The rising burden of cancer in the developing world

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Cancer remains one of the leading causes of morbidity and mortality worldwide. It is predicted that by 2020, the number of new cases of cancer in the world will increase to more than 15 million, with deaths increasing to 12 million. Much of the burden of cancer incidence, morbidity, and mortality will occur in the developing world. This forms part of a larger epidemiological transition in which the burden of chronic, non-communicable disease—once limited to industrialized nations—is now increasing in less developed countries. In addition to the accumulating risks associated with diet, tobacco, alcohol, lack of exercise, and industrial exposures, the developing world is already burdened by cancers some of which are attributable to infectious diseases. These disparities in cancer risk combined with poor access to epidemiological data, research, treatment, and cancer control and prevention combine to result in significantly poorer survival rates in developing countries for a range of specific malignancies. This paper summarizes the recent trends in the epidemiology and survival of cancers in the developing and developed world, and explores potential causes and policy responses to the disproportionate and growing cancer burden in less developed countries. Such responses may include raising awareness as well as education and training to foster better informed decision-making, together with improved cancer surveillance, early detection and emphasis on prevention. Improved health care financing and international initiatives and/or partnerships could also provide additional impetus in targeting resources where needed urgently.

Key words: cancer epidemiology, health services, healthcare policy, developing countries, burden of disease

Introduction

Cancer remains a major cause of mortality worldwide. Despite being potentially among the most preventable and treatable chronic diseases, nearly 7 million lives will be lost to cancer in 2005 alone [1]. For many cancers, incidence rates could increase substantially in the future, with up to 15 million new cases in 2020, most of which will be in developing countries (Figure 1) [2].

Cancer affects all communities worldwide, but there are marked differences in the prevalence and types of cancers among communities. While the total cancer burden remains highest in affluent societies, less developed economies are closing the gap very rapidly. 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) [3]. The increased prevalence and incidence of cancer in developing countries reflects a wider transition in the global burden of disease from infectious disease toward a greater frequency of non-communicable, chronic illness. The 'globalization' of chronic disease is demonstrated by the fact that deaths in the previous two decades from chronic illnesses surpassed those from acute and infectious diseases in all continents except Africa [4].

Several factors enter into the transition of global cancer epidemiology. The rapid aging of populations is a major factor in global cancer trends, as are diet, tobacco and other substance use, and infectious agents. Certain types of cancer, such as breast, colon, and prostate tumours, are associated with Western lifestyle as demonstrated by higher rates of cancers in more developed versus less developed countries [5]. Whereas developed countries have made strides in prevention of some cancers, such as tumours caused by smoking, the incidence of these cancers are on the rise in developing countries. Another important distinction between developed and less developed economies is the incidence of preventable cancers caused by infectious disease. Additionally, early detection, and access to advanced diagnostic modalities and cancer therapies has also led to declines in the incidence and mortality of certain cancers in developed countries not seen in less developed communities.

Epidemiological data are useful to identify disparities in cancer burden, detection and prevention, as well as treatment outcomes such as survival. Often, the epidemiological trends in the global burden of cancer reflect local economic and policy factors. The goal of this review is to reflect the primary differences in the burden of cancer illnesses in developing countries and the potential implications for existing and future economic and social policy.
global cancer: a growing disparity
disparities in incidence

The causes and types of cancer vary globally. The reasons for differences in the incidence, pathology, mortality, and clinical characteristics of cancers in different geographical regions are manifold and complex. Historical background, genetics, environment, lifestyles, socio-cultural and behavioural factors, as well as economics may all play a role, and these elements may interact to contribute to higher or lower risk for specific cancers [6]. Nevertheless, the enormous disparities in wealth between developing and developed countries may also be relevant in the types, frequency, and outcomes of cancer that occur in these settings [7].

Indeed, the overall age-standardized incidence and mortality rates of cancers among developing nations remain below those of developed countries (Figure 2) [8]. The starkest contrast in cancer incidence between developing and developed countries is seen in cancers associated with infectious diseases and with Western lifestyle, respectively. In developed countries, tobacco may cause 1 in 3 cancer deaths [9]. A high incidence of malignancies associated with industrialized societies such as breast, colorectal, and prostate cancers is also evident. Lifestyle factors associated with developed countries such as smoking, lack of exercise, and diet continue to be implicated in the high incidence of these cancers.

disparity in mortality

Worldwide, cancer is a major cause of morbidity and mortality. Over 10 million new cases and over 7 million deaths from cancer occurred in 2000 [10]. The contribution of developing countries was 53% for incidence and 56% for deaths. But the future is more alarming since, by 2020, the total number of new cases is expected to increase by 29% in developed countries whereas, in developing countries an increase of 73% is expected, largely as a result of ageing, urbanization and change in dietary habits [11]. Lung, breast, stomach, colorectal and liver cancer are the most frequent types of cancer in developing countries.

