivors compared to the general population, although a significantly higher proportion of cancer survivors compared to those without such history reported needing mental health services but not having access to them because of cost [7].

On the other hand, various reports across countries have demonstrated patients' dissatisfaction with care in oncology, especially with regard to aspects of their interaction with providers (e.g. information provision, attention to psychosocial needs) [8], underscoring the need to improve the psychosocial care of cancer patients, provided not only by experts in psycho-oncology but also by first-line healthcare professionals (physicians, nurses, etc.).

To this end, there are a large number of evidence-based interventions available for cancer patients and their families [9] as well as for healthcare providers [10,11] that may improve outcomes in cancer care.

Depending on the culture, economics and healthcare systems, psychosocial issues in oncology may vary widely across countries and thus call for different priorities of interventions. On one hand, low-resource countries should rather focus attention on cancer prevention and education to improve early detection of cancer, especially cervical cancer; and on palliative care, considering the limited opportunity for cancer treatment in these countries [3]. On the other hand, in high-resource countries, cancer care is confronted with complex decisions (e.g. treatment or surveillance in prostate cancer, prophylactic mastectomy or intensive surveillance in women at high risk for breast cancer, types of adjuvant hormone therapy in early stage breast cancer) while therapeutic alternatives present equivalent survival efficacy but different effects on quality of life. Physician-patient shared decision making has to have high priority, requiring superior physician communication skills to prevent exacerbation of patients' psychological distress.

This chapter presents the main psychosocial concerns patients and families face when confronted with cancer, and addresses health care providers' own difficulties in facing and dealing with these psychosocial cancer consequences. It also provides information about interventions that have proved useful and efficient to manage these problems.

Psychosocial issues in patients and relatives

Quality of life. An increase in attention to cancer patients' quality of life has been witnessed in the past few decades. The ultimate goal of medicine is not solely health or the prolongation of life but also the preservation or improvement of quality of life. Instruments have been developed and validated to measure this key concept in oncology with objectives such as describing and monitoring patients' symptoms, difficulties or needs, or assessing medical treatment or psychosocial interventions. The term "quality of life" is commonly used in the cancer literature to mean health status, physical functioning, severity of symptoms, psychosocial adjustment, well-being or satisfaction with life. Broad quality of life domains have been described, comprising the physical, psychological, economic, spiritual and social domains.

Studies have shown how cancer and its treatment may entail problems along these different quality of life dimensions. At the psychological level, the cancer diagnosis in itself even if associated with a good prognosis and absence of aggressive therapy (e.g. a small cutaneous melanoma, or an intra-epithelial lesion of the uterine cervix), may be perceived as synonymous with death, pain and suffering, and cause significant psychological distress. Mood disturbance (depression, anxiety) or cognitive abnormalities (poor concentration, memory impairment) may be observed. At the physical functioning level, the principal means of treating cancer—surgery, chemotherapy and radiation—are powerful but often associated with significant sequelae. All these interventions, including hormonal therapy, have physical side-effects, which may be short-term or time-limited, or chronic and persistent, or develop after treatment has ended [12]. Decreased performance status and physical functioning may lead to problems in carrying out daily activities; treatments may involve physical mutilations (e.g. disfigurement, creation of a stoma, hair loss) and symptoms (e.g. pain, nausea and vomiting, fatigue, sleep disturbance). At the social level, concerns with regard to relationships with a partner, family members or with the social network may be raised. Cancer patients may experience feelings of loneliness, abandonment or lack of support; financial or work problems may also emerge; in the survivorship phase, for example, patients may encounter problems in returning to work, feeling marginalised or even stigmatised as a result of having been affected by cancer.

Psychological distress and disorders. Psycho-oncology mainly addresses the psychopathological or psychosocial consequences that arise specifically as a result of cancer and its treatment. Usual diagnostic criteria, like those listed in the Diagnostic and Statistical Manual of Mental Disorders [13], do not necessarily adequately reflect the psychological disorders resulting from a somatic condition such as cancer. Psychological suffering may be perceived as a "normal" reaction to the traumatic event that represents a cancer diagnosis. To underline a continuous psychological phenomenon from "normal" feelings to psychological disturbance

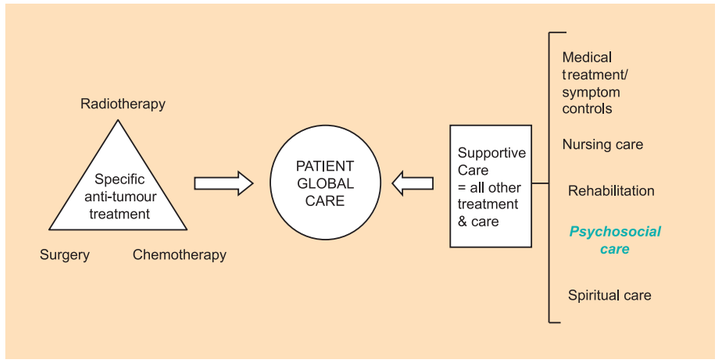

Fig. 1.9.1 *Specific anti-tumour treatment and supportive care including psychosocial care for the global care of the cancer patient*

requiring specialized intervention and to avoid psychopathological stigmatisation, Holland and colleagues [14] has proposed the word "distress" to account for the psychological experience of oncology patients. They defined this term as a *"multifactorial unpleasant emotional experience of a psychological (cognitive, behavioural, emotional), social, and/or spiritual nature that may interfere with the ability to cope effectively with cancer, its physical symptoms and its treatment. Distress extends along a continuum, ranging from common normal feelings of vulnerability, sadness and fears, to problems that can become disabling, such as depression, anxiety, panic, social isolation, and existential and spiritual crisis"*.

Faced with a diagnosis of cancer, most people react initially with numbed shock and disbelief, followed by anxiety, anger or depression. In most cases, this stress reaction subsides within a few weeks as patients learn to come to terms with their disease. Nonetheless, a significant number of cancer patients may develop persistent psychological disorders that call for professional attention.

Studies conducted in recent decades have revealed that pathological levels of distress were more prevalent in patients with cancer than in the general population [15]. One third of all cancer patients experience prolonged high levels of distress that contribute to ongoing adjustment difficulties and can potentially interfere with treatment compliance [16].

As presented in Table 1.9.1, among mood and anxiety disorders, figures range from 6.3% and 47.2% for anxiety, 7.8% and 57% for depression and 7.1% and 48% for general distress and are found in North America [1,17] as well as in Australia [18], European countries [19-23], the middle East [24,25], South Africa [26]; South America [27] and Asia [28]; and across the trajectory of the illness–from the time of the diagnosis of treatment to termination of treatment, survivorship, or recurrence and palliation [20,29].

Author, country, year	Sample size assessment mode	General distress	Anxiety	Depression
Berard, South Africa, 1998[26]	N=456 HAD-S, BSI, Psychiatric interview	-	-	14%
Brédart, Italy, 1999[19]	N=190 HAD-S	-	16%	
Pascoe, Australia, 2000[18]	N=504 HAD-S		11.5%	7.1%
Zabora, US, 2001[17]	N=4496 BSI	35.1%	-	-
Uchitomi, Japan, 2003[28]	N=212 DSM-III SCID, POMS	-	-	4.7-8% within 1 year post-surgery
Carlson, Canada, 2004[1]	N=3095 BSI-18	37.8%	-	-
Grassi, Mediterranean countries, 2004[21]	N=277 HAD-S	-	34%	24.9%
Burgess, UK, 2005[20]	N=222 DSM SCID	48% first year/ 15% fifth year post-diagnosis	-	-
Santos, Brazil, 2006[27]	N=107 HAD-S, IES		20.5%	16.8%
Mehnert, Germany, 2007[22]	N=127 DSM SCID	7.1% adjustment disorder	6.3% generalised anxiety disorder	7.8% major depression + dysthymic disorder
Strong, UK, 2007[23]	N=3071 HAD-S	22%	-	-
Tavoli, Iran, 2007[25]	N=142 HADS	-	47.2%	57%
Ozalp, Turkey, 2008[24]	N=204 HAD-S	37.3%	-	-

Table 1.9.1 *Prevalence figures for anxiety or depressive disorders in cancer patients across countries*
HAD-S = Hospital Anxiety and Depression Scale, BSI = Brief Symptom Inventory, DSM SCID = structured clinical interview for the Diagnostic and Statistical Manual of Mental Disorders, POMS=Profile of Mood Scale, IES= Impact of Event Scale

Post-traumatic stress disorders as a result of the stress event that represents confrontation with a life-threatening illness such as cancer are also found in the cancer setting, with prevalence rates of 19% in breast cancer patients post-surgery and 16% at 6 months [22].

