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Inequity in Cancer Care: A Global Perspective

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INEQUITY IN CANCER CARE: A GLOBAL PERSPECTIVE

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FOREWORD

The strategies of United Nations system organizations such as the International Atomic Energy Agency (IAEA) and the World Health Organization (WHO) are based on guiding principles, the attainment of health equality being an important one. Therefore, their strategies focus on the needs of low and middle income countries and of vulnerable and marginalized populations.

The IAEA is committed to gender equality. In keeping with the United Nations policies and agreements on both gender equality and gender mainstreaming, the IAEA has the responsibility of integrating gender equality into its programmes, as well as for contributing to worldwide gender equality. In addition, the IAEA strongly emphasizes the attainment of the United Nations Millennium Development Goals, of which gender equality is a central tenet.

This publication focuses on the issue of inequality (disparity) as it applies to cancer care in general, and access to prevention, screening, palliative and treatment services in particular. The problem of inequality in access to radiation oncology services is addressed in detail. Access to cancer care and radiotherapy services for women and children is specifically considered, reflecting the currently published literature.

The report is aimed at radiotherapy professionals, health programme managers and decision makers in the area of cancer control. It was developed to create awareness of the role of socioeconomic inequality in access to cancer care, and to eventually mobilize resources to be equitably allocated to public health programmes in general, and to cancer control and radiotherapy programmes in particular.

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1. INTRODUCTION

The Universal Declaration of Human Right states that “everyone has a right to a standard of living adequate for the health and wellbeing of himself and his family”. Cancer patients are not an exception. Inequalities in health are probably one of the most convincing indicators reflecting the inequalities present in society as a whole. Indicators related to cancer and its incidence patterns are proof of this. A close look at the cancer incidence rate according to socioeconomic, racial and ethnic groups reveals significant differences.

There is enough evidence to assert that people with a lower socioeconomic status experience greater cancer incidence and shorter survival rates after diagnosis. Yet, socioeconomic status, a function of income, education and occupation, does not itself cause cancer or poor outcomes. Rather, it is a marker for the underlying physical and social factors that cause the disease, its recurrence and its eventual outcome. Lower socioeconomic status can lead to access problems along the entire spectrum of care, starting from early detection issues to the delays in diagnosis after the appearance of initial symptoms. Apart from logistical barriers to access, people of lower socioeconomic status are more likely to remain uninformed about early detection programmes and disease management, including the early signs, symptoms and availability of cancer treatment. Lastly, but certainly not least important, the quality of available care may vary with socioeconomic status [1].

Health care disparities arise from a complex interplay of economic, social, and cultural factors [2]. It is well known that cancer is a major cause of death throughout the world, second only to cardiovascular diseases. Around ten million new cancer patients are diagnosed every year [4]. The overall incidence of cancer in developing countries is half of that observed in the developed world, and it is increasing rapidly. Site specific cancer survival rates in developing countries are often less than one third of those in the developed world [5]. In contrast, cancer mortality is already comparable between the developing and the developed world.

It would be unrealistic to attempt to find a molecular explanation for the difference in incidence and mortality for most cancers between more and less affluent socioeconomic groups. However, it is likely that many more genetic and epigenetic alterations that have been identified so far are required to complete the process of carcinogenesis. This would eventually explain in molecular terms the demonstrated effect of environmental exposures [3].

The cost of cancer care is another key issue when addressing cancer disparities. This varies dramatically according to the disease and its stage, and whether curative therapy is to be attempted. There is no doubt that there are enormous limitations in the use of cancer resources in developing countries. Apart from the cost of the treatment itself, cancer management generally requires the participation of a number of trained professionals, who are typically in short supply.

The magnitude of socioeconomic differences varies between populations, and over time also within populations [6]. This suggests that identifying factors that influence socioeconomic status and health, and the pathways by which they operate, may be an important public health measure to reduce inequality in health.

Recent studies report that a number of patients from lower socioeconomic groups not only are diagnosed with and die from preventable cancers, but also are diagnosed with late stage disease for cancers that are potentially detectable at an early stage through screening. These patients, who receive either no treatment or treatment that does not meet the currently accepted standards, either die of cancers that may be curable or suffer from terminal cancers in the absence of adequate pain control and other palliative care measures [7].

While the social and economic burden of cancer will continue to increase in developing countries, promising efforts are under way in the scientific, medical, economic and policy arenas. This is likely to have a positive impact on the availability and effectiveness of interventions available for care, and the quality of life of cancer patients.

The present publication examines the issues related to disparities in cancer, focusing on socioeconomic factors, and addresses the problem of access to cancer therapy, in particular to radiation oncology services, underlining access to cancer therapy for women and children in particular.

2. DISPARITIES IN CANCER INCIDENCE AND MORTALITY

The World Cancer Declaration, presented at the UICC World Cancer Congress in 2006, recognized cancer as a global priority and called for urgent action to control the increasing worldwide cancer burden [8].

— A better understanding of the general causes of global cancer inequalities will facilitate efforts to reduce them. There is an awareness of the magnitude of the growing cancer problem in the developing world. However, any action cannot stand alone without proper cancer surveillance and cancer control systems. As a first and essential step, however, better national and regional heath surveillance systems are needed, particularly in poorer regions of the world. Without such steps, it will be difficult to know if, and how much, progress is being made in improving global health status and reducing growing health inequalities. There is a significant lack of relevant cancer data from most developing countries while the research capacity is almost non-existent. Only a few developing countries have reliable cancer registries, and when available they are mostly hospital based and not population based.
— Increased cancer incidence in developing countries is partially due to the socioeconomic development of these countries, resulting in longer life expectancy coupled with unhealthy lifestyle behaviours such as smoking, unhealthy nutrition, and sedentary lifestyle. On the other hand, reduced mortality from infectious diseases results in relatively higher mortality from cancer and other chronic diseases. In addition, in the developing world, transmissible diseases still contribute to cancer incidence, particularly those preventable cancers caused by infectious disease.
— Certain types of cancer, such as breast, colon, and prostate tumours, are associated with 'western-type' lifestyles as demonstrated by higher rates of these cancers in more developed versus less developed countries [9]. Whereas developed countries have made strides in the prevention of some cancers, such as smoking related tumours, the incidence of these cancers is fast growing in developing countries [10–12].
— Additionally, early detection and access to advanced diagnostic modalities and cancer therapies have also led to an increase in early diagnosis and declines in mortality of certain cancers in developed countries not seen in less developed communities [13]. Some of the most prevalent cancers in developing countries are associated with infections caused by viruses such as the Human Papilloma Virus (HPV) (cancer of the cervix) and Hepatitis B Virus (liver cancer).
— Low and middle income countries are faced with a difficult choice of where to allocate the scarce financial resources along the continuum of cancer control: prevention, screening, early detection, treatment or palliative care. These countries have less than 5% of the resources available in the world for cancer control, and more than 80% of their cancer patients will be beyond cure at the time of diagnosis [14]. Nevertheless, differences can also exist among developed countries and disparities exist not only between countries but also within countries. Thus, there are also differences between regions, cities, social groups, hospitals and even health care institutions within the same city.
— In general, lower socioeconomic status (SES) groups in developed countries have less access to care and are unhealthier than higher SES groups. Consequently, all population segments do not share the burden of cancer equally. Even controlling for SES, minority and medically underserved groups tend to present with late stage disease, and consequently suffer higher morbidity and mortality rates than others [15].
— In a review of the survival of 132 006 patients in New Zealand diagnosed with cancer during the years 1994–2003, socioeconomic inequalities in survival were evident for all the major cancer sites. These survival differences were not explained by ethnicity (Maori are the indigenous people of New Zealand), which was an independent factor for reduced cancer survival, and were only partly explained by the extent of disease at diagnosis. This detailed analysis was possible in New Zealand because of the mandated national cancer registry collection and a unique identifier for each person seeking health care.
— There are several reports on current cancer behaviour [5, 16, 17]. All of them describe the increasing trends of cancer incidence in recent years (Table 1). Despite the fact that this increase occurs for all cancer sites, changes in patterns of incidence differ between developed and developing countries and among cancers sites. If by 1980, 50% of all new cancer cases were diagnosed in developing countries, by 2000 this figure rose to 55% and it has been estimated that it will reach 70% by 2020 [11]. While the top five cancers in developed

TABLE 1. CHANGES IN CANCER INCIDENCE BETWEEN DEVELOPED AND DEVELOPING COUNTRIES

	Entire world				Developed countries				Developing countries			
	1980		2000		1980		2000		1980		2000	
Site	No	%	No	%	No	%	No	%	No	%	No	%
Stomach	669.4	10.5	876.3	8.7	333.0	10.4	333.3	7.1	336.4	10.6	543.0	10.1
Lung	662.5	10.4	1238.9	12.3	456.6	14.2	646.2	13.8	205.9	6.5	592.6	11.0
Breast	572.1	9.0	1050.3	10.4	347.9	10.8	579.3	12.4	224.2	7.1	471.1	8.8
Colon and/or rectum	572.1	9.0	944.7	9.4	389.2	12.1	610.6	13.0	182.9	5.8	334.1	6.2
Cervix	465.6	7.3	470.6	4.7	96.1	3.0	91.5	2.0	369.5	11.7	379.2	7.1
Mouth and/or pharynx	378.5	5.9	454.4	4.5	106.2	3.3	134.8	2.9	272.3	8.6	319.7	5.9
Oesophagus	310.4	4.9	412.3	4.1	56.8	1.8	71.2	1.5	253.6	8.0	341.2	6.3
Liver	251.2	3.9	564.3	5.6	59.6	1.9	107.0	2.3	191.6	6.1	457.4	8.5
Lymphoma	237.9	3.7	349.6	3.5	116.1	3.6	173.4	3.7	121.8	3.9	176.2	3.3
Prostate	235.8	3.7	543.0	5.4	177.2	5.5	415.6	8.9	58.6	1.9	127.4	2.4
Bladder	219.4	3.4	335.8	3.3	148.2	4.6	211.8	4.5	71.2	2.3	124.0	2.3
Leukaemia	188.2	3.0	257.1	2.6	82.7	2.6	105.8	2.3	105.5	3.3	151.3	2.8
Corpus uterus	148.8	2.3	189.0	1.9	103.5	3.2	113.6	2.4	45.3	1.4	75.3	1.4
Ovary	137.6	2.2	192.4	1.9	70.4	2.2	91.3	2.0	67.2	2.1	101.1	1.9
Pancreas	137.4	2.2	216.4	2.2	90.0	2.8	127.4	2.7	47.4	1.5	89.0	1.7
Larynx	120.0	1.9	161.4	1.6	52.9	1.6	69.0	1.5	67.1	2.1	92.4	1.7
Other	1068.3	16.8	1799.0	17.9	530.0	16.5	798.1	17.1	538.3	17.0	1000.9	18.6
Total	**6375.2**	**100.0**	**10055.6**	**100.0**	**3216.4**	**100.0**	**4679.7**	**100.0**	**3158.8**	**100.0**	**5375.8**	**100.0**

Source: Parkin, et al. 1988 [18]; Ferlay, et al. 2001 [19].

countries are (in descending order) lung, colorectal, breast, prostate and stomach cancer, in developing countries the most common cancers are lung, stomach, breast, liver, and cervical cancers (Table 1). On the other hand, the incidence rates of cancers associated with low socioeconomic status have not suffered great modifications between 1980 and 2000. One of the most striking examples is that after 20 years, 80% of all cervical cancer still occurs in developing countries, as well as 60% of all new cases of stomach cancer, which represents an increase of 11% when compared to 1980.

The observed differences in cancer incidence, mortality and survival among developed countries compared with those in less developed countries are mainly due to the difference of existing individual and social risk factors in both geopolitical areas. The situation for developing countries is becoming dramatic. They show an increase in the incidence rates for cancers that used to be more frequent in the developed world (lung, breast, prostate); indeed, lung cancer is already the most common cancer in most developing nations. The starkest contrast in cancer incidence between developing and developed countries is seen in cancers associated with infectious diseases and with a 'western lifestyle', respectively. [20, 21].

Socioeconomic inequalities and their influence on health are not exclusive of low income countries. Mackenbach, et al. [22] conducted a study in 22 European countries, correlating socioeconomic status (as measured by education, occupation and income) with the mortality rates by various causes. In almost all countries, the death rates and poorer self-assessments of health were substantially higher in groups of lower socioeconomic status. The magnitude of this inequality between groups of higher and lower socioeconomic status was much larger in some countries than in others. Inequalities in mortality were small in some southern European countries and very large in Eastern European countries and the Baltic region. These variations among countries appeared to be attributable to medical interventions.

While global cancer mortality is expected to increase by 104% by 2020, increases in death rates will be about five fold greater in the developing world, compared to the established market economies [16]. Much of this disparity in cancer mortality is attributable to a lack of prevention and early detection. Late diagnosis and inadequate treatment for advanced cancer also contribute to mortality as up to 80% of patients in developing countries already have incurable disease when first diagnosed.