While global cancer mortality is expected to increase by 104% by 2020, increases in death rates will be about 5-fold greater in the developing world, compared to the established market economies (Figure 3) [12]. This disproportionate mortality reflects belated reactions by overburdened health care systems that are ill equipped to deal with changing patterns of illness. Death rates from most cancers remain significantly greater in developing countries than in developed countries (Figure 4). Much of this disparity in cancer mortality is attributable to lack of prevention or early detection. For example, more than 80% of new cases of cervical cancer will occur in developing countries, where it is the most common cancer in women and results in 250 000 deaths annually [7, 9]. Late diagnosis and inadequate treatment for advanced cancer also contribute to mortality as 80% of patients in developing countries already have incurable disease when first diagnosed.

Figure 1. Estimate of predicted cancer incidence in developing and developed countries [2].

Figure 2. Incidence and mortality (age-standardized per 100 000 population) from the most common cancers in less developed (A), and more developed countries (B) [8].
cancer causes in developing countries

infectious disease-related cancer

In the last few decades, many infectious diseases have been successfully eradicated through governmental and public health interventions [6]. Nevertheless, it has been shown that infection is responsible for nearly 25% of cancers in developing countries, compared with less than 10% of cancers in developed countries [9, 12]. The highest incidence and mortality burdens for neoplasms with infectious etiologies are those for cancers of the cervix, stomach, and liver (Figure 2) [8].

HPV has been linked to cervical and colorectal cancer in developing countries and developed countries [13]. While the attributable fraction of cancers caused by oncogenic HPV is the same in developed and developing countries, the percentage of all malignancies resulting from HPV is approximately 5-fold higher in the developing world [14]. The burden of cervical cancer in developing economies is largely due the absence of Pap cytologic screening (smear test). Other co-factors, such as early sexual debut and male circumcision may increase the risk of cervical cancer. There may also be regional differences in the malignancy potential of certain HPV types. Lesions caused by HPV31 and HPV58 are more likely to advance to cervical carcinoma in Latin America and China, respectively, when compared with Europe [15].

There is hope for prophylactic immunization against cancer-causing HPV, as shown by recent clinical trials of bivalent and tetravalent vaccines [16–18]. However, the promise of an HPV vaccine must be tempered by experience with vaccine preventable diseases in the developing world. Hepatocellular carcinoma is recognized to result from long-term infection with HBV. Today, about 90% of the world’s liver cancer burden attributable to HBV still occurs in the less developed countries, despite the fact that effective and relatively inexpensive vaccines against HBV have been available for decades [14]. It is unclear when and to what degree emerging HPV vaccines will become available outside the developed world, and what their effectiveness will be across heterogeneous populations. Certainly, cytologic screening and prevention through condom use should continue to be the cornerstones of efforts to decrease the burden HPV infections and their potential malignant outcomes.

Nasopharyngeal cancers, which are more common in patients with Epstein Barr virus (EBV) infections, also have a higher incidence in developing countries, compared with developed countries (Figure 2). The number of cases of lymphoma and nasopharyngeal cancers attributable to EBV in less developed countries is 10- to 60-fold higher, compared with more developed countries [14].

The pandemic of HIV/AIDS has led to widespread emergence of Kaposi sarcoma, caused by human herpes virus 8 (HHV8). For many less developed countries – in particular those of sub-Saharan Africa – there have been marked increases in the incidence of all HIV-related cancers caused by viruses, such as cervical and colorectal cancer (HPV), Kaposi sarcoma (HHV8), non-Hodgkin’s lymphoma (EBV), squamous cell carcinoma conjunctiva (HPV), and hepatocellular carcinoma (HBV) [19].

While they remain relatively uncommon, cancers of the bile duct and urinary bladder associated with liver flukes and Schistosoma, respectively, occur only in developing countries [14].

Infectious disease is also important because of its association with the increased overall economic burden of cancer. Although few studies exist on the economic burden of cancer in developing countries, the evidence suggests that this may be significant [20]. It has also been shown that the economic burden of cancer increases considerably when the effect of infectious disease and its relationship to cancer is considered [20].