In advanced cancer, about half of patients express some level of suffering, with physical symptoms, psychological distress and existential concerns contributing to the prediction of this experience [30].

Acute confusional states are less common in patients with cancer overall but develop frequently in advanced cancer, and are a leading source of distress for family caregivers [31]. Patients become restless, suspicious and confused, with impaired concentration, memory and orientation in time and space. Opioid analgesics essentially, but also chemotherapy agents, cerebral tumours or encephalopathy are common causes.

Predictors of psychological disturbance in cancer patients have been highlighted including medical (staging of disease, physical or psychological symptoms), individual (age, gender, past history of psychiatric disorder, personality) or interpersonal and social factors (marital status, social network, education, current concerns) [1,17,20,32]. Potential predictors are not very useful clinically as they only partly explain the development of psychological disturbances. There is meanwhile a consensus to consider the systematic screening of these disturbances as useful in order to allow early treatments of these conditions [33,34].

Couple and family issues. Cancer is a family affair and not the patient's problem alone [35]. The effect of cancer on family members, in turn, may affect the patient's adjustment to illness. The well-being of close relatives is of concern especially since contexts of scarce psychosocial resources lead to reliance of this only source of support to patients.

Marital relationships may be altered, especially in the case of pre-existing problems whereas good marital relationship may buffer the stress of cancer, and are associated with less distress in the patient.

An insufficiently recognised complication of cancer is sexual functioning [36]. Sexual problems can be a consequence of cancer-related anxiety and depression or result from psychological and physical damage following certain treatment such as disfiguring surgery, ostomies, surgically induced nerve damage, radical pelvic irradiation, side-effects of chemotherapy or hormone treatment. Treatment for prostate cancer such as prostatectomy or hormone therapy can diminish a man's self-esteem as a sexual partner [37]. Body image and sexual problems were experienced by a substantial proportion of women in the early months after diagnosis of breast cancer and were associated with mastectomy and possible reconstruction, hair loss from chemotherapy, concern about weight gain or loss, poorer mental health, vaginal dryness and partner's difficulty in understanding patients' feelings [38].

Less well recognised than marital problems is the effect that breast cancer may have on the mother-daughter relationship. Daughters' distress levels have been found to be significantly related to mothers' distress levels [35]. Considering children/adolescents more generally, the family characteristics such as the family's communication or expressiveness are associated with children/adolescents psychosocial outcomes; a particular risk factor may be maternal depression which can affect the parenting role [39].

Specific issue: breast cancer genetic risk. Development of medical knowledge and technology brings definite benefit to the health of individuals; however, new associated psychosocial problems may be elicited, which the psycho-oncology field must address. One of these is related to the psychosocial issues associated with breast cancer genetic testing and subsequent health care management, in terms of intensive medical surveillance or prophylactic interventions. The familial breast cancer syndrome associated with a BRCA1 or BRCA2 mutation is thought to confer in a woman a lifetime risk of breast cancer of between 50 and 85% [40]. Since the discovery of these mutations a decade ago, familial cancer services have been set up in many countries (e.g. Australia, Canada, France, Germany, Netherlands, UK and the USA) to respond to the increasing demand for breast cancer genetic counselling and testing [41].

Breast cancer susceptibility testing offers the potential for early detection of breast cancer, since a positive test result points to the need for increased surveillance, i.e. regular mammography or magnetic resonance imaging (MRI) or indicates the possibility of reducing cancer risk through chemoprevention and risk-reducing surgery. A positive test may also present psychological benefits in reducing the individual's uncertainty and doubts. However, cancer-susceptibility testing also encompasses limitations and potential risks, depending on the test result. The test result may be: 1) positive in an unaffected, at-risk individual when a disease-related mutation has been identified in the family, 2) positive in an individual who is the first identified mutation carrier in a family, 3) negative when a disease-related mutation has been identified in the family or, 4) uninformative or of uncertain significance.

A positive test result may lead to heightened anxiety about being a mutation carrier or induce guilt about possible transmission of genetic risk to children. Mutation carriers may be confronted with the medical and psychological risks of increased screening or surgical prophylactic interventions or of potential insurance,

employment or social discrimination. When the genetic test result is uninformative or of uncertain significance, continuing anxiety, depression or confusion considering the lack of evidence-based guidance regarding prevention or surveillance strategies may appear. A negative test result may offer reassurance and reduction of anxiety about personal cancer risk due to heredity; however, it may result in strained family relationships or guilt, and potential inappropriate routine surveillance.

Research results to date do not indicate harmful psychological consequences following a positive test result [41-44]; however, most studies have been undertaken in settings devoted to clinical research and care by specialists in hereditary cancer and have addressed individuals of prevailing cultures. These studies do not provide long-term information on the emotional and health behavioural effects of this new technology. Although counselees seem to improve their knowledge about genetic aspects after genetic counselling, their risk perception remains incorrect [42], suggesting the need for professional support in helping individuals make informed decisions when considering the option of performing genetic tests or managing their high risk of cancer.

Studies on the psychological consequences of intensive screening or prophylactic interventions require careful attention. In the general population, if mammography screening does not appear to have a negative psychological impact on the majority of women, those who are recalled for further investigations after screening are subject to significant adverse consequences which may remain in the long term [45]. Additionally, regarding prophylactic mastectomy in particular, although the literature indicates a high level of satisfaction among women overall, a subset may report regret post surgery and are likely to experience high levels of psychological distress, sexual dysfunction and concern with body image [44].

Psychosocial issues in oncology professionals

In the context of cancer care, the relationship between patients and healthcare providers and the standards of communication are of the utmost importance. Inadequate explanations may lead to patients being confused about their diagnosis, prognosis and potential therapeutic options, thereby promoting dissatisfaction and psychological distress. This can affect attitudes towards treatment and care, difficulty adhering to medical recommendations, and may result in poorer outcomes. However, the information that must be conveyed to patients—disclosing a cancer diagnosis or explaining aggressive treatments—often has 'threatening' content, making the task of healthcare providers particularly difficult.

The care of patients with cancer may be particularly stressful. In particular, dealing with cancer patients' psychosocial issues entails an emotional burden that can lead to burnout [46]. A high level of morbidity and mortality, confronting death, treatments with limited efficacy that are powerful but toxic or mutilating, difficult therapeutic decisions, medical or nursing staff conflicts, patients' or family emotional or behavioural reactions may all contribute to the stress associated with cancer care. For example, healthcare professionals may report feelings of helplessness, anger, or occasional identification with the patient. In communicating with cancer patients, doctors are often confronted with a number of difficult issues for which they are usually unprepared, such as communicating bad news, preparing for aversive procedures, exploring treatment options, enrolling in clinical trials, discussing prognosis, or switching from curative treatment to supportive care [47]. In cancer care, professionals need to accept that care can be of good quality and effective without necessarily leading to a cure; this may challenge their original motivation in entering the medical profession.

Management of psychosocial issues

Interventions targeted at health care professionals.
Lack of skills and training in the detection of cancer patients' and families' psychosocial needs has been identified as a substantial barrier to the provision of evidence-based psychosocial care in oncology [2]. Studies suggest that clinicians do not identify patients with high levels of anxiety or depression [48-50] and need for psychosocial counselling [50]. Physical symptoms are more frequently addressed by the treatment team than are psychological concerns, although patients expect clinicians to initiate discussions about psychosocial issues [51].

Oncologists play an important role not only in identifying psychological distress but also in preventing it by providing adequate information and basic emotional support to patients and their relatives. Adequate communication skills are required to deal with issues that regularly arise in the cancer setting (e.g. complex treatment decision-making, treatment refusals, euthanasia requests).

Interventions have been designed to facilitate the detection of physical and psychological problems through the use of quality of life questionnaires in routine oncology practice [52], the provision of assessment tools [16] and guidelines for psychosocial management [14], as well as to train healthcare professionals in psychosocial issues [53] and in communication skills [54,55].

Psychological distress screening tools and psychosocial guidelines. Oncologists' estimation of whether and how severe a patient is distressed is often complicated by patients' denial [50]; besides, common somatic symptoms found in cancer, such as pain, fatigue, weakness, reduced energy and appetite/weight changes, are also common psychopathological symptoms: breathlessness, muscle pain, dizziness and palpitation for anxiety and panic attack; fatigue or appetite/weight for depression.