Table 2 estimates the rise in cancer incidence in eight developing countries in four regions. The table shows the crude incidence in 2002 and the projected incidence for 2020 according to the Globocan 2008 database (IARC).

TABLE 2. CANCER CRUDE INCIDENCE AND PROJECTIONS

COUNTRY	CANCER INCIDENCE IN 2008 (Crude incidence[a] in number of cases)	PROJECTED CANCER INCIDENCE IN 2020 (Crude incidence in number of cases)
	LATIN AMERICA	
Bolivia	8.689	12.220
Costa Rica	7.653	11.634
	AFRICA	
United Republic Of Tanzania	21.180	30.303
Nigeria	101.797	138.365
	ASIA	
Vietnam	111.581	161.515
Sri Lanka	24.447	32.219
	EUROPE	
Albania	7.732	9.934
Ukraine	142.960	143.233

[a] 'Crude incidence' is the number of new cancer cases in a specified time period without adjustment for age or other factors.

There is an increasing awareness of the magnitude of the growing cancer problem in the developing world. Several well recognized and persistent obstacles to adequate health care in developing countries exist. The global disparities in the incidence of certain preventable cancers, as well as disparities in survival from several treatable and curable cancers, are a demonstration of the lack of equality in health, apparently determined solely by the hazard of where one is born. While the total cancer burden remains highest in affluent societies, less developed economies are closing the gap very rapidly. There is a lack of adequate health care coverage available to many persons living in less developed countries, and when available, it is often inequitable and not affordable [7, 10, 20, 23].

3. CANCER RISK FACTORS

Socioeconomic differences in cancer have not usually been an argument to explain cancer etiology. Cancer mortality distribution by social class in England and Wales was first shown in 1911. Even at that time it was evident that deaths due to cancer were distributed unequally in the population [24].

Primary prevention through lifestyle changes and environmental interventions might offer the best option for reducing the large and increasing burden of cancers worldwide. Policies and programmes to implement such interventions depend on reliable and comparable analyses of the effect of risk factors for cancer at the population level.

As developing countries 'succeed' in achieving lifestyles similar to those in advanced economies, they will also encounter much higher cancer rates, particularly cancers of the breast, colon, prostate and uterus (endometrial carcinoma). The increased prevalence and incidence of cancer in developing countries reflect a wider epidemiological transition in the global burden of disease from infectious diseases toward a greater frequency of non-communicable, chronic illnesses [11].

On the other hand, the demographic transition process confronts and will confront the majority of developing countries in the upcoming years [25–27], characterized by decreasing fertility, increasing life expectancy and therefore an ageing population. This suggests a future increase in the total number of cancer cases, in other words, an increase in the crude incidence rate.

Various types of cancer may have a common contributing cause at the individual level (for example tobacco smoking or unhealthy nutrition habits), but these exposures may also have common socioeconomic and political roots at the population level [28]. Knowledge of the impact of these exposures is necessary for prevention, both as a part of cancer control as well as the establishment of regional health policies aimed at decreasing inequalities in cancer treatment.

The most important environmental human carcinogens include tobacco, asbestos, aflatoxins and ultraviolet light. Almost 20% of cancers are associated with chronic infections; the more significant ones being hepatitis viruses (HBV, HCV), papilloma viruses (HPV) and Helicobacter pylori. There is increasing recognition of the causative role of lifestyle factors, including unhealthy nutrition, lack of physical activity, and alcohol consumption. Genetic susceptibility may significantly alter the risk from environmental exposures [9]. Goodarz et al. [29] point to nine known and potentially modifiable risk factors: tobacco smoking, alcohol drinking, obesity, low fruit and vegetable intake, physical inactivity, unsafe sex, air pollution and hepatitis B virus. Related factor cancer sites are mainly the upper aero-digestive tract, lung, stomach, cervix, liver, colorectal, breast and prostate cancer. The main cancer risk factors and cancer related outcomes are discussed below in more detail.

3.1. TOBACCO CONSUMPTION

Tobacco is the main specific contributor to total mortality in many developed countries. It has also become a major contributor in developing countries, where tobacco use is increasing rapidly [6]. Consumption of tobacco products is causally related to many types of cancer. The risk is proportional to the duration and intensity of

exposure. Non-filtered, high tar and black tobacco cigarettes represent a greater risk for most tobacco related cancers. Most commonly, smoking causes lung cancer [30]. In addition, it is highly correlated with cancer of the larynx, oral cavity and pharynx [31, 32], oesophagus, pancreas, kidney and bladder [9, 33].

Lung cancer varies dramatically among communities. Within many communities, smoking and hence lung cancer, are sharply related to social class [34]. High rates are observed in certain parts of North America and Europe.

From the mortality study in England and Wales (United Kingdom) mentioned above, Lynge [24] pointed out that lung cancer mortality among men was fairly distributed in 1931. Forty years later, a steep social class gradient was developed and lung cancer was roughly three fold more common among men of lower social class. The upper social classes were the first to quit smoking, when tobacco was shown to cause lung cancer in the early 1960s.

Prevalence of smoking varies throughout the world. It is usually higher among men. The ratio of men to women is close to seven. Except in the Western Pacific and Eastern Mediterranean regions where prevalence among women is relatively high (around 25%), prevalence of smoking in women is normally half or less of that reported among men [9]. The proportion of smoking is decreasing among men in industrialized countries. Tobacco smoking spreads with increasing wealth, from persons who can afford it and subsequently to all layers of society. Although tobacco smoking is an individual habit, exposure nevertheless depends on political, economic and social factors [6]. A recent upward trend in smoking prevalence among women in many developing countries will result in a much greater number of smoking related cancers among women in the future [9].

3.2. ALCOHOL DRINKING

A great number of epidemiological studies have demonstrated a correlation between chronic alcohol consumption and the occurrence of cancer. Alcohol is a strong risk factor for cancer in the upper aerodigestive tract (oral cavity, pharynx, hypopharynx, larynx, and oesophagus) and also a major etiological factor in hepatocarcinogenesis. In addition, alcohol increases the risk for colorectal and breast cancer [32, 35–38]. These studies clearly suggest that ethanol itself is the crucial compound, which causes the carcinogenic effect [39].

Patterns of alcohol drinking by socioeconomic status are not consistent between countries or genders. The role of alcohol drinking in the observed negative social class gradient for the alcohol related cancers is very similar among men in France, Italy, and New Zealand. Suggestive evidence of the role of alcohol drinking related to cancer has been described about men in Brazil, Switzerland, the United Kingdom and Denmark [6, 36]. Alcohol drinking is frequently associated with tobacco smoking and poor dietary habits. Alcohol drinking and tobacco smoking show a synergistic interaction in the etiology of cancers of the oral cavity, pharynx, larynx and oesophagus [37]. Very heavy drinkers, for whom alcohol could be the source of up to 30% of the total calorie intake, tend to have a poor diet lacking fruits and vegetables, which may further enhance their risk of developing these cancers [9].

3.3. NUTRITION AND PHYSICAL ACTIVITY

The strength of the evidence for the association of specific dietary components and cancers at specific sites varies [40]. Current data suggest that breast cancer is associated with obesity and moderate alcohol intake. There is less convincing evidence for the association with high intake of fat, meat and dairy products, and low intake of fruits and vegetables. For colorectal cancer, overweight, obesity and high intake of alcohol and red meat appear to be important aetiological factors, while high intake of fruits and vegetables, folates and calcium may have a protective role [41, 42]. There is consistent evidence that overweight and obesity, combined with low physical activity, play a role in the development of several cancers, colorectal cancer, breast cancer and prostate cancer [29, 41, 43]. The theory suggests that the higher risk of cancer in low social classes nowadays, in both the developed and developing worlds, is related to the fact that the amount of variation from the diet to which people has been historically adapted is greater in that portion of the population which has less access to the world's goods and services [6]. This is particularly true regarding the intake of fresh vegetables and fruit, which are consumed in smaller quantities among the poor in most parts of the world.

Obesity is recognized as the 'new social epidemic'. Even as an excess of risk for obesity related cancers appeared first among the upper social classes, it is now a burden of the lower social classes as well. The social

gradient in obesity related cancers might be changing, as it was observed for colorectal cancer in the USA between the 1950s and 1960s. While excess food intake and physical inactivity are individual choices, social, economic and political factors play a crucial role [24].

3.4. SEXUAL BEHAVIOUR AND REPRODUCTIVE HEALTH

Cervical cancer is the most important cancer linked with sexual behaviour. In all regions, it is more frequent among women of low socioeconomic status, especially in the poorest regions where access to screening for cervical cancer is limited [29]. It is associated with multiple sexual partners and early age at first sexual intercourse [6].

Certain high risk strains of human papilloma virus (HPV) have been identified as the main causal agent of cervical cancer. Information on social class differences in sexual behaviour is available for a limited number of countries, mostly industrialized countries. Other co-factors such as high parity, tobacco smoking and use of oral contraceptives probably modify the risk in women infected with HPV. Poorly defined immunological factors are the major determinants of viral outcome [44]. Other sexually transmitted infections (STI) as Chlamydia trachomatis, chronic pelvic inflammatory disease, and nutritional factors might also play a role.

In a hospital based case control study conducted to devise a risk scoring system for the prediction of cervical cancer in Nagpur, India [45], five risk factors were identified to be significantly associated with cervical cancer: illiteracy, poor hygiene, long duration of marital life, multi-parity and early menarche.

The increase of cervical cancer is parallel to the increase in persistent HPV infection, other STI, smoking and differences in screening practices [46]. Prediction of the effect of changes in HPV incidence on cervical cancer incidence is complicated by the presence of other risk factors, the protective effect of screening and the population dynamics of HPV infections. New prevention strategies can be derived from the evolving knowledge of HPV carcinogenesis. Public awareness of HPV is generally very low, particularly of its relationship with abnormal smears and cervical cancer. Knowledge levels vary according to socio-demographic characteristics. The sexually transmissible nature of the infection is also of major concern and confusion for women [47].

Sexual behaviour has been correlated with prostate cancer in several studies [48, 49]. An increased risk of prostate cancer among men with a history of venereal disease has been described, supporting the hypothesis that an infectious factor related to sexual behaviour could be involved in the occurrence of prostate cancer.

Sanderson, et al. [50] found a significantly reduced risk for prostate cancer associated with having college or technical school education level and a borderline reduced risk for the higher categories of educational level (taking individual educational level as a socioeconomic status measure). In addition, there was a significant trend to decreased risk with increasing educational level.

Women's reproductive history plays an important role in the risk of breast, ovarian, and endometrial cancers [51]. There is overwhelming evidence that sex steroids (androgens, estrogens, progestagens) play an important role in the development of some women's tumours [9]. There are large socioeconomic differences in the risk of female reproductive cancers. As a general pattern, breast cancer, ovarian cancer and endometrial cancer are more common among women with higher socioeconomic status. A low level of fertility in developed countries has largely influenced these differences.

3.5. ENVIRONMENTAL POLLUTION

Environmental pollutants refer to a specific subset of cancer causing environmental agents; namely contaminants of air, water and soil generally characterized by a lack of individual control over their level of exposure [9]. The carcinogenic pollutants for which most information is available include asbestos, toxic agents in urban air (SO_2, NO_2), indoor air pollutants, chlorination and other drinking water contaminants, and radiations (including ionizing radiation). Heavy environmental pollution has been associated with an increased risk of cancers, in particular lung cancer. There is evidence [52] suggesting that individuals from lower social classes are exposed to higher levels of environmental pollutants than are individuals from higher social classes. This may be due to the placement of the new sources of pollution or of the toxic processes in disadvantaged areas, or to the selective migration of the poorer sectors of society to these areas. Exposure to ultraviolet (UV) radiation, principally from sunlight, is very much related to the workplace (farmers, fishermen, constructors), but this could

be modified strongly by personal behaviours such as the use of protective clothing and choice of recreation. Workers in outdoor occupations probably receive the highest cumulative skin exposure to UV radiation.

It has been estimated that occupational exposures are responsible for about 4% of all human cancers in industrialized countries [53]. These cancers are concentrated in the lower social classes, thus contributing to the social class related gradient in cancer incidence and mortality. However, there is no direct evidence on the extent of the contribution of occupational exposure to carcinogens due to social class difference. Several problems, such as the possible interaction between carcinogens and the effect of extra occupational confounding factors add further elements of uncertainty. For example, more than 70% of Chinese households rely on solid fuels (coal and biomass) for cooking and heating and more than 60% of Chinese men also smoke [29]. Smoking and coal smoke magnify one another's hazards for lung cancer.

3.6. INFECTIONS

Hepatitis B virus (HBV) and Hepatitis C virus (HCV) are major etiological factors in the occurrence of hepatocellular carcinoma (HCC) worldwide [54], especially in developing countries where the majority of liver cancer cases are found. In parallel with the geographic distribution of HCC a high level of HBV prevalence is concentrated in the developing world. The association of chronic infection by HBV and low social class is quite strong. Socioeconomic factors such as low educational level, lower social stratum, and crowded urban residence have been reported to predict higher HBV chronic carrier prevalence. Moreover, the effect of poverty on HBV prevalence is clearly evident among younger age groups, and earlier chronic HBV infection seems to increase the risk of developing HCC.