environmental and dietary factors

Oncogenesis is often multifactorial, involving genetic and environmental factors. In addition to infectious agents, there are a host of other influences from the environment that may be carcinogenic alone, or in combination with one or more predisposing factors (Table 1). Many environmental factors cluster in specific geographical regions. For example, oral cancers are highly prevalent in regions such as India and Southeast Asia as a result of widespread betel nut and tobacco chewing practices [6]. Higher incidences of lung cancer occur where there is abundant indoor air pollution or radon, such as in India and China, as well as smoking [12].
Compared with Europe and North America, stomach cancer continues to be an exceedingly prevalent malignancy in developing countries. China, Chile, Ecuador, and Costa Rica are striking examples, but some developed countries such as Korea and Japan also have a high prevalence of stomach cancer. The reasons for these patterns are unclear, but may be associated with food conservation with refrigeration, a more varied diet, and, possibly, smoking [21]. There is now convincing evidence that *Helicobacter pylori* infection is associated with a 2- to 3-fold increased risk of cancers including carcinoma of the stomach and gastric lymphoma [12]. The overall prevalence of infection with *H. pylori* is 74% in developing countries and 58% in developed countries [14]. The role of highly salted foods in the development of gastric cancers is supported by the observation that these neoplasms remain prevalent in countries like Japan and Korea, where people continue to consume large amounts of salty foods despite the availability of refrigeration [12]. As with most malignancies, it is likely that a combination of factors, including diet and environment, have a strong influence on gastric cancers.

**Figure 4.** Cancer death rates in developing and developed countries for males (A) and females (B) [8].

Of all the environmental factors, the use of tobacco poses the greatest threat and contributes considerably to cancer prevalence and mortality in developing countries. Both tobacco...
smoking and chewing are associated with increased risk of cancer. This risk is on the rise in developing countries. Worldwide, it is estimated that tobacco causes about 8.8% of deaths (4.9 million) and 4.1% of disability-adjusted life years (DALYs) (59.1 million); the rapid evolution of the tobacco epidemic is illustrated by comparing these estimates for 2000 with those for 1990: there are at least a million more deaths attributable to tobacco, with the increase being most marked in developing countries [22].

There were large increases in smoking in developing countries, especially among males, over the last part of the 20th century [23, 24]. Smoking rates also remain relatively high in most transition countries. This contrasts with steady but slow decreases, chiefly among men, in a number of industrialized countries. Overall, the prevalence of tobacco use has declined in some high income countries, but is still increasing in some low and middle income countries, especially among young people and women. The first estimates of the health impacts of smoking in China and India have also shown substantially increased risk of mortality and disease among smokers [25–28]. Smoking causes substantially increased risk of mortality from, among others, lung cancer and oral cancer. Consequently, in populations where smoking has been common for many decades, tobacco use accounts for a significant proportion of mortality, as illustrated by estimates of smoking-attributable deaths in industrialized countries [29]. The adverse effects of tobacco on oral health are well documented and numerous studies in various populations have shown that smokers have a substantially higher risk of oral cancer than non-smokers [30, 31].

While cigarette smoking causes the majority of the adverse health effects of tobacco, chewing is also hazardous. The adverse effects associated with areca (betel) nut use include oral and oropharyngeal cancer, oral premalignant lesions and conditions (oral leukoplakia and submucus fibrosis), gum disease and addiction [32]. Several studies have shown that the practice of chewing tobacco containing areka nut is highly prevalent among adults [33–35] although this habit starts at young age [36, 37]. As many users develop dependency this raises important concerns regarding its consequences for oral health [38].

Policy issues

The above trends highlight a number of policy deficiencies in developing countries. These include the lack of effective cancer surveillance and control, but, more fundamentally, the lack of adequate health care, funding and coverage at the national level, as well as the lack of effective preventive policies. Globalisation, thought by many to improve economic growth in developing countries, may adversely affect it, thereby also compromising investment in health care and health services in individual countries.

Of the top four causes of death worldwide, three – cardiovascular disease (CVD), cancer, and chronic respiratory diseases – are associated with chronic disease. And CVD, chronic respiratory diseases, cancer, and diabetes made up 60% of the 58 million annual worldwide deaths estimated for 2005, with more than three-quarters of these deaths occurring in developing countries [39].

In October 2005, the World Health Organization (WHO) released a report – Preventing Chronic Disease: A Vital Investment – to raise awareness about this largely invisible epidemic in developing countries and to issue a call to action for national governments, international organizations, civil society, and the private sector [40]. WHO proposes a new global goal: to reduce the projected trend of chronic-disease death rates by 2% each year until 2015. Such a reduction would prevent 36 million people from dying of chronic disease in the next 10 years, most of them in middle- and low-income countries.

Cancer surveillance and control

While the growing burden of cancer in developing countries has been recognized for at least 2 decades, there is little evidence that prevention alone will have a major impact on this trend in developing countries (Figures 1 and 2). For instance, legislation (and its enforcement) to control tobacco use in developing countries has lagged behind the dramatic rise in tobacco consumption. India, the third largest grower of tobacco in the world, amassed 1.7 million disability-adjusted life years (DALYs) in 1990 due to disease and injury attributable to tobacco use in a population where 65% of the men and 38% of the women consume tobacco. [41] As a result, combined efforts in both prevention and treatment will be needed to control cancers in developing countries, emphasizing the need for advancements in two specific areas: cancer surveillance and cancer control systems.