These somatic signs create difficulty in diagnosing depression and anxiety in cancer patients, and lead to highlighting more reliable symptoms such as, for depression, anhedonia, guilt, suicidal thinking and hopelessness [49].

In the United States, through the National Comprehensive Cancer Network (NCCN) (www.nccn.org), specific tools and procedures have been tested to trigger referral by the oncology staff to the psychosocial services. Similar to the pain management guidelines, a rapid psychological screen measure, the Distress Thermometer coupled with a Problem List to identify sources of distress (psychological, family, social, spiritual, practical, physical), are provided to patients in the ambulatory setting to identify those at risk for psychosocial problems and facilitate appropriate interventions.

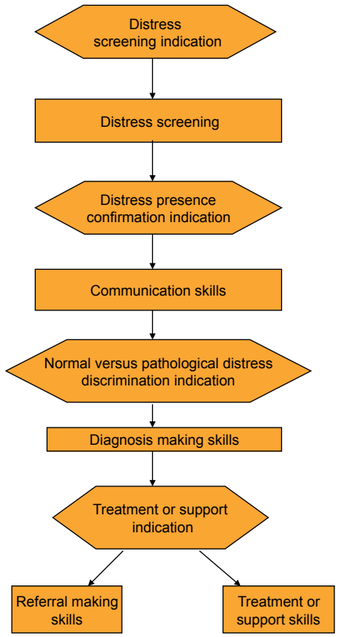

Fig. 1.9.2 *Optimisation of distress treatment : importance of screening. Used with permission: Razavi D, Delvaux N. Précis de psycho-oncologie de l'adulte. Masson. 2008, p 311*

Clinical practice guidelines based on comprehensive review of evidence-based psychosocial interventions have been produced in different countries as benchmarks against which the quality of psychosocial care in cancer can be assessed. In Canada, such guidelines allow regional and federal governments in planning and budgeting psychosocial care in cancer (www.capo.ca); in Australia, the implementation of the guidelines has been performed through demonstration projects, doctor communication skills training and forming partnerships with patient advocacy groups (http://www.nhmrc.gov.au/); in the United Kingdom, the National Institute for Health and Clinical Excellence also offers clinical guidance from a critical and comprehensive appraisal of studies assessing the effectiveness of psychosocial, supportive and palliative care services for cancer patients (http://guidance.nice.org.uk/csgsp). Other countries with guidelines in use are Germany, Hungary, Italy, Israel, Spain and Japan; in still others, guidelines are at different stages of development. Figure 1.9.2 illustrates the steps of interventions and skills needed to optimize the care of emotional distress [57].

Communication skills training. Good doctor-patient communication is essential, since it increases patients' coping and satisfaction with care, enhances informed consent and cooperation with care, reduces the probability of malpractice litigation and decreases professionals' burnout. Doctor-patient communication encompasses: 1) creating a good interpersonal relationship (a clear, warm and reassuring setting); 2) exchanging information (eliciting patients' information on their difficulties, preferences and expectations as well as providing complex medical information); and 3) making treatment-related decisions (which require an adequate understanding of the medical and psychosocial stakes associated with possible therapeutic options) [56].

Communication skills training is aimed at improving health care providers' ability to elicit patients' concerns and needs as well as to offer emotional support. Facilitating (e.g. use of open questions, expressions of empathy, appropriately responding to patients' cues) or blocking (e.g. exclusive focus on physical symptoms) communication behaviours have been described; these are promoted in training programmes [11].

A patient-centred care approach is encouraged; this entails the following specific features:

- an individualized, bio-psycho-social attention to the patient confronting the difficulties the disease imposes in his/her daily life;
- the consideration of a patient who is no longer a passive recipient of care, but perceived as possessing resources to deal with his/her condition, such as the capacity to understand medical information and share medical decision making; and
- a non-judgmental, genuine and comprehensive caring attitude.

Cancer patients generally prefer a collaborative role in deciding on a treatment plan; however a significant number prefer to remain passive, deferring to their physicians on treatment decisions [58]. Physicians are not necessarily attuned to patients' wishes regarding their involvement in shared decision-making. An uneven balance of power in treatment decision-making (either making all the decision or leaving it all to the patients) may affect patients' well-being and satisfaction with care.

Recent systematic reviews have provided evidence for the effectiveness of communication training in improving basic communication skills in the cancer setting [10]. These must comprise the following specific features: learner-centered, skills-focused, and practice-oriented, organised

in small groups and lasting at least 20 hours. Communication skills training courses should be proposed during academic training and pursued in continuing education programmes.

Interventions targeted at patients or relatives

Improving quality of life. There is now a considerable body of evidence concerning the effectiveness of psychosocial interventions for individuals or families confronted with cancer [9]. Because of the various individuals' needs and contexts, different types of professional psychosocial interventions have been developed and tested. These comprise individual interventions such as education, counselling (crisis-oriented or psychodynamic), cognitive (cognitive reframing, problem solving) therapy or mind-body techniques (relaxation, hypnosis, meditation), group interventions (expressive-existential, cognitive-behavioural, psycho-educational) and couple or family interventions. They are usually targeted to specific episodes of the illness trajectory: diagnosis/pre-treatment, immediately post-treatment or during extended treatment (chemotherapy or radiotherapy), and advanced disease or death, through the bereavement period when addressed to relatives [1]. More specific interventions have also been designed for particular problems (e.g. sexual dysfunction, sleep disturbance). Careful psychosocial assessment at appropriate time points in the patient's journey may channel to specific interventions.

Cancer patients' psychological adjustment results from the interaction between their appraisals of the stresses associated with the disease and their internal or external resources, in terms of their coping style, personality traits or available support resources. Psychological therapy in people with cancer strives at facilitating coping in favour of improved patient well-being. For example, cancer patients with a hopeless/helpless or anxious preoccupied adjustment style perceive the disease as a major threat, loss or defeat, which may lead to depressive or anxious mood disorders. During psychological therapy, these negative thoughts may be challenged, new ways of thinking about the disease and its impact on life explored and new methods to cope with the illness experimented [59].

In group therapy, expressing feelings and fear about the illness and encouraging mutual support is emphasised [60]. Emotional expression helps adjust to the stressful experience of cancer through the opportunity to identify one's feelings and to process them at a deep level.

Recently, the importance of finding meaning in life to the preservation of positive effects has been underlined in face of the catastrophic event of experiencing cancer. Additionally, a posttraumatic growth phenomenon, or positive changes has been reported as a result of this experience. These observations have triggered the development of new forms of psychological therapy for advanced cancer patients [61].

Considering the effects of psychological therapy in oncology, research evidence suggests that it does not promote survival but may affect this outcome in addressing patients' depression, hopelessness/helplessness and promoting improved adherence to anti-cancer treatments. The relevant outcomes are indicators of quality of life such as anxiety and depression or adjustment to the disease, as well as aspects of interpersonal and social functioning.

Following a critical review of 329 trials in cancer psychological therapy and considering various aspects of quality of life, Newell et al. [9] concluded that group therapy, education, structured and unstructured counselling, and cognitive behavioural therapy offer promise for many of the psychosocial outcomes explored (e.g. depression, anxiety, overall quality of life and physical symptoms such as fatigue or conditioned nausea).

Further studies need to address the appropriateness of existing forms of psychological therapy for subgroups of patients so as to design or adapt interventions accordingly (e.g. patients from rural areas, with psychopathological antecedents or from varying cultural backgrounds). For example, these may rather attract patients belonging to higher socioeconomic classes [62], although cancer patients from lower socioeconomic status have been shown to present greater morbidity and poorer perseverance with anti-tumour treatment. Psychosocial factors, like optimism, unmitigated communion, or negative social interaction have been shown to moderate the effect of psycho-oncological interventions, highlighting a specific group of participants more susceptible to benefit from currently proposed interventions [63]. Henceforth, it would also be useful to determine the optimal time to offer psychological interventions to patients for they may not be open to address their distress at any time, especially as long as a treatment decision has not yet been made [64].

Conclusions and recommendations

Cancer and its treatment may considerably affect patients' physical and psychosocial functioning, hence overall quality of life. The psycho-oncology discipline has been developed and implemented in an increasing number of countries to respond to the psychosocial needs raised in oncology at the different phases of the cancer journey, including prevention and early detection, diagnosis and first treatments, survivorship, recurrence, terminal stages and bereavement.

Evidence-based psychosocial interventions addressing patients, families or their social milieu, or focusing on caregivers and healthcare professionals have been designed and tested, and are presently available in many settings to address psychosocial concerns, foster adaptation to the disease and treatment course, and therefore improve healthcare outcomes.