Although three genres of parasites (Schistosoma, Opisthorchis and Clonorchis) are known or suspected risk factors for cancer in humans [53], no adequate information is available on the determinants of these infections related to social class. Infection by *Helicobacter pylori* (*H. pylori*) is an important etiological factor for stomach cancer. Studies done in the UK and USA strongly suggest that social class factors, especially those occurring during childhood, are determinants for this infection, with odds of sero-prevalence of the order of 1.5–5 for lower social class as compared with higher social class. A nested case control study, from The European Prospective Investigation into Cancer and Nutrition, concluded (adjusted for *H. pylori* infection) that a higher socioeconomic position was associated with a reduced risk of gastric adenocarcinoma [55].

Summary of risk factors

From the 7 million cancer deaths in 2001 worldwide, 35% have been attributable to nine potentially modifiable risk factors [29]. Of these, 0.76 million deaths were in high income countries and 1.67 million in low or middle income nations. Among low and middle income regions, East Europe and Central Asia had the highest proportion of deaths (39%) from cancers attributable to the risk factors studied. Smoking, alcohol use and low fruit and vegetable intake were the leading risk factors for death from cancer worldwide, and in low and middle income countries. In high income countries, smoking, alcohol use, overweight and obesity were the most important risk factors for cancer. Sexual transmission of HPV is a leading risk factor for cervical cancer among women in low and middle income countries.

Figure 1 compares the contributions of the main risk factors to related cancer mortality by income level. Cancers with the most attributable deaths were cervical cancer, lung cancer, and oesophageal cancer. Attributable deaths in low and middle income countries are twice as much as in high income countries. These differences are more evident for oral, oesophageal, stomach, liver and cervical cancer.

A number of effective interventions can modify cancer incidence and mortality: HBV vaccination for liver cancer, various screening methods for cervical cancer, mammography screening for breast cancer, fecal occult blood test and surgical prevention (for those at high risk) for colorectal cancer and HPV vaccine for cervical cancer are examples. Increasing worldwide coverage by the above technologies could help reduce the burden of cancers, especially those involving prevention and early detection, particularly in developing countries. Paradoxically, the chance of having these technologies available is far from reality in the developing world. The relative efficacy of surgery, chemotherapy and radiotherapy varies from cancer to cancer and depends upon multiple technical and

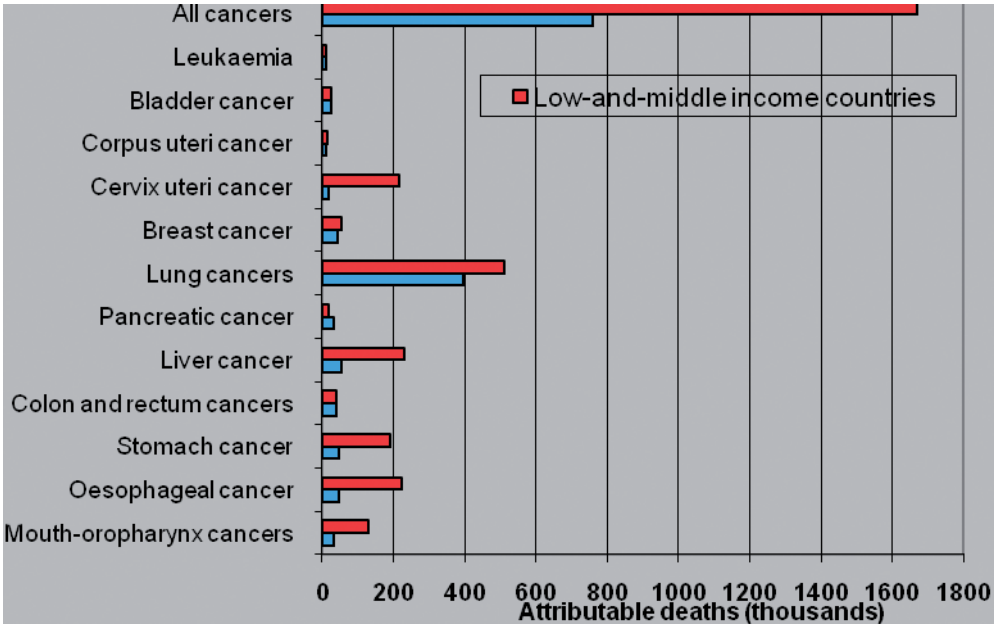

FIG. 1. Total attributable cancer deaths (thousands) by cancer site, and country (income level) to nine selected cancer risk factors. (Adapted from Goodar [29].)

biological factors such as stage. The common situation in low income countries is that patients are diagnosed at advanced stages [29].

4. CANCER SCREENING

The objective of a screening programme is early diagnosis that leads to a cost effective and measurable reduction in disease burden. If improved outcomes and cost effectiveness cannot be demonstrated, the rationale for screening is lost. It requires an efficient organization to ensure high coverage (>70%) of target populations and to monitor and evaluate outcomes. Hence, screening programmes require large human and financial resources.

Screening has been implemented mostly in developed countries, for cancer sites such as uterine cervix, breast, and large bowel, always after medical care for these diseases was fully covered. Screening for cervical and oral cancer has been introduced in a small number of developing countries, but they have been largely ineffective in reducing mortality by these diseases [56–58]. For screening programmes to have an impact on cancer mortality, adequate diagnostic, staging and treatment services must also be in place.

4.1. CERVICAL CANCER SCREENING

Screening for cervical cancer is the most widespread screening for cancer worldwide. Cytology based screening programmes involving sexually active women, screening women annually, or once every 2–5 years, have led to a large decline in cervical cancer incidence and mortality in developed countries over the last 40–50 years. In contrast, cervical cancer remains largely uncontrolled in high risk developing countries because of ineffective or non-existing screening programmes. Developing countries having data on cancer incidence and/or mortality have registered either a stable or slowly declining trend in cervical cancer incidence, most likely due to socio-demographic changes rather than due to early detection/prevention efforts [59].

New developments in liquid based cytology, automated reading, and testing for HPV are being implemented to try to improve on the limitations of routine cytology. Nevertheless cervical cancer is still an important public health problem among adult women in developing countries in South and Central America, Sub-Saharan Africa, and South and South-East Asia, where it is the most or second most common cancer among women. Some regions in sub-Saharan Africa have registered increasing incidence in recent years. Despite the declining trends in incidence observed in some other regions, the total burden of cervical cancer is rising in high risk developing countries [56, 60, 61].

4.1.1. South and Central America

Cytology based screening programmes for cervical cancer have been introduced in some developing countries, particularly in South and Central America, over the last 30 years, but generally they had very limited success [56]. Since the 1970s, there have been efforts to organize cervical cytology screening programmes nationally or regionally in selected Latin American countries [56, 62]. Some examples are cited below:

***Chile*:** A cytology screening programme was implemented in the early 1970s. Cervical cancer mortality rates have subsequently started to decline. Nevertheless, within the country, the poorer regions have the highest mortality rates, and the risk of dying of cervical cancer is four times higher among the less educated women compared to educated women [63].

***Colombia*:** The Colombian National League against Cancer and other private organizations have been offering cytology screening since the 1970s. In 1990, a five year nationwide cervical cancer control programme was initiated to provide cytology smears to more than 60% of women aged 25–69 years over a three year period and to provide follow-up to over 90% of the women screened; five years later, cervical cancer mortality data suggested that the situation has remained unchanged.

***Costa Rica*:** A nationwide cytology service was available since 1970 to women aged 15 years and above. Information/education campaigns have been used to encourage sexually active women to have annual cytology smears. During all pelvic examinations a Pap smear should be obtained. Around 250 000 smears have been performed and reported annually. Coverage has varied considerably according to region, with coverage of rural areas being inadequate in each given round of screening. Cervical cancer incidence has been virtually unchanged from 1983 to 1991, though a significant decline has been observed recently. However, cervical cancer mortality rates have remained unchanged over the last 25 years [64].

***Cuba*:** A cervical cytology screening programme, offering smears every two years to women aged 20 years and above, was implemented through the primary health care services in 1968. The programme was modified in 1997, screening women between 25–59 years over a three year period. More than 80% of Cuban women aged 20–60 years have been screened at least once [57]. Despite the fact that cervical cancer is the fourth cause of cancer mortality among women in Cuba, no reduction in cervical cancer incidence and mortality has been observed since the introduction of the programme.

***Mexico*:** A national cervical cancer screening programme was initiated in 1974 and now operates in the Federal District and all the 31 states of the country. Cytology smears are offered annually to women aged 25–65 years. The programme is integrated within the existing health care services. However, the infrastructure and resources were sufficient to carry out only 3.5 million smears annually from a target population of 16.5 million women (data for 1996); annual screening was nevertheless the 'norm' for the programme. There is a wide variation in the coverage of women on a national level. Studies indicate that less than 30% of women in rural areas have been screened so far. There is no systematic effort to coordinate the programme through a central organization for call, recall, and follow-up of screened women. There has been no decline in mortality from cervical cancer in Mexico since the initiation of the screening programme [65, 66].

Puerto Rico: An early detection programme for cervical cancer was established in Puerto Rico in the 1960s. This covered the metropolitan areas until 1962, and was later expanded to all health regions of the island. Cytology

smears are offered to women aged 15 years and above. Mortality from cervical cancer has declined steadily over the last three decades. The average, annual age standardized incidence also dropped from 38 per 100 000 women during 1950–1954 to 19.9 per 100 000 women in 1990. Between 1950 and 1990 mortality rates dropped from 19.1 to 5.2/100 000 women in the same period.

No organized cervical cancer screening programmes are reported from Brazil and Peru. Sporadic screening with opportunistic cytology smears has been carried out. A high incidence of the disease, however (incidence >40 per 100 000 women) is reported from north-eastern Brazil and Peru. Low level sporadic screening with opportunistic cytology smears is carried out as well in other regions of Latin America.

4.1.2. Africa

There are no organized or opportunistic screening programmes for cervical cancer in any of the high risk Sub-Saharan African countries [56]. The South African Institute of Medical Research organized the infrastructure for mass screening of the female population of Soweto (Project Screen Soweto) so that 90 000 cytology smears could be tested annually. However, the lack of a planned population education and motivation programme resulted in poor participation of the target population. Currently, cytology smears are provided on demand in gynaecology and family planning clinics in South Africa. Cross-sectional/randomized screening intervention studies are currently ongoing in several African countries — Burkina Faso, Democratic Republic of the Congo (Brazzaville), Ghana, Guinea (Conakry), Kenya, Mali, Niger, and Nigeria — to address the accuracy of various screening approaches such as cytology, HPV testing, VIA, and visual inspection with lugol's iodine (VILI) as well as the detection rates [56].

4.1.3. Asia

India accounts for one fifth of the world burden of cervical cancer [4]. There are no organized or high level opportunistic screening programmes for cervical cancer in any of the provincial states. Two sub-districts of western India attempt to evaluate the role of improved awareness in the early detection and control of cervical cancer [67]. In Singapore, opportunistic screening for cervical cancer has been operating for the past few years, but has had only a minimal impact on the overall incidence and mortality from the disease [56]. A cytology based demonstration programme on screening is currently being implemented by the Ministry of Health of the Nakornpanam Province in north-east Thailand.

4.1.4. Breast cancer screening

Screening for breast cancer has been relatively successful in developed countries. Breast cancer screening, especially using mammography, has been recommended for several decades. It is now recognized that screening women aged 50–69 years by mammography every two years is the sole well established means of reducing mortality due to breast cancer [42]. There is also limited evidence for the efficacy of mammography screening in women aged 40–49 years (without familial risk) in reducing mortality from breast cancer. On the other hand, the efficacy of screening older women (69–74 years) is supported by the results of a trial in Sweden, where a 32% reduction in mortality for this group was observed [68]. Screening up to the age of 74 has been proposed in some countries, particularly when life expectancy is greater than 80 years. The cost of breast cancer screening varies widely, depending on the health system, economic and demographic characteristics and screening modalities considered. Its cost may be prohibitive enough to prevent the implementation of organized mass mammography based screening programmes in most developing countries [69, 70].

4.1.5. Oral cancer screening

Although cancer of the oral cavity is largely related to lifestyle and can be easily detected and diagnosed during its early stages through visual inspection of the oral mucosa, actual figures concerning its prevention and early detection are dismal. Early diagnosis of oral carcinoma greatly increases the probability of cure. Primary prevention, which involves reducing the exposure to tobacco, alcohol and betel quid has been shown to be effective

in reducing the incidence of oral cancer. Secondary prevention involves screening for the early detection of oral cancer. Oral cancer screening can take many forms. Clinical examination and biopsy allow the early detection of pre-malignant lesions and early oral cancers [71].