However, at an international level, the integration of psychosocial oncology within oncological care is still deficient. Clinical and educational recommendations based on current scientific knowledge have been provided [3,65]; these should be more largely endorsed. The psychosocial components of oncological care should be included in every national cancer care plan and psycho-oncology services made available in every cancer care service. Cancer patients and close relatives should be offered psycho-oncology consultations and a range of psychosocial services during and after the treatment course; they should be provided with clear, free-of-charge information on their condition, respecting their needs and preferences. Healthcare professionals should be provided with validated psychosocial assessment tools, training and continuous supervision to be supported in addressing and adequately responding to the psychosocial needs of patients and relatives, engaging good communication and shared medical decision making.

The International Psycho-Oncology Society (IPOS) was implemented in 1984 to bring together investigators and clinicians dedicated to the clinical, educational and research aspects of psycho-oncology, in order to spread knowledge and practice in the psychosocial care of cancer patients worldwide while taking into account the diversity of problems and needs according to the cultural, economical or healthcare system background. Thanks to an initiative from the Psycho-Oncology Co-operative Research Group in Australia, a world map showing psycho-Oncology research groups is now available (http://www.ipos-society.org/professionals/tools-resources/research-centers.htm)

Cross-national psycho-oncology research is now possible thanks to the international development and validation of psychosocial instruments allowing monitoring of patients' difficulties and assess interventions effectiveness [66, 67] or evaluate the quality of cancer care provided [68].

The further mission of the IPOS is to assist the WHO in shaping priorities of action regarding the psychosocial element of national cancer control programmes [3].

Psychosocial oncological care is an essential component of high-quality cancer care that should be made available across countries to improve cancer patients' and relatives' health outcomes, their quality of life and satisfaction with care, and to ensure healthcare providers' well-being while carrying out the activities of their caring profession.

Fig. 1.9.3 *Communication skill training is aimed at improving health care providers' ability to elicit patients' concerns and needs as well as to offer emotional support*

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3. Australian Practice Guidelines for the Psychosocial Care of Adults with Cancer: http://www.nhmrc.gov.au/

4. The National Institute for Health and Clinical Excellence guidance: http://guidance.nice.org.uk/

5. The National Comprehensive Cancer Network (NCCN), guidelines for supportive care, distress management: www.nccn.org

6. World map of psycho-oncology research groups: http://www.ipos-society.org/professionals/tools-resources/research-centers.htm

1.10 Rehabilitation in Oncology

Summary

> Rehabilitation is an essential part of a comprehensive concept of cancer care starting from early detection of cancer and covering the entire continuum from diagnostic assessment to treatment, rehabilitation and aftercare including end-of-life phases

> Cancer rehabilitation is defined as a process of helping the patient to regain physical, social, psychological and work-related functionality after cancer treatment

> Rehabilitation programmes include an interdisciplinary and comprehensive approach providing support to patients and their families to cope with treatment sequelae and to allow them to regain quality of life and functional status

> Rehabilitation needs must be assessed individually by instruments measuring physical performance and quality of life

> Research results provide good empirical evidence for effects of rehab programmes, especially on important outcome domains such as health-related quality of life, psychosocial status and psychiatric comorbidity

Due to early detection and improvement of cancer therapy, survival times for many types of cancer have increased over the past few decades, whereas the cure rates have improved in only a few instances. Oncologic treatment including surgery, chemotherapy and radiation has become more aggressive and is often long-lasting. Cancer therapies are producing toxicities which cause substantial short- and long-term side effects, functional loss and psychosocial distress. As a consequence, in many cases cancer has to be regarded as a chronic disease involving great challenges for patient care. Many cancer patients require repeated oncologic treatment with substantial impact on quality of life and functional status. The demands on the patients to adapt to those changes may vary depending on their extent as well as whether they are temporary or permanent. Patients themselves have higher expectations of medical treatment for participation in an active life. Against this background, cancer rehabilitation has become more important during the last decades. Today, rehabilitation is an essential part of a comprehensive concept of cancer care starting from early detection of cancer and covering the entire continuum from diagnostic assessment to treatment, rehabilitation and aftercare including end-of-life phases.

Basic concepts and structure of cancer rehabilitation

Cancer rehabilitation may be defined as a process of helping the patient to regain physical, social, psychological, and work-related functionality after cancer treatment [1]. Rehabilitation as a process starts during or immediately after the end of the primary treatment in terms of secondary and tertiary prevention. Cancer rehabilitation includes a comprehensive approach to providing support to patients and their families to cope with treatment sequelae and to allow them to regain quality of life and functional status [2].

As a conceptual basis for rehabilitation, the WHO classification for functioning, disability and health (ICF, former ICIDH=International classification of impairment, disability and handicap) describes how people live with their health condition [3]. ICF is a classification of health and health-related domains that describes body functions and structures, activities and participation. The domains are classified from body, individual and societal perspectives. ICF also includes a list of environmental factors. ICF is useful to understand and measure health outcomes. It can be used in clinical settings, research, health services or surveys at the individual or population level [3]. A first version of the ICF classification for breast cancer has been published [4].

Cancer rehabilitation services can be effectively introduced in a variety of institutional settings. In most European countries as well as in the USA rehabilitation services are mostly based in outpatient settings. Many cancer centres and hospitals offer a variety of cancer rehabilitation services to their patients. Germany provides a unique system of rehabilitation clinics delivering inpatient rehabilitation programmes for all chronic diseases [5,6].

Rehabilitation needs

There are multiple rehabilitation-related issues in different stages throughout the course of the disease. Problems during the initial phase after treatment are different from those that may arise from phases after recurrence or at the end of life [7]. Therefore rehabilitation needs must be assessed individually [8]. The need for rehabilitation in cancer patients is assessed by instruments measuring physical performance and quality of life [9,10]. Cancer-specific scales attempt to assess how illness and treatment affect an individual's quality of life. Those instruments are useful in clinical and research settings and are also used for evaluation of the effects of rehab programmes. Some of those scales can be used along with more in-depth interviews and case-management interventions. They may be also used to document cancer-related problems, assess patient needs and provide information to enhance outcomes.

Goals and interventions

Cancer rehabilitation is aimed at regaining or restoring physical function and independence, often following surgical and medical therapies. Over and above that, an important task of rehabilitation is also to prevent impairment. Although reemployment may not be attained for all patients, vocational reintegration is an important goal of rehabilitation, especially for younger patients [11]. In detail, the goals in cancer rehabilitation are:

- to cope with the physical and emotional changes;
- to improve physical condition and performance status focused on strength, endurance and mobility;
- to improve social, emotional and mental functioning ;
- to identify and treat rehabilitation problems and treatment sequelae (e.g. pain, fatigue, lack of stamina, polyneuropathy, sleeping disorders)
- to enhance self-help strategies, competence and resourcefulness in disease management;
- to improve dietary habits through nutritional counselling; and
- to help the patients to become reemployed or retrain.

Goals are based on individual needs and, ideally, should be attainable within a reasonable amount of time. As each person with cancer has unique physical and emotional needs, each requires an individual rehabilitation plan. Patients and their family members are encouraged to be active and fully-informed partners in the rehabilitation process and thereby contribute to reaching their goals.

Having completed a need and goal assessment the composition of the rehab interventions is to be designed according to the patient's stages of recovery. Rehabilitation programmes include a wide spectrum of treatment options (Table 1.10.1).

- Medical treatment including pain management and complementary medicine
- Exercise programs
- Physical therapy
- Diet counselling
- Pain management
- Smoking cessation education
- Psychological counselling/individual psychotherapy
- Psychological education
- Art therapy/Occupational Therapy
- Neuropsychological training

Table 1.10.1 *Interventions in cancer rehabilitation*

Specialised programs have been developed for diagnostic subgroups (e.g. breast cancer, prostate cancer) and treatment subgroups (e.g. after stem cell transplantation). For example, specified rehabilitation programmes for breast cancer in women may focus on comprehensive management of lymphedema, exercise, diet counselling, post-operative management of breast reconstruction, psychological counselling and psychotherapy, or dance therapy addressing body image and self-esteem. As another example, patients after stem cell transplantation with their severe fatigue and decreased physical performance often require special training, psychological education and a prolonged period of recovery.

Psycho-oncology in rehabilitation

Psychosocial interventions are an essential part of a comprehensive rehabilitation programme. During the last few decades psychosocial interventions based on individual or group therapy have been developed [12,13], which are carried out also in rehabilitation centres. Meta-analyses and systematic reviews have proven those interventions on highest EBM levels I or II [14-17]. Psychoeducational group interventions in rehabilitation are mostly based on the cognitive behavioural approach including various elements (Table 1.10.2). They encompass 6 to 12 sessions based on a structured agenda focusing on the most prominent issues of cancer patients and initiating active coping behaviour.

- Information about cancer and its treatment
- Social and emotional support, sharing of experience
- Stress management
- Cognitive behavioural self-instruction and self-control techniques
- Relaxation, guided imagery

Table 1.10.2 *Elements of psychoeducational programs in cancer rehabilitation*

Cancer rehabilitation as a multidisciplinary task

Comprehensive cancer rehabilitation is provided by a multidisciplinary team of healthcare professionals. Health-care professionals involved in cancer rehabilitation are all committed to help an individual return to the highest possible level of function and independence and to ensure the best possible quality of life. These professionals may include oncologists, psychologists, rehabilitation nurses, dieticians/nutritionists, physical therapists, occupational therapists, art therapists (including music therapy, dance therapy, bibliotherapy etc.), social worker/vocational counsellors and also clergy of different persuasions. All of those professionals are coordinated mostly under the guidance of an oncologist. They work together very closely and should provide a regularly based interchange through multidisciplinary case conferences throughout rehabilitation. Structured meetings as well as external supervision are elements of quality assurance of the rehabilitation.

Evaluation of cancer rehabilitation

Systematic investigation and evaluation in rehabilitation began about 1980. Research programs have been developed to assess the effectiveness and quality of rehabilitative interventions. Compared with other research areas, only a few empirical studies have been conducted in the field of oncological rehabilitation programs. Some studies provide good empirical evidence for effects of rehab programmes, especially on important outcome domains such as health-related quality of life, psychosocial status, and psychiatric comorbidity [18-23]. However, some longitudinal studies showed that the effects of rehabilitation programs could not be proven as stable in catamnestic follow-up assessments [23,24]. In some studies, scores of many outcomes measures tend to decrease to baseline level or even below [23]. Only some studies with short term follow-up [20] showed that the improvements achieved in rehabilitation measures could be preserved during the follow up period. Factors like gender, age,

social status as well as psychological status have been shown to be of prognostic relevance concerning the success of rehabilitation over time [22]. Some studies have found that specified outpatient rehabilitation programs are effective in reducing fatigue while changes in fatigue were associated with changes in physical parameters [25]. Some other studies verify the effects of exercise and training programs for cancer patients [26,27]. There is some evidence that patients prefer multidimensional programmes to programmes with only one component [28]. In the future, further research is required, especially in terms of prospective longitudinal studies to improve effectiveness of the rehabilitation programs.

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1.11 Modern Imaging in Oncology

Summary

> The growth of tumour tissue is a multi-step process traditionally studied by anatomic imaging modalities

> Since molecular processes are the basis of oncology, anatomical imaging has nowadays been enhanced by new technology that illuminates these subcellular events

> The state of the art of modern anatomic imaging modalities includes new applications of well-known techniques, recent developments in molecular imaging studies

Ultrasound. Ultrasound is a safe, noninvasive imaging modality used worldwide for initial investigation of many symptomatic oncologic patients who will subsequently undergo Computerized Tomography (CT) or Magnetic Resonance (MR) imaging for further, more refined assessment. Performance of ultrasound includes detection of tumours of any accessible solid organ, based on lesion morphology and on a specific gray-scale. Optimal contrast resolution is achieved in deep solid organs, such as thyroid, liver, spleen, pancreas, uterus, ovaries and prostate, and superficial structures such as lymph nodes.

Ultrasound can also be used for intra-operative diagnosis because of the superb vision of tiny lesions when the probe is placed intimately close to the region of interest. Furthermore, ultrasound is the ideal mode of guidance for interventional procedures because of its real-time multiplanarity. However, despite the low cost and widespread availability of this modality, its high operator-dependence makes it less reliable in routine staging of proven malignancies, search for metastases and evaluation of response to treatment [1].

CT. CT is currently used for diagnosis, staging and follow-up of almost all tumours. CT imaging is based on X-ray attenuation (Figure 1.11.1 a). The introduction of the spiral scanning mode in the 1990s allowed continuous data acquisition and improvement of dynamic studies (Figure 1.11.1 b). The introduction of multislice CT scanners in 1998 allowed much faster scanning with thinner slices (up to 0.6 mm) and higher power levels (Figure 1.11.1 c), with the current most important application in cardiac imaging. However, the use of iodinated contrast medium is still frequently necessary because of the intrinsic low resolution of tumour tissue to normal tissue.

Traditional use of CT imaging, lacking of multiplanarity, has been enhanced by many image-processing methods. These include: multiplanar reformatting views (MPR) for sagittal, coronal and oblique visualisation (Figure 1.11.2 a,b,c); maximum-intensity projections (MIP) for displaying only structures with the maximum density within a mass, such as vascularisation of lesions (Figure 1.11.3 a); volume rendering (VR) reconstructions to display entire organs at varying opacity levels (Figure 1.11.3 b); surface rendering (SR) reconstructions to display enhancing voxels on the edge of structures with different densities, for virtual bronchoscopy and colonoscopy.

Because of its reproducibility, CT has also been included as a standard examination for monitoring response to therapies by the standard World Health Organization (WHO) criteria, and by the Response Evaluation Criteria in Solid Tumors (RECIST) [2].

MRI. Magnetic resonance imaging (MRI) is based on the use of a magnetic field and high-frequency electromagnetic pulses to generate images of anatomic structures with superb soft-tissue contrast, even without using contrast medium. Modern MR sequences have significantly reduced acquisition times and motion artefacts.

MRI does not apply ionizing radiation; therefore repeated examinations may be performed without risk of radiation damage to tissues, although frequent exposure is now being examined by an expert committee in the United Kingdom to check for any possible predisposition to cancers. Unavailability due to high costs makes MRI difficult to disseminate for routine use worldwide.

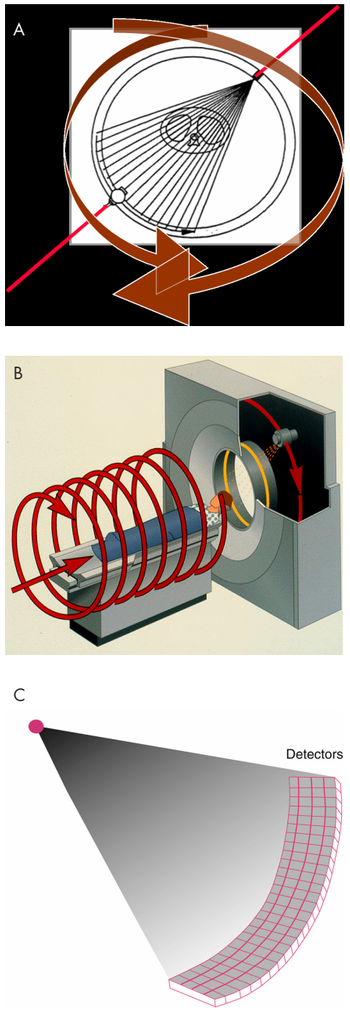

Fig. 1.11.1 *a,b,c. Beyond many years of studies performed by Conventional CT (a), the introduction of spiral CT allowed continuous data acquisition (b) and the consequent development of multislice CT allowed faster scanning by adding more rows of detectors (c)*

Recent developments in MRI imaging are Diffusion Weighted Imaging (DWI-MRI) and Dynamic Contrast-Enhanced (DCE-MRI). In DWI, image contrast derives from differences in water-motion of molecules (Figure 1.11.4 a,b,c); it can be performed quickly and yields insights about tumour cellularity and integrity of cell membranes [3]. In DCE, differences between tissues are highlighted by heterogeneous contrast medium uptake and varied degree of tumour angiogenesis; it can therefore monitor the effectiveness of treatments such as traditional cytotoxic chemotherapy, novel antiangiogenic drugs, hormonal and other targeted therapy, and radiotherapy [4].