Oral cancer screening is implemented less worldwide. Although the efficacy of screening for oral cancer in increasing survival and reducing mortality remains unproven [72], it is believed that oral cancer screening programmes could result in a higher proportion of cancers being localized at diagnosis, and a comparatively higher survival rate could be provided to those patients [58].

Most oral cancers are detected at a later stage, requiring complex, costly and often ineffective therapies. Public awareness programmes that stress the importance of at least one annual dental examination, identification of warning signs of oral cancer and recognition of the hazards of tobacco and alcohol use, are necessary to reverse the high morbidity and mortality rates associated with this disease.

5. WOMEN'S CANCER

Today, women's life expectancy worldwide is over 70 years old. Women's lifestyle in Western societies has changed — the women now being more physically, intellectually and sexually active. The influence of social, cultural and environmental factors on women's health is also different than in the past. Consequently, the profile of most frequent diseases with the highest mortality rates among women has changed also.

Cancer affects women in various population subgroups in different ways. Understanding cancer related health disparities in women is an important step toward improving health and the quality of life for millions of minority women.

Women of low socioeconomic status and minority women are at particular risk of not adhering to recommended cancer screening guidelines. Such behaviour may contribute to disparities when cancers are discovered at later stages, contributing to higher mortality rates among these women. The global cancer burden in women shows increasing trends [17].The absolute numbers of new cases jumped from 3 100 000 women in 1980 to 5 060 657 in 2002 (Table 2). As described before, the most frequent site in women was breast cancer with 1 151 298

TABLE 3. ESTIMATED ANNUAL CANCER INCIDENCE BURDEN WORLDWIDE IN WOMEN IN 1980, 1990 AND 2002

Site			
	1980	1990	2002
Mouth and pharynx	121 200	105 400	146 697
Oesophagus	108 200	103 200	146 723
Stomach	260 600	287 200	330 518
Colorectal	285 900	381 000	472 687
Liver	79 500	121 100	184 043
Lung	146 900	265 100	386 891
Breast	572 100	795 600	1 151 298
Cervix	465 600	371 200	493 243
Lymphoma	98 000	116 300	149 559
Leukaemia	81 300	100 900	129 485
All sites	3 100 000	3 789 800	5 060 657

Source: Created with data from Parkin et al. [17].

new cases. Nevertheless, an important relative change in lung (163.4%), liver (131.5%) and breast (101.2%) was observed between 1980 and 2002.

There is a significant difference between developed and developing countries in cancer patterns and women are not an exception. In more developed nations, women are now living an average of six to eight years longer than their male counterparts and have an average life expectancy at birth of about 80 years. Since individual behaviour has a profound impact on health and wellbeing, lifestyle modification has received much attention. Women in more developed nations have more access to a plentiful diet, and their physical activity in daily life has declined. Unhealthy lifestyles have increased, such that up to 25% of women are obese. As women have gained status in society, risk factors previously associated with men, such as tobacco and alcohol abuse, are becoming less sex specific [73].

Existing barriers to screening tests are factors in preventing women from accessing available screening tests for breast and cervical cancer. Once barriers are identified, interventions can be developed to reduce certain health disparities [74]. Even in those countries with broad health care coverage and organized screening programmes, women from low income groups or low levels of education continue to have poorer health outcomes. In the USA, African American women have a life expectancy five years shorter than white women. In European countries, markers of morbidity (e.g. self-reported general health, chronic conditions, and long term disability) are consistently less favourable among women with lower incomes and educational levels. Women with low incomes and from ethnic minorities are more likely to have infants with low birth weight, cervical cancer, and HIV disease. These factors are usually associated with developing countries [73].

Further progress in reducing the cancer toll (loss of life, suffering, and health care costs) will depend on reducing health disparities by applying the best available strategies for prevention, early detection, treatment and palliative care more effectively. Advancements in screening, diagnosis and treatment in more developed areas are the most effective factors in reducing incidence and mortality as well as prolonging survival, at least for some specific cancers. These effects were not detected in less developed areas because of the limited access to primary and specialized care [75]. Reasonable plans of action to control cancer must recognize the diversity of needs and carefully evaluate the balance between feasibility and expected benefit.

Glanz et al. [76] surveyed cancer information on nine populations of minority women in the USA: Mexican American, Puerto Rican, Cuban American, African American, Asian American, Native Hawaiian, American Samoan, Native American, and Alaska Natives. Approximately 35 million women belonging to these racial/ethnic groups live in the USA, and their number is increasing. From 1992 to 1998, white women experienced a slight increase in breast and lung cancer incidence and a decrease for other cancer sites. African American women had an increased incidence of breast cancer, and Asian American women had a modest increase in all major cancers combined. Gaps in early detection have been narrowed, but minority women still lag behind white women. Smoking and obesity remain common in these populations.

5.1. BREAST AND CERVICAL CANCER

5.1.1. Breast cancer

Although breast cancer incidence, mortality and survival rates vary four fold in different regions, breast cancer incidence is increasing in the world as a whole. In those regions without early detection programmes, mortality is also growing [77]. In developing regions, breast cancer risk has historically been relatively low in relation to industrialized countries. The most rapid rises in breast cancer are seen in developing countries, towards a distribution closer in profile to that observed for women living in industrialized countries. Increasing trends in developing areas are often considered the result of the ‘westernization’ of lifestyles, an ill defined surrogate for changes in factors such as childbearing, dietary habits and exposure to exogenous estrogens.

The dynamics in breast cancer incidence and mortality over time seem to be complex. The association between socioeconomic status and breast cancer risk is well established. Women in higher socioeconomic groups are at higher risk. When social class is measured by income or education levels, the variations in risk largely correlate with the differential distribution of known risk factors [78]. Broadly speaking, the largest increase in risk has been seen in populations of women historically at low risk, often within developing countries. Relatively recent departures from the long term trend have been observed in several, mainly western, countries.

According to the latest estimation [17], breast cancer is the most frequent cancer in women (23% of all cancers), with more than a million of new cases diagnosed every year. It is also the most common female cancer in both developing and developed countries, and 55% is occurring in the latter. Age standardized rate (ASR) is three times higher in developed than in developing areas. In general, the incidence is high (more than 80 per 100 000) in developed regions of the world and low (less than 30 per 100 000) in developing regions.

Higher socioeconomic position has been reported to be associated with an increased risk of breast cancer mortality. Longitudinal data on breast cancer mortality according to educational level and marital status obtained from Austria, Belgium, Denmark, England, Wales, Finland, France, Norway, Switzerland, Turin, Barcelona and Madrid showed a positive association in all populations, except for Finland, France and Barcelona. Overall, women with a higher educational level had an approximately 15% greater risk of dying from breast cancer than those with lower education. This was observed among both married and unmarried women. A higher risk of breast cancer mortality among women with a higher level of education was a persistent and generalized phenomenon in Europe in the 1990s [79].

Breast cancer mortality rates have been steadily growing for nearly a century in many countries. As a result, breast cancer ranks as the fifth largest cause of death from cancer overall, and it is still the leading cause of cancer mortality in women worldwide (411 000 annual deaths 14% of female cancer deaths). Nevertheless, during the past decade signs of a sustainable decrease in breast cancer mortality rates were seen in a number of 'western-lifestyle' countries as result of the progress achieved in breast cancer control interventions. In these countries, survival of breast cancer patients is considerably better. Although several factors are contributing to this outcome, it is mainly due to breast cancer awareness, early detection and more appropriate breast cancer therapy. The declines seen in breast cancer mortality are a considerable success, but there is no room for complacency until research can impact positively on reducing incidence [80].

Health literacy and level of decision makers' involvement, both embedded in social and economic realities, are key components in breast cancer treatment policy and may contribute to breast cancer disparities found in the USA [81]. Those treatments shown to be related to best outcomes are less likely to be chosen by certain groups of women. Results indicate that women with low income in metropolitan areas with over 1.5 million population are less likely to have a mammogram than more affluent women in the same areas [82]. The effects of economic and cultural factors on breast cancer treatment choice must be understood if health care professionals are to intervene effectively to address disparities and improve breast cancer outcomes for all women.

5.1.2. Cervical cancer

Although there are effective screening methods for cervical cancer, it continues to be a public health problem in developing countries. Cancer of the cervix is the seventh greatest in frequency overall, but the second most common cancer among women worldwide. There were 493 000 new cases and 274 000 deaths in the year 2002 [17]. In general terms, it is much more common in developing countries, where cervical cancer represents 15% of all female cancers and the risk of developing the disease before the age of 65 is 1.5%. In developed countries, cervical cancer accounts for only 3.6% of all new female cancers, with a cumulative risk (0 to 64) of 0.8%.

The adoption of cervical cytology screening has resulted in a rapid decrease in cervical cancer mortality rates in more developed countries, where incidence rates are now generally low. Before the introduction of screening programmes in the 1960s and 1970s, cervical cancer incidence in most of Europe, North America, and Australia/New Zealand was similar to that observed in developing countries today. For example, incidence was 38.0 per 100 000 in the Second National Cancer Survey of the USA. Very low rates are also observed in China (6.8 per 100 000) and Western Asia (5.8 per 100 000). The lowest recorded rate is 0.4 per 100 000 in the north-west of the Islamic Republic of Iran.

The substantial decline in cervical cancer incidence and mortality, most clearly observed in Western countries is due to well developed screening programmes and effective treatment coverage. Declines are also evident in some developing countries. This is particularly striking in China, where the estimated age standardized incidence rate was 6.8 in 2002, compared with 17.8 in 1985. Although some of the differences reflect changing data sources, cancer registry results also indicate a fairly dramatic decline of rates in recent years. As a result of these trends, cervical cancer has ceded its place as the leading cancer in developing countries to breast cancer; only in sub-Saharan Africa, Central America, south-central Asia, and Melanesia is it still the most frequent cancer affecting women.

6. CHILDHOOD CANCER

Total incidence of childhood cancer varies rather little among different regions of the world, with a cumulative risk to the age of 15 in the range 1.0–2.5 per thousand [83, 84]. Mainly, the differences are due to diverse environments, lifestyles, dietary habits, and hygienic conditions.

The publication of the international incidence of childhood cancer, by the International Agency for Research on Cancer (IARC), shows that childhood cancer incidence is roughly similar in Australia, Canada, Japan, the USA and Western Europe. Major differences in incidence were observed in acute lymphoblastic leukaemia (ALL) and brain tumours [83]. The incidence of ALL in developing countries seems to be lower than in the west, and the incidence peak at age 2–3 years seen in western countries is not present in the developing world.

Due to international efforts, the childhood mortality rate under 5 years has fallen significantly in the last decade, and the trend is still downwards. The main reason is the prevention of deaths from infections. Cancer is the second major cause of deaths in the developed world after accidents. Although it is at the moment not so significant in low and middle income countries, there is a very high probability that it will be one of the major issues in the near future. For example, in Egypt cancers occurring under the age of 20 years constitutes 6% of all cancer cases, as opposed to only 1% in the USA. The situation is similar in other low and middle income countries. The death rate from infections is decreasing and the incidence of cancers in the young population is increasing faster than ever.

The Automated Childhood Cancer Information System (ACCIS) study shows significant survival improvement for all tumour groups in the three decades studied in both the east and the west. However, survival rates were better in the west for all three cohorts [85]. In general, the encouraging result obtained in childhood cancer treatment constitutes one of the most important successes for the oncology community. Most of the children and young adults under the age of 20 diagnosed with cancer prior to 1970 had little hope of being cured. Since then, cure rates, as measured in five year survival, have increased up to 78% [86]. Therefore, major attention is being placed at present on reducing the side effects and late toxicities of therapy [87–89].

More than 85% of paediatric cancer cases occur in developing countries. This rate will exceed 90% in the next two decades due to an increase in the young population in favour of developing countries [90]. Largely, children with cancer living in developing countries cannot fully profit from those advances in paediatric oncology.

Following the recommendations of the International Society of Paediatric Oncology (SIOP) to concentrate resources in specialized paediatric cancer units, there is an emphasis on assistance and twinning of units in developing countries with established units in more affluent countries. These centres also provide cancer registry expertise and are contributing to the knowledge of cancer incidence and epidemiology. The challenge is to ensure equality of access to cancer care for all children.

All these cooperative efforts to improve cancer survival in childhood are very significant, but they are not a solution for developing countries. An important issue is the availability and the price of anti-neoplastic drugs. The geographical access to cancer treatment is another problem. Generally, patients living in rural areas have to stay away from home for extended periods and their relatives have to abandon their daily activities and income generation. In low and middle income countries as a rule, the people are too poor to pay even a minimal amount for treatment, even if drugs were distributed at a reasonable price. Nutritional status in children with cancer has an impact on treatment outcomes, the course of the disease and survival. Decreased tolerance to chemotherapy has been described associated with altered metabolism of anti-neoplastic drugs, increased infection rates, and poor clinical outcome in malnourished children [91]. Often, treatment protocols (including drugs and radiotherapy) have to be adapted to local circumstances; therefore high cure rates seen in western countries will not be achieved in developing countries. Limited tertiary care from medical institutions and limited human resources make up the common reality in developing countries [92].

The survival gap between rich and poor countries is widening. The reason is mainly the success of paediatric cancer therapy in developed countries, but low and middle income countries are not benefitting from this improvement. Another reason for the survival gap is abandonment of treatment and toxicity. Even if the child has access to cancer therapy, the abandonment rate is high and there are limited supportive care services to prevent treatment related morbidity or mortality.

There is a survival advantage for patients treated in the framework of cooperative group research protocols. Yet even in the western world, many adolescents with cancer are not treated at member institutions of the paediatric or adult cooperative groups; they are excluded from the benefits of such treatment protocols and the best supportive care [93]. Despite the 80% survival rates in the west, a large number of children with cancer in developing countries will die due to lack of appropriate medical care.

7. CANCER SURVIVAL

Cancer prevention and early detection are the most effective ways to reduce cancer mortality. Nevertheless, in the short term, cancer treatment and therefore cancer survival has an important role in reducing cancer mortality. Cancer survival depends on the widespread application of effective diagnosis and treatment modalities, while the availability of these depends on macro-economic determinants, including public health investment [86, 94, 95]. Several studies have found a correlation between survival of cancer patients and macro-economic variables measuring the wealth of countries, the level of investment in health and social inequalities [6, 96–99].

Long term cancer survival rates are less than 20% in developing countries, 20–30% worldwide, and approximately 50–60% in high income countries. Although a combination of screening and opportune treatment may be significantly effective in reducing cancer mortality, limitations in the availability of health services, and accessibility to existing technologies, including public education and cultural/ethnic considerations, clearly constrain the effects of treatment on population trends in cancer mortality, even in developed countries.

According to the EUROCARE studies [100–102], survival varies greatly across Europe for common and rare malignancies. These variations can be explained by a number of factors, including differences in screening programmes, the quality of cancer treatment facilities, availability of evidence based guidelines, radiotherapy facilities, and access to new anticancer drugs, as well as clinical factors as tumour stage and biology. Survival represents the end result of the complex interplay of all these factors, whose individual contribution to survival cannot be easily distinguished [103].

When comparing cancer disparities by race/ethnicity and socioeconomic status in the USA for all cancer sites combined, the residents of poorer counties (those with greater than or equal to 20% of the population below the poverty line) have 13% higher cancer death rates in men and 3% higher rates in women compared with more affluent counties (less than 10% below the poverty line). Differences in cancer survival account for a part of this disparity. Among both men and women, five year survival for all cancers combined is 10 percentage points lower among persons who live in poorer than in more affluent census tracts [104].

Lung cancer remains a highly lethal disease. Survival at five years reported by the SEER programme in the USA is 15%, the best recorded at the population level. The average survival in Europe is 10%, not much better than the 8.9% observed in developing countries [105].

The situation is quite different for colorectal cancer, where early diagnosis and adequate treatment could have a positive impact on the prognosis. Survival estimates (in men) at five years are 65% in North America, 54% in Western Europe, 34% in Eastern Europe, and 30% in India.

A similar situation is observed in prostate cancer. Much of the difference is a consequence of latent or early cancer being detected by ‘screening’ procedures. In fact, the relative survival in the USA in 1995–2000 is reported to be 99%**.** As a result, mortality rates are probably a better guide to the risk of invasive prostate cancer in different populations. Mortality rates are high in the Caribbean, Southern and Central Africa, North and West Europe, Australia, New Zealand, and North and South America, and low in Asian and North African populations. Variations in mortality rates between China and the USA are 16-fold (almost 80-fold for incidence).

8. ACCESS TO CANCER THERAPY

Differences in morbidity by age, sex, occupation, geographic and social groups are more or less associated with lifestyle and carcinogenic exposures, which may occur due to a wide range of political, economic and social factors. Within this framework, differences in cancer mortality and survival are also often related to coverage, accessibility, available sanitary structures, prevention policies and timely medical care.

Cancer care requires that the patient have access to a multidisciplinary team of care providers across the full continuum and coordination of services. Optimal treatment can improve cancer survival significantly. Unfortunately, diagnosis of cancer in developing countries is too frequently made in advanced stages [106].

National Cancer Control Programmes (NCCP) are comprehensive public health approaches designed to reduce the incidence and mortality of cancer and to improve the quality of life in cancer patients through the systematic and equitable implementation of evidence based strategies for prevention, early detection, treatment, and palliation and by the optimal use of available resources [107].

Historically, cancer incidence has a larger burden (2:1 age standardized incidence rate) in developed countries than in developing countries [4]. This is essentially due to a progressive decrease of infectious diseases and a simultaneous increase in age of the population. In the next decades, this increase has been estimated to be proportionally greater in developing than in industrialized countries. However, the mortality/incidence ratio is still 17% higher in developing countries, probably associated with a lack of accessibility and timely treatment.

8.1. CANCER CARE

Advances in scientific knowledge during the last decades have marked significant progress in almost all fields of clinical medicine. Developments in the field of molecular biology and translational medicine continue to generate opportunities to transfer 'from the bench to bedside' the latest results of scientific investigation. In parallel, novel technologies for diagnosis and treatment have increased the cost of health care.

Not only is oncology one of the medical fields which benefited most from these advances, but also one of the fields in which increased care costs have generated great concern among physicians, patients, family, health decision makers, insurance companies, politicians and society as a whole.

In the USA, the continued introduction of high cost novel cancer therapies and diagnostics (plus those in other areas of medicine), reflecting scientific progress and reward for innovation, is likely to exert increasing financial pressure on patients, oncologists, businesses, and society. The total cost of cancer care estimated by the National Institutes of Health, USA in 2005 was $209.9 billion. Direct medical costs, including inpatient and outpatient care, drugs, and devices, accounted for $74 billion. Of this total, $17.5 billion was attributed to indirect morbidity costs (i.e. lost productivity), and indirect mortality costs (i.e. lost productivity due to premature death) accounted for $118.4 billion [108].

In Europe, the vast majority of the costs of cancer therapy fall on third parties, normally governments, or health funds. Therefore, the main focus of cost effectiveness studies is to assist payers in deciding whether new therapies are worthwhile, despite their high cost. Drug budgets are regulated in most European countries. The main form of central control is price setting, with some form of reference pricing being the most common approach. This sets the price of drugs, either to an international standard or to a common price for drugs in the same group or cluster. At the hospital level, the main control over cancer drugs is the hospital's own drug list. Studies have shown a wide variation in access to cancer drugs among European countries. Explanations for these variations include differences in research funding, a drug's approval process, the role of health economics in decision making, and budgetary issues [109].

Several studies have documented that individuals from lower socioeconomic groups and specific racial and ethnic minorities have greater cancer risk and worse cancer related outcomes [104, 110–113]. Besides, the access to high quality health care services is often compromised among minority, rural, and other underserved populations. It can be deduced that increasing cost of cancer care tends to worsen disparities in care. It might also be related to the existence or not of universal access to free care as well as national control programmes which, although rare, do exist in developing countries, (e.g. Brazil, Chile, Sri Lanka, and Cuba).

The differences in cancer treatment facilities are also marked between industrialized and developing countries. The book Cancer in Developing Countries — The Great Challenge for Oncology in the 21st Century [7] presents ample arguments concerning these differences. There are enormous limitations on both quantity and quality of cancer care in the developing world. The use of these limited resources is not well balanced. According to Ref. [7], developing countries command only 5–10% of the global resources for cancer treatment but have to cope with more than 50% of the world's patients.

Only through well designed, managed and funded National Cancer Control Programmes (NCCP) with universal reach and accessibility will the concerted efforts have an impact on cancer control. The establishment of a NCCP should include guidelines or recommendations for the management of the most common cancer sites in any given country. These recommendations could help avoid non-evidence based treatment strategies and allow available resources to be used more rationally, with the consequent medical and social benefits.

Chemotherapy is one of the most important components of modern cancer care. Since the introduction of anti-neoplastic drugs around the middle of the last century, the use of cancer chemotherapy has being increasing. There are various types of tumours in which it is possible to achieve cures even in advanced stages (e.g. leukaemia, lymphomas, germinal cell tumours and paediatric tumours). There is another group in which anti-neoplasic adjuvant treatment significantly increases the overall survival rates or disease free survival rates obtained with surgery. This is the case for breast cancer and colon cancer. Moreover, the use of chemotherapy can increase survival in many advanced tumours such as lung, bladder, colon, and breast.

Incorporation of new drugs to clinical practice has always been associated with an increase of costs. With the introduction of targeted therapy using drugs like rituximab, trastuzumab, erlotinib, bevacizumab and other similar ones, the cost of cancer therapy has increased.

An important tool to assist in the formulation of a drugs policy for cancer was developed in 1985 when the WHO's Expert Committee on the use of Essential Drugs completed a list of the essential drugs in cancer therapy [114]. The latest version of this list was presented, revised and updated in 1999 by a group of medical oncologists from five continents [115]. This document clearly shows that curable cancers and those cancers where the cost-benefit ratio favours drug treatment can be managed appropriately with regimens based on only 17 drugs. These drugs are available as generic preparations at relatively low cost.

However, the availability of anti-neoplastic chemotherapy alone is only one side of the coin. An important issue in the treatment of patients with cytotoxic drugs is the need for adequate hospital, diagnostic and clinical laboratory facilities, as well as qualified human resources and patient compliance, strongly influenced by education and socioeconomic factors.

Increasing awareness of the financial component of cancer care prompts patients to begin to consider the treatments they receive more carefully, balancing the potential benefits with both medical risks and financial costs.

TABLE 4. THE WHO ESSENTIAL DRUG LIST: 17 ANTINEOPLASTIC DRUGS, AND 4 ADDITIONAL SUPPORTIVE MEDICATIONS [115]

Bleomycin	Vincristin
Chlorambucil	Vinblastine
Cisplatin	Cytarabine
Cyclofosfamide	Dactinomycin
Doxorubicin	Daunorubicin
Etoposide	6-Mercaptopurine
5-Fluoruracil	2 antiemetics
Methtrexate	Dexamethasone
Prednisolone	1 dopamine receptor antagonist
Procarbazine	1 5-HT3 receptor antagonist
Tamoxifen	

Most patients continue to place a higher value on the medical aspects of treatment than on the financial side, and only a small minority will elect not to receive anti-cancer treatment that they deem to be effective because of its cost. However, the relative infrequency of this choice does not diminish its significance. Some patients, with or without endorsement and acknowledgment from their loved ones, refuse to accept treatment that will saddle their families with unmanageable debt. Other patients will ration their medications to make them last longer, compromising their health for the sake of finances [116].

An example of well established use of economic evaluation in health care decision making is the Technology Appraisal Programme of National Institute for Clinical Excellence (NICE) in the United Kingdom. *http://www.nice.org.uk/*). Under the process laid down by NICE, a scope is developed for each technology appraisal. The scope determines the patient population(s) to be studied and the relevant comparators to the technology of interest. The manufacturer, or sponsor of the technology then makes a submission in accordance with NICE guidelines, addressing the evidence on the clinical and cost effectiveness of the new technology [109].

8.2. ACCESS TO RADIATION THERAPY

Around 85% of the world's population lives in developing countries, but is served by only approximately 30% of the world's radiotherapy facilities. Conversely, the developed countries, with 15% of the world's population, have 70% of these facilities. Approximately 30 countries (15 countries in Africa as well as several in Asia) do not have even one radiation therapy machine [121].

Radiotherapy saves lives by curing certain cancers and extending or improving the quality of a patient's life for other cancers. It is estimated that over 50% of patients who are diagnosed with cancer in the world would benefit from radiotherapy, either on its own or combined with surgery or chemotherapy [117]. In high income countries, 52% of new cases of cancer should receive radiotherapy at least once and up to 25% might receive a second course [118]. Because the relative distribution of cancer sites varies from region to region, the proportion of patients with radiotherapy indication could vary between 47% and 61% [119].

The analysis of inequalities related to radiotherapy resources is a complex issue, considering that the indicators for referring the necessities can move simply from the availability of megavoltage units (medical accelerators and ^{60}Co machines) to a more detailed study considering facilities, equipment and human resources required in a standard radiotherapy service, such as simulators, brachytherapy, treatment planning systems, immobilization devices, radiation oncologists, medical physicists, biomedical engineers and radiotherapy technologists. External beam radiotherapy can be accurately and safely delivered with ^{60}Co machines and simple medical accelerators for most cancer sites.

However, availability alone does not determine access to radiotherapy. Geographical or spatial accessibility and affordability by patients and their families to cover the direct and indirect cost of the treatments are also barriers to radiation therapy access. Another component of access is awareness — not only the patients must be aware of the existence of treatment and its benefits, but their treating physicians must be aware of the availability and indications for radiotherapy [120].