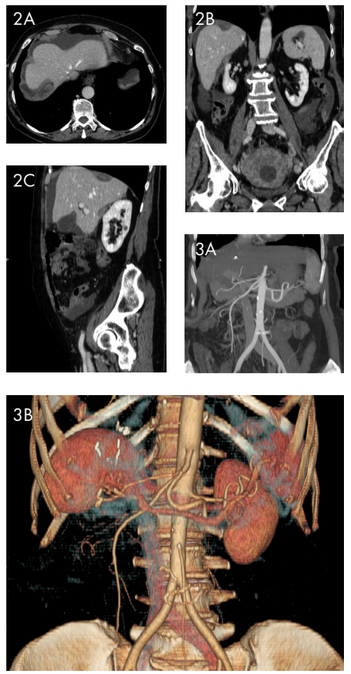

Fig. 1.11.2 *a,b,c. Multiplanar (MPR) CT reconstructions of an ovarian cancer patient, showing an hepatic lesion on the axial image (a), which is clearly located on the liver surface on the coronal (b) and sagittal (c) images, thus making the patient a stage III instead of stage IV*

Fig. 1.11.3 *a,b. Volume Rendering (VR) and coronal Maximum-Intensity Projection(MIP) from a multislice CT study, acquired using 2.5 mm slices in the early post-contrast phase, showing arterial vascularisation of liver*

PET. Most tumour cells use glucose uptake to supply energy. Therefore, the administration of a radiolabeled glucose analogue such as 18-fluorodeoxyglucose (18FDG), shows tumour tissue as "hotter" than normal tissue. Several cancers can be diagnosed and staged using 18-FDG with accuracy rates of 80–98%.

Positron Emission Tomography (PET) imaging can be used for staging and assessing response to treatment, as well described in lymphoma and melanoma patients. Advantages of PET for monitoring response to therapy rely on characterisation of post-therapy masses as metabolically active (residual tumour) or inactive (post-treatment fibrosis). PET imaging can give this information before other anatomic modalities because metabolic changes usually precede anatomical response [5]. However, FDG is excreted by the kidneys in urine, so tumours of the urinary tract may be misdiagnosed. New PET contrast agents that will further expand the range of applications of the technique are currently under evaluation.

Virtual Colonoscopy. Virtual Colonoscopy (VC) is a noninvasive CT method for detection of colorectal polyps and cancers (Figure 1.11.5). In contrast to endoscopic colonoscopy, it is fast, noninvasive, does not require sedation and, although the experience is still short, its rate of morbidity and mortality is very low.

Currently, with the use of multislice CT, the mean scan time is 4–10 seconds, and thin slices of 0.6mm enable high-quality MPR (Multiplanar reconstruction) and 3D reconstruction.

VC can demonstrate lesions behind haustral folds and beyond bends of the colon by providing endoluminal views of the interior of the bowel in both forward and reverse direction. It is also able to detect extra-colonic abnormalities.

Limitations of this technique can be false negatives related to retained fluid, incomplete distension, and difficulty to demonstrate flat lesions [6]. The most important disadvantage of virtual colonoscopy, compared to endoscopic colonoscopy, is the lack of ability to perform biopsies and remove detected polyps under vision. Another less critical disadvantage, when VC is considered as a screening modality for colorectal cancer, is the exposure to ionizing radiation. However, VC is usually performed at a low radiation dose due to the high natural contrast between the colon wall and the endoluminal gas.

Molecular imaging

Most of diagnostic imaging is based on anatomic techniques. Recently radiological research has been focussing on complementing anatomical imaging with functional imaging. Molecular imaging in oncology encompasses new techniques and probes to study processes at the cellular and molecular levels. Molecular imaging methods can be used to stage patients, to predict response to treatments and to provide information on bio-distribution of targeted molecules. The use of specifically targeted contrast agents along with high-resolution imaging modalities are aimed at delivering earlier diagnoses and guiding the choice of new cancer-targeted drugs.

Depending on the properties of the tracers, various aspects of cancer cells including signal transduction, apoptosis and protein interactions can be targeted and visualised.

Several modalities can be used for molecular imaging; mainly single photon emission com-

puted tomography (SPECT), positron emission tomography (PET), magnetic resonance (MR) and computed tomography (CT).

For instance, the use of superparamagnetic iron oxide (SPIO) particles for cellular trafficking has enabled the visualisation of a single cancer cell by using a clinical MR [7].

Furthermore, positron-emitting analogues of chemotherapeutic agents, such as paclitaxel or fluorouracil, are under evaluation for assessment of a tumour's ability to sequester the radiolabelled analogue [8] and of the consequent advantage for the patient to undergo that specific chemotherapy.

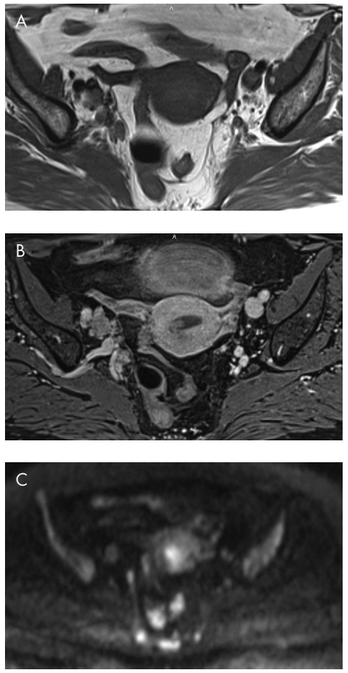

Fig. 1.11.4 *a,b,c. Pelvic MR study of an endometrial cancer patient. T1 pre-contrast (a) and post-contrast (b) images show an enlarged pathologic right obturator lymph node. Diffusion-Weighted Image (DWI) acquired with a 900 b-value (c) shows hyper-intensity of the lymph node due to low water-motion of molecules, thus confirming its positivity*

The use of radiolabelled somatostatin analogues for imaging has become the gold standard for staging of neuroendocrine tumours, because the somatostatin receptor is strongly over-expressed in most tumours, resulting in high tumour-to-background ratios. Based on this attitude, a peptide receptor radionuclide therapy with radiolabelled somatostatin analogues is emerging as a treatment modality for patients with unresectable, somatostatin-receptor-positive neuroendocrine tumours [9].

Future directions for imaging in oncology

Advances in different imaging modalities and the possibility of their integration are predicted to show better outcomes than the sum of their single parts. CT, MR, US and PET may guide high-precision radiotherapy techniques, such as intensity-modulated RT (IMRT) [10].

An additional synergy may come from fusion of PET/SPECT and CT, where the use of common detectors may be used to detect emission of gamma rays and transmission X-rays to provide better localisation of metabolic processes.

The traditional low-spatial resolution of PET has been improved with co-registration and fusion of PET and anatomical images either on a software basis with CT and MR, or with integrated hardware with CT (PET-CT) (Figure 1.11.6).

Whole-body MR imaging is under evaluation as a diagnostic tool in cancer staging as an alternative to scintigraphy, in staging the skeletal spread of disease and in assessing tumour burden [11].

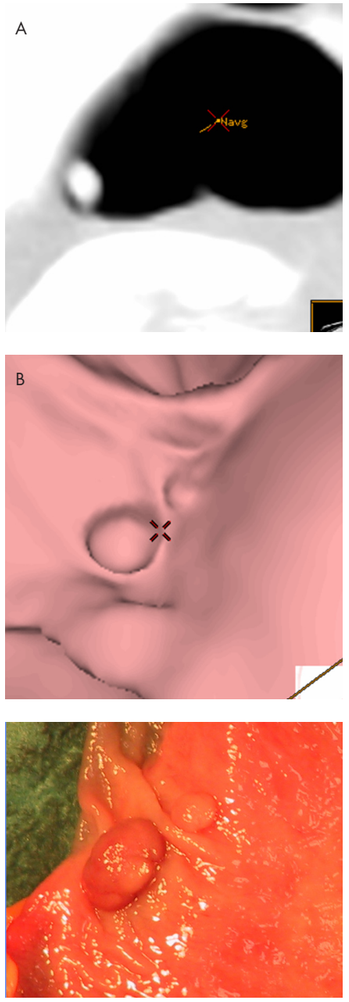

Fig. 1.11.5 *a,b,c. Virtual Colonoscopy (VC) can detect polyps as in the regular axial view (a) as in the volume view (b), and the visualization is comparable to endoscopic colonoscopy (c)*