Previous publications [122–124], have discussed the radiotherapy resources and shortfall of equipment in developing countries and regions, including an analysis of inequalities in countries in Asia, Africa and Latin America. A large difference in equipment and personnel among countries was demonstrated, showing that inequalities are present even within regions, for instance, the number of megavoltage units per million inhabitants ranges by a factor of 82 in Asian countries. Inequalities in provision of human resources (radiation oncologists, medical physicists, radiotherapy technologists) are also discussed in the mentioned papers.

For the scope and extent of this report, inequalities are approached in relation to the availability of megavoltage and brachytherapy units only, as those are the most representative tools for treatment in radiotherapy facilities.

According to WHO [125], "radiotherapy is fundamental to the optimum management of cancer patients, and provision of radiotherapy services is central to national cancer control strategies. Although it requires long term planning and appropriate assessment of health care resources, without recourse to sophisticated technologies, effective radiotherapy for many cancers can be comprehensively provided at moderate cost." Nevertheless, it is radiotherapy, as compared with chemotherapy and surgery, which is the most equality sensitive cancer therapy and the most affected by economic factors.

According to the IAEA's database registry of centres that offer radiation therapy worldwide (DIRAC, Directory of Radiotherapy Centres) [126], as of November 2008 there were about 2400 radiotherapy centres with fewer than 4000 megavoltage machines for cancer therapy in the developing world (low income and middle income countries). This provides treatment capacity for about 1.25 million patients per year (assuming 500 patients per megavoltage unit per year), but radiation therapy would be medically appropriate for around 3 million of the almost 5 million cancer patients in developing countries who will develop cancer this year (assuming that 60% of all patients will require radiotherapy at some stage of the their treatment).

8.2.1. Megavoltage radiation units according to population

The distribution of megavoltage machines among the geographical regions of the world is shown in Fig. 2. Inequalities in the distribution are even more pronounced if we regroup the countries considering their geographical location as shown in Fig. 3.

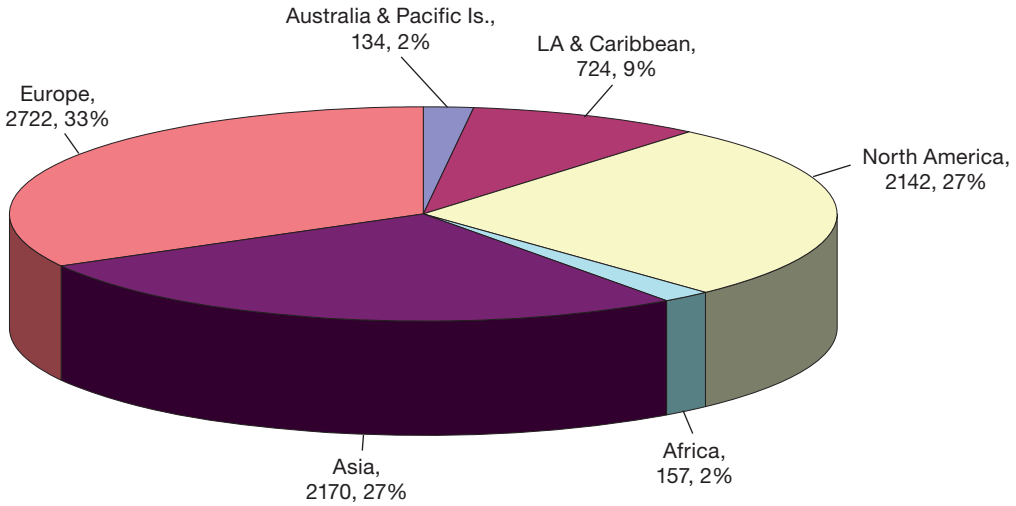

FIG. 2. Distribution of megavoltage units (linacs and ^{60}Co machines together) per region of the World. (Source: IAEA, DIRAC directory, 2006 [126]).

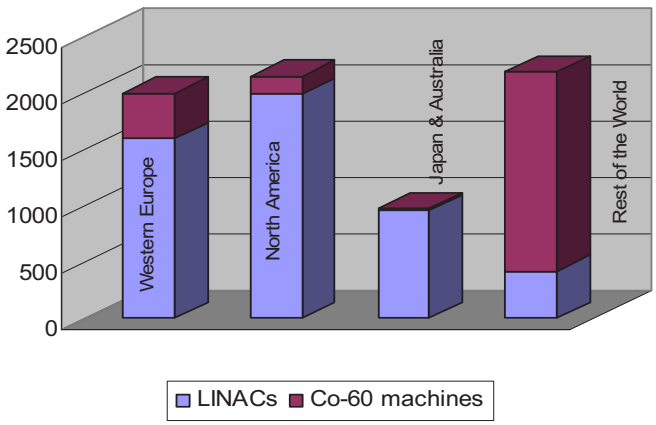

FIG.3. Distribution of megavoltage units (linacs and ^{60}Co machines) considering their industrial development. (Source: Created with data from IAEA, DIRAC, 2006 [126]; Hitoshi, 2005[127]).

A more realistic view of inequalities in radiotherapy equipment availability is expressed when considering the number of megavoltage units per million inhabitants. Figure 4 shows that the average number of machines in developing countries is 0.5 per million inhabitants, compared with more than six units per million inhabitants in North America.

Regulations exist in most industrialized countries about the provision of megavoltage radiotherapy equipment. A study carried out by The Royal College of Radiologists, UK [128] concluded that 28% of radiotherapy patients were outside the target limits for the maximum waiting times to commence radiotherapy treatment, concluding that clinical outcomes were compromised, demonstrating a direct relationship between the provision of megavoltage radiotherapy equipment and waiting times. This report recommended that "by 2006 there will be a requirement for five accelerators per million population" in the UK; according to DIRAC data, this amount is currently around 3.5 for the UK.

But if in some regions/countries there is concern about the recommended limits for maximum waiting times to commence radiotherapy, in others the alarm is that most of the population has no access to radiotherapy services at all. While in some countries with strong health systems the number of megavoltage units per million inhabitants is over five, such as Sweden (Fig. 5) with 83 megavoltage units (72 linacs) for 9 million inhabitants; 15 countries of the Central Africa region, with over 490 million inhabitants, account for only 26 megavoltage units (4 linacs), which means an average of one machine for almost 20 million inhabitants. This situation is worsened in low and in middle income countries, due to the infrastructure of the health system, where an important portion of the radiotherapy facilities belong to the private sector, so the lower socioeconomic groups may not have access to these limited treatment facilities. Even the access to public facilities in many countries is charged through social security fees, therefore being unavailable to the poorest sector of the population. The number of megavoltage units per million of population in regions of low and middle income countries is shown in Fig. 6.

8.2.2. Megavoltage radiotherapy units according to cancer incidence

Even when the regulations about the provision of megavoltage radiotherapy equipment in most developed countries are based on the required minimum number of machines per million inhabitants, this model is not applicable to all regions or countries. As illustrated previously, although cancer incidence is growing in developing countries, its crude rate is still about 40% of that reported for more developed countries. This means that the demand for radiotherapy services should not be estimated on a population basis, but rather on a cancer crude incidence basis.

In this sense, the IAEA has suggested a figure for the estimation of provision of megavoltage units, according to which a machine is required for every 500 new treatment courses per year [129].

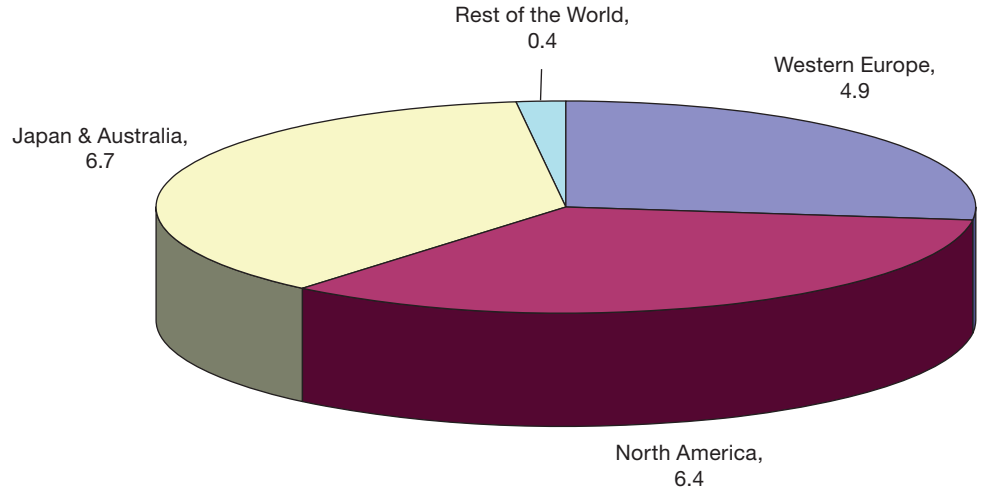

FIG. 4. Average number of megavoltage units per million. (Source: IAEA, DIRAC directory, 2006 [126]).

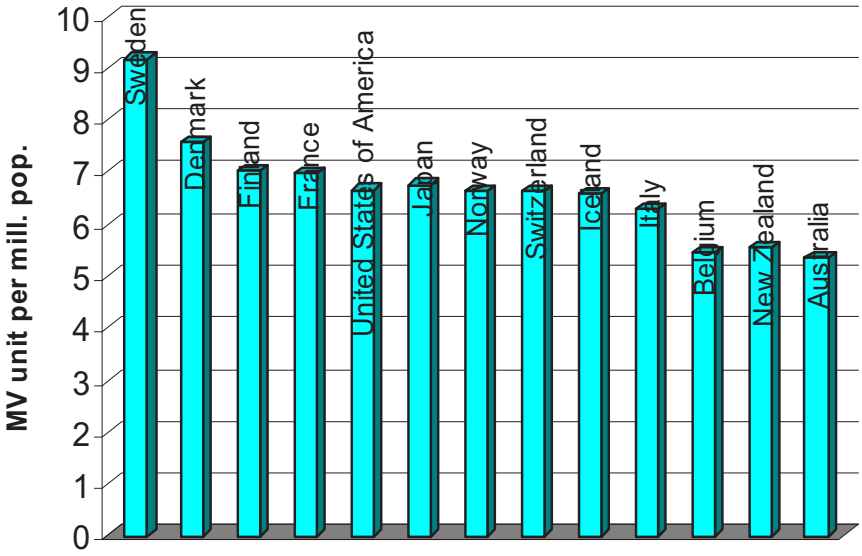

FIG. 5. Countries with the highest average number of megavoltage units per million inhabitants. Source: IAEA, DIRAC directory, 2006 [126].

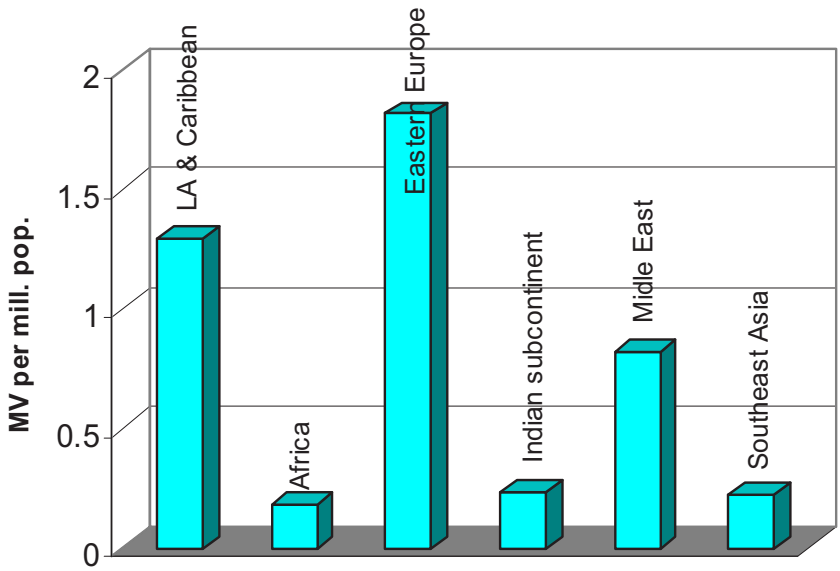

FIG. 6. Average number of megavoltage units per million inhabitants in regions of low and middle income countries. Source: IAEA, DIRAC directory, 2006 [126].

The estimated number of patients that would require radiotherapy has been calculated in Table 5 for the main regions of the world. The figures were estimated considering that 60% of all cancer cases would require radiotherapy in some phase of their treatment and the number of cases estimated by IARC and published in GLOBOCAN [4].

With this concept in mind, the distribution of megavoltage units was analysed in relation to cancer incidence, and more specifically with the estimated number of patients that would require radiotherapy at some stage during their treatment. The number of existing megavoltage units per 500 patients requiring radiotherapy is shown in Fig. 7 for the different regions.

TABLE 5. NUMBER OF RADIOTHERAPY TREATMENT COURSES PER YEAR (ASSUMING THAT 60% OF ALL CANCER PATIENTS WOULD REQUIRE RADIOTHERAPY AT SOME STAGE OF THEIR TREATMENT)

Region	Cases of cancers	Cases that would require radiotherapy
Australia & Pacific Islands	103 725	62 235
Caribbean	66 486	39 892
Central America	153 649	92 189
South America	612 927	367 756
North America	1 570 520	942 312
Northern Africa	119 614	71 768
Middle Africa	466 351	279 811
Southern Africa	63 796	38 278
East Asia	2 890 311	1 734 187
Indian Subcontinent	1 263 553	758 132
Middle East	200 210	120 126
Southeast Asia	524 881	314 929
Eastern Europe	889 659	533 795
Western Europe	1 804 206	1 082 524
Total	10 729 888	6 437 933

Source: Created with data from Ferlay *et al*. 2004 — GLOBOCAN 2002 [4].

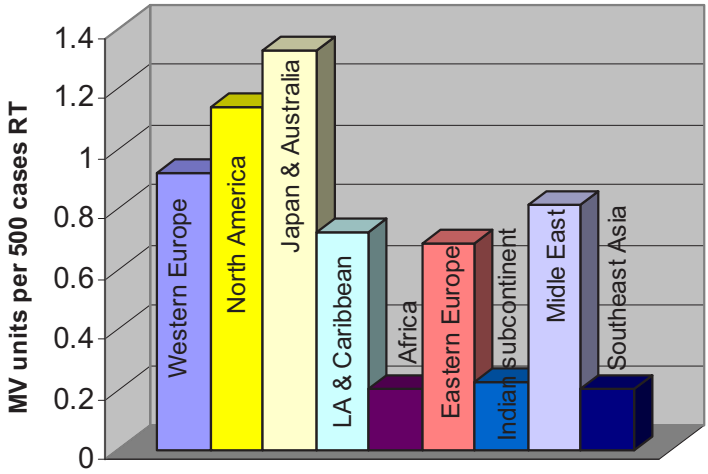

FIG.7. Existing megavoltage units per 500 patients requiring radiotherapy annually. Source: Created with data from IAEA, DIRAC directory, 2006 [126] and Ferlay et al. 2004–GLOBOCAN 2002 [4].

In most developed countries this number is close to or over the recommended level: 1.33 for Japan and Australia, 1.14 for North America, 0.92 for Western Europe. But even in these developed countries access to radiotherapy is unequal. There have been reports of widespread waiting lists for radiotherapy that suggest access to radiotherapy is less than optimal in many parts of the world [120]. In several market economy countries, radiotherapy services are highly fragmented; this means a large number of radiotherapy departments (usually private) operate with only one or two teletherapy machines. When calculating the number of teletherapy machines per million inhabitants, the numbers look good. However, fragmentation limits the efficiency of the radiotherapy services and also limits access.

It is evident that even in regions with the lower cancer incidence, the provision of megavoltage units is far from the recommended figure of one machine per 500 courses of radiotherapy per year. In the extreme case of countries in the central Africa region, this figure only reaches 0.05, which means that on an average, each existing machine should treat 10 000 patients per year; in reality, most of those potential patients will endure cancer without access to appropriate treatment and half of them, who could have been cured, will die without access to this therapy.

8.2.3. Megavoltage radiotherapy units related to gross domestic product (GDP)

More than half of the cases of cancer in the world arise in people in low income and middle income countries. This proportion will rise to 70% by 2020 [119]. In Fig. 8, the number of megavoltage radiotherapy machines per million inhabitants for randomly selected countries of all levels of development is displayed as a function of their GDP per capita. Although some spread is observed mainly for low income countries, the data confirms a strong correlation between the level of economic development and the provision of radiotherapy.

8.2.4. Provision of brachytherapy

In 2005, almost 260 000 women died of cervical cancer, nearly 95% of them in developing countries, making this disease one of the most serious threats to women's lives as well as a public health challenge in those countries.

Brachytherapy is a modality of radiotherapy in which the source of ionizing radiation is placed in close proximity or even inside a malignant tumour or tissue. The major role of brachytherapy has been in the management of gynaecological cancers which may be treated with either: low dose rate (LDR), medium dose rate (MDR) or high dose rate (HDR) systems, in addition to external beam radiotherapy. In the treatment of cervical cancer, brachytherapy has historically provided a successful alternative to surgery, in conjunction with external beam radiation therapy in order to reduce cancer recurrence and complications associated with treatment. For many cervical cancer patients, the combination of external beam radiotherapy and brachytherapy is the best curative treatment option and the only one for the advanced cases.

Brachytherapy is performed in a majority of the cancer centres in the USA [131]. In some UK centres [132] and in Western Europe, brachytherapy applications account for up to 10% of the total number of radiotherapy treatments, reaching 25% in some European centres [133].

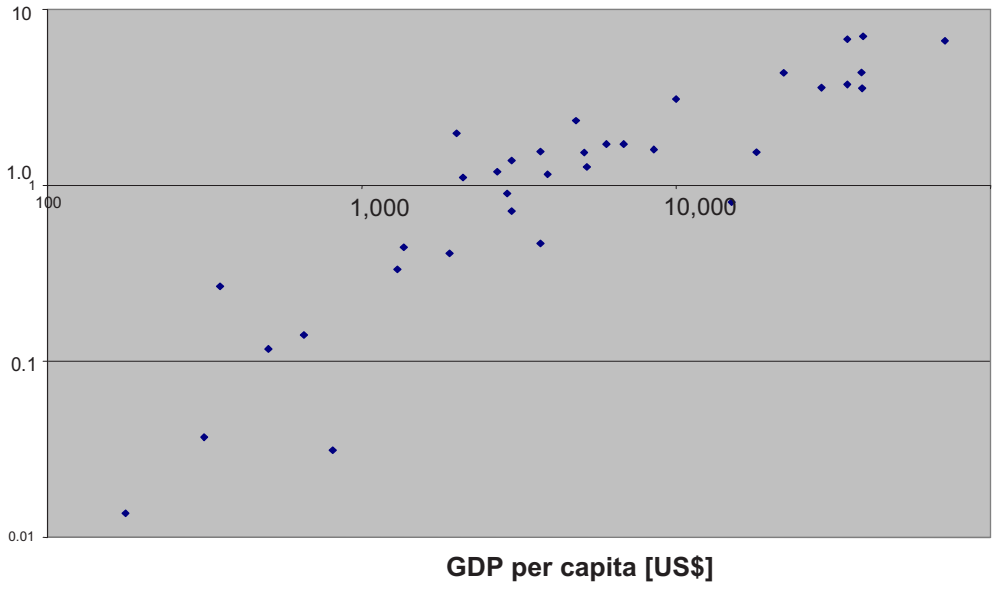

FIG. 8. Correlation of megavoltage units per million inhabitants with GDP per capita. Sources: Created with data from IAEA, DIRAC directory, 2006 [126]; International Monetary Fund, World Economic Outlook Database, September 2006 [130].

Inequalities in the provision of brachytherapy services are explained in Fig. 9. The source of these data [126] is supposed to underestimate the actual capacity of equipment; nevertheless, it is a trustworthy approach to the situation.

For an estimation of the needs of brachytherapy equipment, some preliminary assumptions should be made:

- Cervical cancer is one of the leading causes of death in women in the developing world. Most of the brachytherapy operation time will be applied for the treatment of gynaecological cancers:
- In many developing countries, almost the sole application of brachytherapy is in cervical cancer.
- Over 80% of newly diagnosed women with cervical cancer live in developing countries; most are diagnosed when they have advanced disease.
- Brachytherapy is recommended for the treatment of stage IB to IIIB/IVA cervical cancer [134], which represents around 60% of all cases of cervical cancer in developing countries and 30% in developed countries [119].
- To treat 200 or more patients per year with brachytherapy, one HDR after-loader (2 or more if LDR) is required [129].

The number of patients who would require cervical cancer brachytherapy has been estimated for the main regions of the World in Table 6. Column 3 shows the required number of brachytherapy devices (HDR/MDR afterloaders) for treating cervical cancer only.

A comparison of estimations in Table 4 with data in Fig. 9 gives an idea of the differences in the availability of brachytherapy services between developing and developed regions. While in developing regions the provision of after-loader units available for gynaecological brachytherapy is less than 50% of the requirements, in developed regions the current provision exceeds the requirements by almost ten times, suggesting that brachytherapy applications could cover other cancer sites.

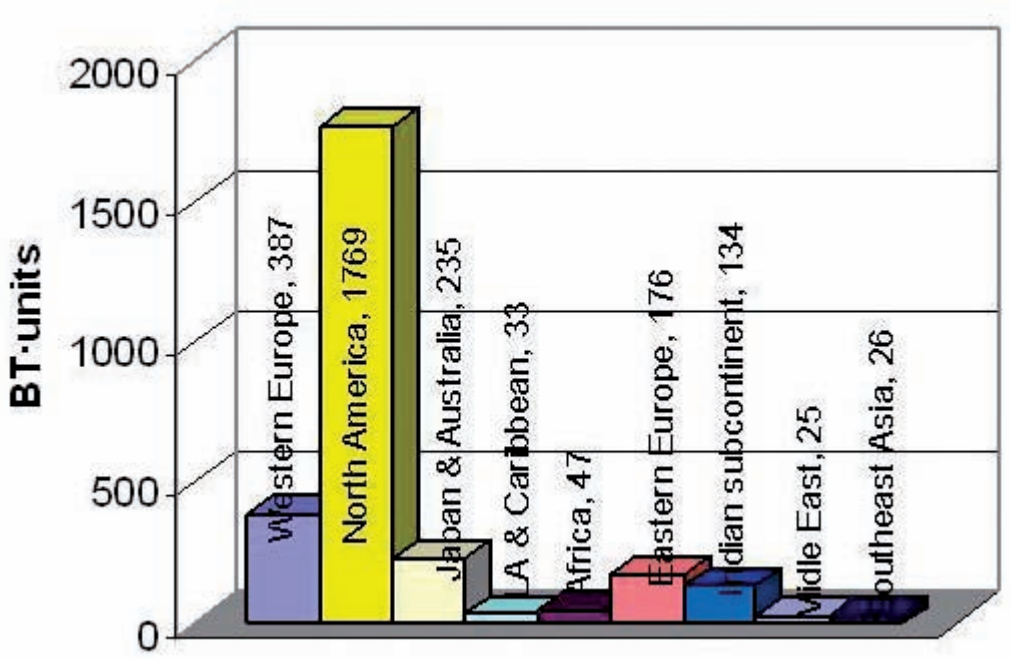

FIG. 9. Distribution of brachytherapy equipment (LDR manual and afterloaders, MDR, HDR) relative to industrial development. Source: Created with data from IAEA, DIRAC directory, 2006 [126]; Ferlay et al. 2004–GLOBOCAN 2002 [4]; IMV Medical Division, Nucletron, USA.

TABLE 6. REQUIREMENTS OF GYNAECOLOGICAL BRACHYTHERAPY PROVISION

Region	Cases of cervical cancers/year	Cases requiring brachytherapy[a]	Required HDR/MDR afterloaders[b]
Australia & New Zealand	1063	319	2
Caribbean	6369	3821	19
Central America	17 165	10 299	51
South America	48 328	28 997	145
North America	14 670	4401	22
North Africa	8175	4905	25
Middle Africa	8201	4921	25
Southern Africa	7698	4619	23
East Asia	61 132	36 679	183
Indian Subcontinent	157 620	94 572	473
Middle East	4456	2674	13
Southeast Asia	42 537	25 522	128
Eastern Europe	35 294	21176	106
Western Europe	24 517	7355	37
Total	493 100	250 260	1251

[a] Assuming an optimal brachytherapy utilization rate of 60% for developing and 30% for developed regions.
[b] Assuming that a unit is required for every 200 treatment courses per year.
Source: Created with data from Ferlay et al. 2004 — GLOBOCAN 2002 [4].

8.2.5. Inequalities in radiotherapy: Gender issues

In developing countries, the proportion of advanced stage tumours is higher than in developed regions. Between 50% and 80% of breast cancers in low and middle income countries are advanced at diagnosis [135], compared with 15% in high income nations [136]. Similarly, 56% of cervical cancers in Bangalore, India, are diagnosed at stage III compared with 15% in high income countries. Such advanced tumours are unlikely to be amenable to surgery and will therefore be treated with definitive radiotherapy.

In many developing countries, cervical cancer represents more than 50% of all radiotherapy treatments, while in most countries radiotherapy is indicated in more than 80% of all breast cancers, which represents another 20% of all treatments with radiotherapy [118]. Considering these figures, it is evident that inequalities in radiotherapy provision affect women especially, since women constitute around 70% of the total number of radiotherapy patients.

8.2.6. IAEA activities in radiotherapy and cancer control

The IAEA works with its Member States and multiple partners worldwide to promote safe, secure and peaceful use of nuclear technologies.