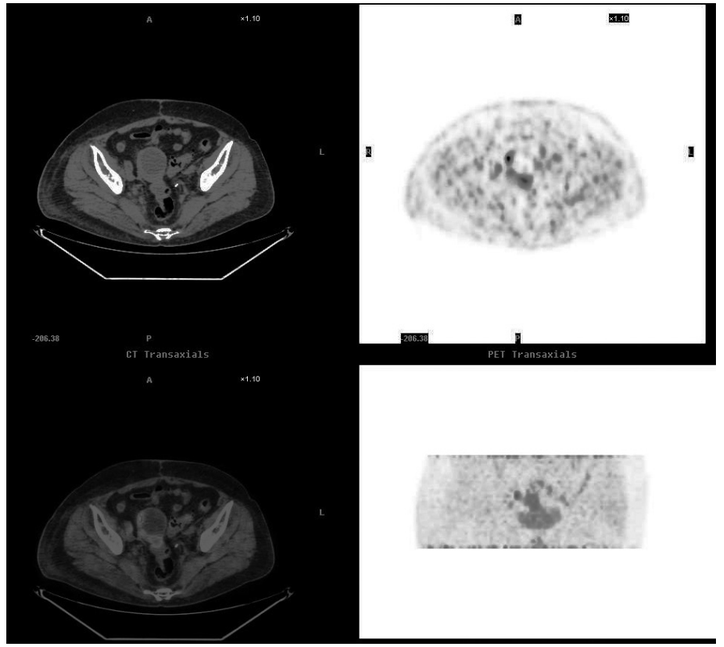

Fig. 1.11.6 *PET-CT integrative image showing a hypermetabolic lesion of the right uterine wall with a post-surgery diagnosis of endometrial adenocarcinoma*

Conclusions

Modern oncology relies on advances in cross-sectional imaging for diagnosis, staging and evaluation of treatment response. New molecular imaging techniques are promising to add information about tumour biology and function to the visualisation of disease by current imaging modalities. Imaging of anatomy and assessment of function are still in progress, and their advancements as single modalities and successive integration is heading for improving the ultimate management of cancer patients.

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1.12 Breast Health Care Delivery in Low- and Middle-Income Countries

Summary

> Breast cancer is an international problem affecting countries at all economic levels, is the most common cancer among women, and worldwide is the most likely reason that a woman will die of cancer

> Despite the common misconception that breast cancer is predominantly a problem of wealthy countries, the majority of breast cancer deaths occur in low- and middle-income countries (LMCs)

> The breast cancer burden in LMCs will continue to increase in coming years on the basis of increasing life expectancy and shifting reproductive and behavioural patterns associated with heightened breast cancer risk

> The Breast Health Global Initiative (BHGI) has developed evidence-based, economically feasible, resource-sensitive guidelines for breast cancer early detection, diagnosis, treatment, and health care systems in LMCs

> BHGI guidelines can provide a framework for systematic, comprehensive improvement and are intended to assist ministers of health, policymakers, administrators, and institutions in prioritising resource allocation

> A systematic program of research to develop appropriate readiness assessment instruments and identify effective implementation strategies is needed to effectively apply BHGI guidelines in LMCs

Among women, breast cancer is the most common cause of cancer-related death worldwide, with case fatality rates highest in low- and middle-income countries (LMCs). Globally, breast cancer is the most common cancer among women, comprising 23% of all female cancers that are newly diagnosed in more than 1.1 million women each year [1]. Over 411 000 deaths result from breast cancer annually, accounting for over 1.6% of female deaths from all causes (Figure 1.12.1) [2]. Projecting to 2010, the annual global burden of new breast cancer cases will be 1.5 million, and an ever-increasing majority will be from LMCs [3]. Approximately 4.4 million women diagnosed with breast cancer in the last five years are currently alive, making breast cancer the single most prevalent cancer in the world [1]. Despite the common misconception that breast cancer is predominantly a problem of wealthy countries, the majority of breast cancer deaths in fact occur each year in developing rather than developed countries [3].

Health care disparities. Breast cancer already is an urgent public health problem in high-resource regions, and is becoming an increasingly urgent problem in low-resource regions, where incidence rates have been increasing by up to 5% per year [2,4]. In most LMCs, breast cancer incidence rates are increasing at a more rapid rate than in areas where incidence rates are already high. Global breast cancer incidence rates have increased by about 0.5% annually since 1990; by contrast, cancer registries in China are recording annual increases in incidence of 3–4% even in the absence of population-based breast cancer screening [1]. Among Asian countries with the most developed data registries, breast cancer rates in Japan, Singapore, and Korea have doubled or tripled in the past 40 years, and China's urban registries document 20–30% increases in the past decade alone [5]. In the urban areas of India, cervical cancer had the highest incidence among female cancers 15 years ago, but has now been overtaken by breast cancer as the most commonly diagnosed cancer among women [6]. Despite the younger age structure of most developing countries, breast cancer already accounts for about 45% of the incident cases and 54% of the annual deaths [3].

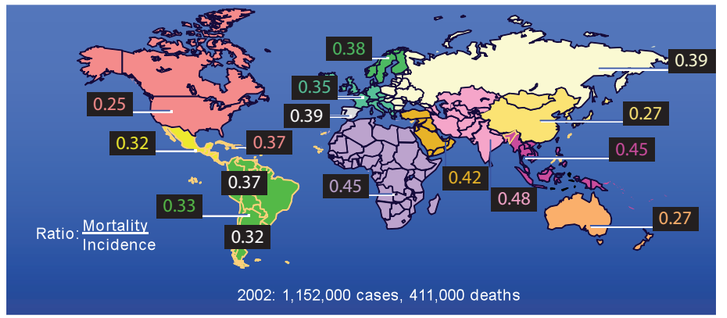
The breast cancer burden in LMCs will predictably continue to increase in coming years on the basis of 1) increasing life expectancy and 2) shifting reproductive and behavioural patterns associated with heightened breast cancer risk. Even conservatively assuming no change in underlying age-specific rates (Figure 2), there could be a nearly 50% increase in global incidence and mortality between 2002 and 2020 due to demographic change alone, with disproportionate shares of that increase occurring in the developing world–with increases of 55% in incidence and 58% in mortality in less than 20 years [3].

These statistics probably underestimate the actual rising breast cancer rates, since the few data available from LMCs reveal increases in breast cancer age-specific incidence and mortality rates, especially in recent birth cohorts. This is especially true among urban women and is probably due at least in part to the adoption of Western lifestyles that tend to promote decreased parity, delayed childbirth, decreased physical exercise, and dietary habits associated with earlier menarche, all of which have been associated with increasing rates of postmenopausal breast cancer [5,7,8].

Despite significant scientific advances in breast cancer management, most of the nations of the world face resource constraints that limit their capacity to improve early detection, diagnosis and treatment of the disease. In LMCs, worsened cancer survival is largely due to late stage at presentation, which leads to particularly poor outcome when coupled with limited diagnosis and treatment capacity [9]. Of the over 75 000 new cases presenting for treatment each year in India, between 50% and 70% have locally advanced (Stage III) or metastatic (Stage IV) breast cancer at diagnosis [10]. By comparison, 38% of European and 30% of American breast cancer cases were reported to be locally advanced at diagnosis in the EUROCARE study and SEER cancer registry between 1990 and 1992 [11].

Compounding the problem of late diagnosis, breast cancer case fatality rates are high because LMCs typically lack major components of health care infrastructure and resources necessary to implement improved methods for early detection, diagnosis and treatment of breast cancer [12,13]. Although most LMCs have not yet identified cancer as a priority health care issue, because infectious diseases are a predominant public health problem, cancer care will become an important health problem over the next decades as the control of communicable diseases improves and life expectancy rises [8].

Breast health care guidelines. Evidence-based guidelines outlining optimal approaches to breast cancer detection, diagnosis and treatment have been well-developed and disseminated in several high-resource countries [14,15]. These guidelines define optimal practice and therefore have limited utility in LMCs. Optimal practice guidelines may be inappropriate to apply in LMCs for numerous reasons, including inadequate personnel resources, limited healthcare infrastructure, lack of pharmaceuticals and cultural barriers. Hence, there is a need to develop clinical practice guidelines oriented towards LMCs, specifically considering and adapting to existing health care resources.