The objective of the IAEA programme in human health is to enhance the capabilities of Member States to address their needs related to the prevention, diagnosis and treatment of health problems through the application of nuclear techniques. The mandate arises from Article II of the IAEA's Statute: "The IAEA shall seek to accelerate and enlarge the contribution of atomic energy to peace, *health* and prosperity throughout the world. It shall ensure, so far as it is able, that assistance provided by it or at its request or under its supervision or control is not used in such a way as to further any military purpose".

The IAEA focuses on the medical use of radiation for the diagnosis and treatment of diseases, primarily cancer. The main objective is to improve the availability and safe use of effective cancer management strategies in Member States, in particular by helping establish and upgrade radiotherapy centres and equipment, introducing resource sparing treatment protocols for use in low and middle income countries, organising teaching and training courses for radiation oncologists and other health care professionals and devising effective treatments for different types of cancer based on radiobiological principles and clinical and laboratory studies.

The lack of sufficient trained staff is a critical problem for the establishment of adequate radiotherapy services in the developing world. The importance of addressing and eventually solving this problem cannot be overemphasized. Many factors contribute to this limitation, including few job positions, low salaries, lack of training programmes, difficulties in the recognition of accreditation obtained in other countries and emigration of professionals to more affluent countries. The appropriate training and subsequent retention of professionals is essential for planned radiotherapy services to be effective in dealing with this 'silent crisis' of cancer in the developing world.

The IAEA has embarked on the preparation of a series of syllabi for the training of the main professions involved in providing radiotherapy services. These professions include radiation oncology physicians, medical physicists, radiation therapy technologists, radiation oncology nurses and applied radiation biologists. While many countries have already developed and implemented their own syllabi for the training of radiation oncologists, these cannot usually be extrapolated to low and middle income countries.

The IAEA supports the building up of indigenous capacity in radiation therapy to cure or alleviate the life threatening effects of cancer in Member States falling under the developing countries list. However, the resources available to the IAEA fall far short of those necessary to meet human needs around the world. In order to help meet these needs, a Programme of Action for Cancer Therapy (PACT) has been initiated to introduce, expand, or improve radiotherapy programmes as integral parts of comprehensive national cancer control programmes in developing countries. This effort will be in synergy with other organizations, institutes and partners, and will seek extrabudgetary contributions of non-traditional donors to acquire the necessary resources to facilitate the implementation of the programme.

PACT has formulated the following three point strategy to implement its aims:

(1) To identify and assess a country's most pressing cancer needs so that partners and donors can effectively respond. This constitutes a comprehensive cancer control needs assessment through the imPACT — integrated missions of PACT review process for each of the countries selected.
(2) To establish PACT model demonstration sites (PMDS) as an example of the value and efficacy of multi-disciplinary, inter-agency cooperation in combating cancer. Such sites highlight PACT's activities and help raise public awareness as a forerunner to larger regional/global initiatives. These will form the basis for increasing donations from development banks, foundations and other sources. PACT's model demonstration sites projects so far include six countries in different regions.
(3) To focus on regional capacity building through the development of regional cancer training networks to establish regional reference cancer centres to train health care professionals and provide mentorship to other centres within the region.

One particular aim of this stage is to encourage trained staff to stay in their home countries with ongoing professional development programmes, the establishment of a Virtual University for Cancer Control, and investment in modern information technology and facilities.

As defined by the World Health Organization (WHO), a National Cancer Control Programme "is a public health programme designed to reduce the number of cancer cases and deaths and improve quality of life of cancer patients through the systematic and equitable implementation of evidence based strategies for prevention, early detection, diagnosis, treatment, and palliation, making the best use of available resources. A comprehensive national cancer programme evaluates the various ways to control disease and implements those that are the most cost effective and beneficial to the largest part of the population. It promotes the development of treatment guidelines, places emphasis on preventing cancers or detecting cases early so that they can be cured, and provide as much comfort as possible to patients with advanced disease."

PACT promotes the concept of national cancer control planning towards the development of integrated national cancer control programmes as the most efficient way to tackle the cancer problem in a country. Each

country has particular features in terms of the cancer burden, cancer risk factors, culture, health system, and available financial and human resources as well as infrastructure. They should be carefully assessed in order to establish realistic and achievable priorities for action. To assist ministries of health in this regard, in collaboration with its partners, PACT offers a comprehensive needs assessment review service called imPACT (integrated missions of PACT). Any IAEA Member State can request an imPACT review by contacting the PACT programme office.

The IAEA's projects and publications focus on supporting public institutions in order to exert the highest possible impact on the weak sectors of the population: the poor, the elderly, women and children. The IAEA is committed to gender equality. In keeping with UN policies and agreements on both gender equality and gender mainstreaming, the IAEA takes responsibility for proactively integrating gender into its programmes as well as for contributing to worldwide gender equality in all areas of influence, including human health in general and cancer radiotherapy in particular.

9. CONCLUSIONS

Cancer is the second leading cause of death worldwide. Cancer killed 7.6 million people in 2005, three quarters of whom lived in low and middle income countries. Cancer survival rates in developing countries are often less than one third of those in the developed world.

Inequality in health reflects broader social inequality, and the cancer pattern both in terms of its incidence and its treatment and survival in a country and within countries clearly confirm this concept. Socioeconomic status cannot be considered to be the direct cause of cancer or of low cancer survival. Nevertheless, it is certainly a marker for underlying physical and social factors that lead to disease, disease recurrence, and substantively affects access to care resulting in inequitable survival. Socioeconomic effects may be explained by differences in access to health services among socioeconomic status groups, considering health care not only as diagnosis and treatment but as the general spectrum of health information/education, early diagnosis, timely and adequate treatments, palliative care and quality of care in general.

Socioeconomic development, including improvements in access to health services in developing countries, results in reduced mortality from infectious diseases and increase in life expectancy, thus contributing to an increase in cancer incidence and mortality. At the same time, it brings changes in people's lifestyle, incorporating unhealthy behaviours such as smoking, unhealthy nutrition, and sedentary inactivity, which also result in increasing cancer incidence and mortality. While many common cancers in developing countries are associated with infections (cervical, stomach and liver cancer), those associated with a western lifestyle are rapidly increasing (breast, colorectal and prostate cancer), and patients are mostly incurable at the time of diagnosis. Developing countries lack the resources and in many cases the political will to face this situation. These countries have less than 10% of the resources available in the world for cancer control.

Women and children are especially vulnerable. Breast cancer is the leading cause of cancer mortality among women worldwide, while cervical cancer is the seventh, but cervical cancer is the first in poor regions like Sub-Saharan Africa, South and Central America, South-Central Asia and Melanesia. While 55% of the world's breast cancer cases are from developed countries, 83% of the world cervical cancer patients are from developing countries. Although 85% of the paediatric cancer patients are from developing countries, they cannot achieve the high cure rates (overall 78%) seen in developed countries, due to lack of drugs, limited radiotherapy services and qualified human resources. Women and children are also more likely to die from curable cancers (e.g. cervical cancer and breast cancer) due to lack of treatment facilities.

Long term survival rates are less than 20% in developing countries, but rise to 50–60% in developed countries. The mortality/incidence ratio is still 17% higher in developing than in developed countries. This is associated to the lack of timely and effective treatment in developing countries.

The cost of cancer care is an important issue when addressing cancer disparities. This is especially true regarding the cost of treatment for advanced cases, which are the most common in low and middle income countries. Nevertheless, the most striking point for cancer care and cancer control in the developing world is not the

technology cost of the treatments itself. Cancer management needs specialized human resources accessible to all citizens irrespective of their socioeconomic status and this is probably the largest barrier they will have to overcome to succeed in cancer control.

Radiation therapy and chemotherapy are very important and specific components of modern cancer treatment, but cancer drugs and radiotherapy equipment need adequate hospital facilities, and more importantly, qualified human resources.

There is strong evidence of the effectiveness of radiation therapy in many situations in clinical oncology. To achieve optimal outcomes at the population level, effective treatments have to be timely accessible to all patients who need them. Inequalities in radiotherapy provision are significant and the current trend of increasing cancer incidence in developing countries, accompanied by the limited resources devoted to improving and upgrading the existing facilities in these regions, will deepen the existing gap with the developed world.

In terms of funds, the required investment to reverse the current trend is not as high as it may seem compared with the expected impact in terms of cure rate and quality of life of potential patients. External beam radiotherapy can be accurately and safely delivered with ^{60}Co machines and simple accelerators for most cancer sites, while the required ancillary equipment for simulation, localization; planning and dosimetry can be shared for several machines located in one centre.

In this sense, new facilities should be designed to enclose more than one teletherapy machine, eventually also including a brachytherapy unit. They need to be accessible to all those who need them if the severe equality gap in cancer therapy is to be reduced. This concept of scale economy would also help to solve the problem of the required trained staff for those facilities.

Deprivation is an important determinant of ill health in general and of cancer outcomes in particular. There is a marked difference between the health of people living in deprived areas of the world and those living in more affluent areas. The reasons for the association between deprivation and poorer cancer outcomes could include increased exposure to environmental carcinogens and infectious agents, later stage at presentation, poorer access to or uptake for screening, diagnostic and treatment services, the presence of significant co-morbidities and/or variations in the quality and effectiveness of available cancer treatment services.

In this context, the global fight against cancer is connected with the broader aims of the UN Millennium Development Goals. A reduction of the inequalities in cancer care could be anticipated with the achievement of goals such as a reduction of extreme poverty, improved education, promotion of gender equality and empowerment of women, general improvement of maternal health, combat of HIV/AIDS and other infectious diseases, ensurance of environmental sustainability and establishment of global partnerships for development.

10. POLICY TO ADDRESS INEQUALITY

For virtually all disease categories examined, inequality (disparity) in the delivery of health care leads to much worse health outcomes for certain groups, particularly minorities, women, children and the poor. In the case of cancer, disparities in early detection, treatment and outcomes for racial/ethnic minorities and low income patients are well documented.

Given that our knowledge of the inherited (ethnic/race) basis of disparity is incomplete and changing, it would be imprudent to base conclusions that shape health care policy on this type of information. Instead, socioeconomic, quality of care analysis and structural modifications are better precepts to lead the disparity discussion, not only because their effectiveness is likely to be immediate but also because emerging evidence shows that these factors are at the root of the disparity problem. Experts in the field have moved from describing the problem in terms of such classifications as ‘race’ and ‘minorities’ (as in the late 19th and early 20th centuries) to the reality, which is that these classifications are for the most part surrogates for what is the true root cause of inequality, poverty [137,139].

Poorer people tend to have poorer health, including higher rates of all forms of chronic diseases, and inferior cancer treatment outcomes when results are adjusted for stage and stratified by poverty level [137].

Geographically based structural deficits are usually a manifestation of complex and fragmented health care systems plagued by a lack of access on multiple levels. At the most basic level, any patient with a disease requiring complex coordination of care, such as cancer treatment, will encounter numerous barriers to securing care as he/she attempts to navigate the medical delivery system. And virtually all such patients must contend with the additional demands of work, family, and emotional stress. But for those patients who are also poor, there will be even more issues such as access to reliable transportation, child care and community based medical resources, and these may be nearly insurmountable.

Implicit in our understanding of inequality is that its multi-factorial causes include variations in biology, socioeconomic status, access to care and the quality of care received. With increasing complexity in contemporary radiation oncology, access to specific technologies and essential coordination of care are somehow missing for many at risk and disadvantaged patients. Many patients in the developing world do not receive critical areas of care or, worse yet, do not receive the care they need at all.

'Quality' in health care is a multidimensional concept comprising seven elements [138]:

(1) Patients get the care they need;
(2) Patients need the care they get;
(3) Health care is delivered safely;
(4) Health care is delivered on time;
(5) Health care is patient centred;
(6) Health care is equitable.

The components of 'inequality' (or disparity) in turn encompass all the other elements of 'quality', making it reasonable to address the inequality problem in a quality improvement context. A programme to improve quality must therefore include activities to address the inequality problem.

Inequality is about poverty and the lack of infrastructure to meet the needs of disadvantaged patients. Setting the necessary infrastructure in place helps bridge the gap between high quality health care and the actual care delivered. Quality of care and inequality are integrally related concepts that benefit from the coordination of interventions to address structural and process based deficits in the health care delivery system [139].

The powerful tools of health services research and the discipline of 'quality' have accurately described and to a great extent explained the inequality problem. However, to address the underpinning of inequality, there must be an effective and systematic improvement of the infrastructural deficits and implementation of patient centred care models that facilitate health care for disadvantaged patients.

Clinical trial programmes (where care is delivered equitably and consistently), an electronic medical record, cancer care specific transportation, elucidation of patients' needs, implementation of methods to identify and address barriers to care and tools to assist patients with fewer resources, navigating the complicated care process are all straightforward interventions effective in eliminating inequalities. Furthermore, the results from quality initiatives in underserved populations will have the additional benefit of informing programmes aimed at quality improvements for all patient groups by promulgating processes and techniques that improve care coordination and promote timely and patient centred care.

These interventions, integrated into the health care process and, whenever possible, combined with financial incentives for providers and institutions, represent a foundation for policies to effectively address the inequality issue [139].

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