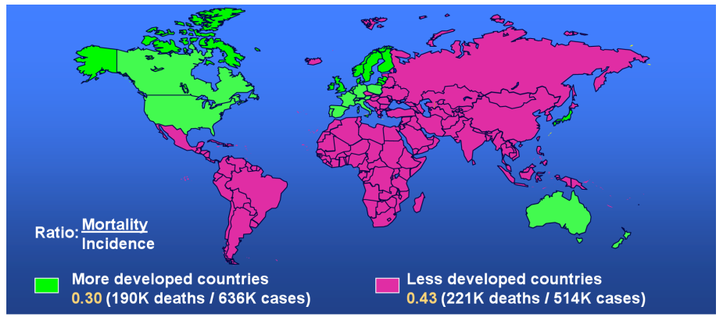


Fig. 1.12.1 *Estimated mortality-to-incidence ratios for breast cancer in 2002 by A) global geographic region of the world and B) more developed vs. less developed countries [3]. The majority of breast cancer cases are diagnosed in high-resource countries, but the majority of breast cancer deaths occur in the low- and medium-resource countries*

Co-sponsored by the Fred Hutchinson Cancer Research Center and Susan G. Komen for the Cure, the Breast Health Global Initiative (BHGI) strives to develop evidence-based, economically feasible and culturally appropriate guidelines that can be used in nations with limited health care resources to improve breast cancer outcomes. The BHGI held three Global Summits to address ***health care disparities*** (Seattle 2002), [16] ***evidence-based resource allocation*** (Bethesda 2005) [17] and ***guideline implementation*** (Budapest 2007) [18] as related to breast cancer in LMCs. Modelled after the approach of the National Comprehensive Cancer Network (NCCN), BHGI developed and applied an evidence-based consensus panel process now formally endorsed by the Institute of Medicine [19] to create resource-sensitive guidelines for breast cancer early detection, [20,21,22] diagnosis, [23,24,25] treatment [26,27,28] and health care systems, [29, 30] as related to breast care in LMCs. The BHGI guidelines are intended to assist ministers of health, policymakers, administrators and institutions in prioritising resource allocation as breast cancer treatment programs are implemented and developed in their resource-constrained countries.

Guideline dissemination and implementation (D&I) research. The dominant paradigm even now in the medical community is that good research and publication should be sufficient to ensure the translation of scientific findings into general practice [31]. Unfortunately, a landmark Institute of Medicine (IOM) report from 2001 clearly identified the failure of much scientific innovation to be translated into practice [32,33]. More recently, Rubenstein and Pugh separated the IOM's second translational block–clinical research to practice–into two parts: 1) clinical research to guidelines and 2) guidelines to practice [34]. D&I researchers maintain that the process is complex and have begun to identify factors and processes critical to the adoption of new technologies and practices [35]. While there has already been some D&I work on assessing readiness for change, it has usually focused on just one component,

such as providers or health units, or has focused on intention without considering self-efficacy or environment. As a conclusion in her extensive review of the implementation literature, Greenhalgh notes the need for more research on system readiness for innovation and for more studies evaluating implementation of specific interventions [36].

A review of available information strongly suggests a crucial role for research in applying the experience and knowledge of high income societies to the challenges of women and breast cancer throughout the world. A recent survey of oncology experts from Latin American countries found that 94% of the surveyed experts consider clinical-epidemiologic research development on breast cancer insufficient in their country [37]. The main reasons identified were insufficient economic retribution and lack of available time.

Very little research on guideline implementation has been done in LMCs. It is necessary to see whether the basic frameworks and instruments being described in high-income countries apply in these very different environments and what adaptation is needed to make them both valid and feasible. A systematic program of research to develop appropriate readiness assessment instruments and identify effective implementation strategies is now needed in a variety of LMCs. As the adoption, implementation and maintenance of the new evidence-based principles embodied in the BHGI guidelines progresses, it is critical that careful evaluation be incorporated in the efforts to ensure that lessons about effectiveness and efficiency are captured. It is precisely because resources are scarce in these countries that it is even more imperative for LMCs to adopt effective practices as quickly as possible, and that implementation approaches are designed with limited resources in mind [31].

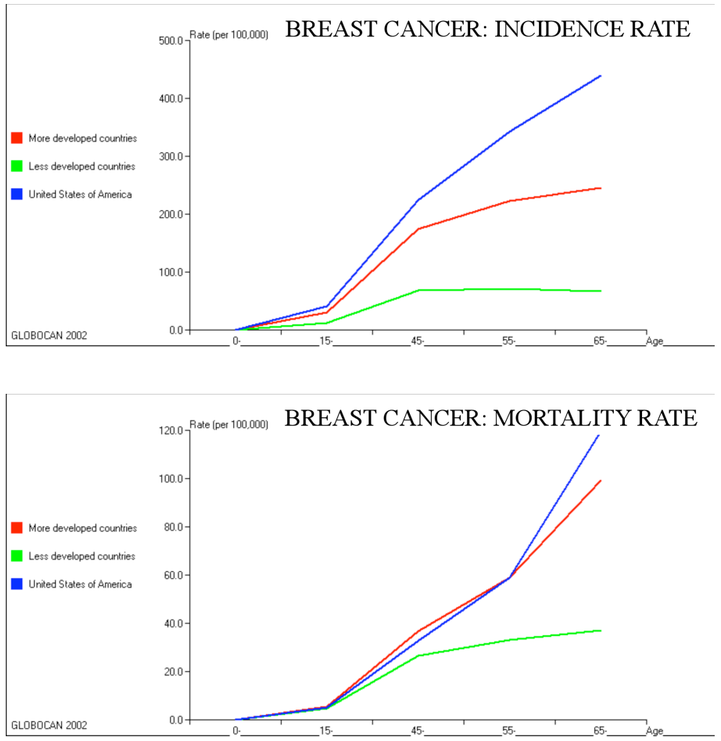


Fig. 1.12.2 *Age-specific breast cancer A) incidence and B) mortality in the United States, more developed countries and less developed countries [3]. Differences in breast cancer incidence between more developed and less developed countries are greatest in older (postmenopausal) women, but breast cancer mortality is very similar for women under age 50.*

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CANCER CONTROL IN LATIN AMERICA AND THE CARIBBEAN:
Pan American Health Organization (PAHO)

In Latin America and the Caribbean, cancer is the 2nd leading cause of death. The most common causes of cancer deaths are lung, stomach and prostate cancer among men, and cervix, breast and stomach cancer among women. Uruguay, Argentina, Colombia, Peru and Barbados are among the countries in the Region experiencing the greatest cancer burden.

The public health response to cancer has been varied, given that most countries in this Region are experiencing an epidemiological transition and facing the double burden of chronic diseases and infectious diseases. In a 2006 survey by PAHO, 75% of responding countries reported having national cancer control programs, yet only half of the countries reported having an acceptable degree of implementation of their programs. All countries report having a cervical cancer screening program; however, screening coverage is very low, as more than half of the countries reported 25% or less coverage. Cancer treatment centres exist in all countries, with the exception of several countries in the Caribbean, although access is far lower than in the industrialised countries. Radiotherapy treatment capacity is quite low in the region, with a reported number of radiation oncologists of 1.6 per million population and high-dose teletherapy units of 1.4 per million population, compared to 9 and 6.4 respectively in industrialised countries. Apart from being scarce, access to treatment services is inequitable, since most of these services are provided in health centres located in the largest cities, meaning a large proportion of the rural population has no access to them. Their high cost also makes them inaccessible to poor urban populations.

The common problems reported by all countries are:

- the advanced stages of diagnosis of cancer and the need for early detection programs;
- the need to improve access, availability and quality of cancer treatment centres, particularly outside of big cities;
- limited access to affordable cancer drugs;
- weak surveillance and cancer registry systems;
- inadequate opportunities for training and continuing education; and
- the need to increase the public health priority and resources for cancer in the public health agenda.

PAHO has been providing technical cooperation to countries in Latin America and the Caribbean, and responding to these problems and the needs expressed by the Ministries of Health. The main areas of cooperation have been in creating comprehensive national cancer control plans, cervical cancer prevention, tobacco control and radiotherapy services. As part of the Alliance for Cervical Cancer Prevention, PAHO has been assisting countries in improving the quality and coverage of screening programs and testing alternative screening approaches. The lessons learned from this work have culminated in the development of a Regional Strategy for Cervical Cancer Prevention and Control, which provides policy and technical guidance for comprehensive programs, and is anticipated to be presented to the 2008 PAHO Directing Council. In the subregion of Central America, the Ministers of Health have called for the creation of a sub-regional cancer plan, which is being coordinated by PAHO through a participatory process with the Ministries of Health. This subregional plan will elevate the political and technical commitments for national cancer programmes, as well as solidify a sub-regional response for common issues on cancer prevention, early detection, treatment and palliative care. PAHO continues to evaluate and improve the quality of radiation therapy through its longstanding radiological health program.

With an aging population and corresponding rise in cancer burden in Latin America and the Caribbean, health systems will need to be equipped to control cancer. The challenges remain in having adequate resources, applying current and new knowledge and sustaining the political will to achieve effective cancer control.

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