Surveillance of cancer is critical to the implementation and evaluation of primary and secondary prevention programs while survival data are an essential measure of outcomes. One of the starkest global disparities in cancer control is the lack of mechanisms for data collection in less developed regions. The lack of cancer information is evident by the paucity of data on cancer occurrence and mortality over the last decade (Table 2).
Table 2. Availability of cancer-related information and services in Africa, Asia, and Latin America [5]

<table>
<thead>
<tr>
<th>Regions (No. countries)</th>
<th>Number of countries with resources available for 1990s</th>
<th>Cancer control services</th>
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<td></td>
<td>Data for 1990s</td>
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<td></td>
<td>Incidence</td>
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<tr>
<td>Africa (56)</td>
<td>8</td>
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<tr>
<td>Central and South America (21)</td>
<td>6</td>
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<tr>
<td>Caribbean (8)</td>
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<td>Asia (44)</td>
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[5]. While international efforts to collect data on cancer incidence and mortality are essential, the quality and validity of these ultimately depend on local surveillance, pathology, and staging, which vary significantly across regions.

Some cancers amenable to early detection and treatment, such as testicular cancer, oral cancer, and cervical cancer, continue to have a high incidence and mortality in less developed countries. Screening programs and pathologic expertise for rapid and accurate diagnosing and staging are lacking (Table 2) [5].

The availability of radiotherapy services falls short of need, even in countries with the best healthcare infrastructure. Not surprisingly, while the need for radiotherapy is greater in developing countries where tumours are often diagnosed in an advanced stage, such resources remain scarce. The International Atomic Energy Agency (IAEA) has a mandate to accelerate and enlarge the contribution of radiotherapy in the diagnosis and treatment of cancer, with funding of over US$30 million for technical services in human health in 2004 [2].

Unfortunately, the need greatly outweighs the availability, and some African countries have no radiotherapy while others are poorly equipped (Table 2). For example, Ethiopia has a single cobalt machine for 60 million people while many African countries lack radiotherapy facilities altogether. Few countries have access to advanced radiotherapy options, such as accelerators. In addition to lack of radiotherapy equipment, current obstacles to optimal cancer management with radiotherapy include a lack of training, suboptimal utilization of radiotherapy resources, deficiencies in quality assurance, and a need for greater use of evidence-based treatment guidelines [2].

**major health policy issues**

There exist several well-recognized and persistent obstacles to adequate healthcare in developing countries, many of which effect patient outcomes as the cancer burden continues to rise. 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. In low income countries, health spending per capita consistently ranks among the lowest globally. The 2005 Human Development Report from the United Nations Development Program revealed the growing disparity in health care expenditures between rich and poor nations. For example, of 177 nations, the per-capita annual health expenditures of 50 nations were under 200 US dollars [42]. Countries with progressively lower income and health spending per capita also have proportionately higher burden of disease and lower life expectancy. In many middle-income countries, however, there are promising new initiatives.

China is one such case with ongoing policy reform initiatives both in urban but also in rural areas, [43, 44] that have resulted in nearly 120 million people being able to access health services through medical savings accounts. Similarly, in Turkey and Russia, reforms are in progress to introduce universal healthcare coverage and prescription drug coverage, respectively, by 2007 [45–47]. In other countries, healthcare access has been improved for select populations. In Mexico, action at the national level resulted in coverage of basic care for several million Mexicans [48].

**the impact of globalization**

Increasingly, globalization is having a wide-ranging impact on developing economies and their populations. The precise effects of globalization and their implications for health and social justice are a subject of intensive debate. However, it is now appreciated that, while once seen as chiefly an economic phenomenon, globalization has broad effects on sociocultural frameworks, including those on health and disease [49]. In the simplest view, those countries most burdened by domestic challenges in health are least capable of bearing the additional demands of international risks and competition. These emerging economies must struggle to maintain equity in the face of increasingly complex webs of international cooperation [50].

Health has been a broadly accepted international goal, and continues to inform many dimensions of the global economy [49]. Interdependence of economies may have deleterious effects on developing nations, but it may also open up new avenues to collective action. One example is how international trade agreements have changed in recognition of the importance of access to affordable care and effective pharmaceuticals. In 2001, a strong international movement for the global mobilization of drugs to combat HIV infection in developing countries resulted in the Global AIDS and Health fund. This was the first time in the history of the United Nations that a General Assembly was devoted to a single health topic. It not only highlighted the link between economics, health, and security, but also served as a model for the impending battle against the cancer pandemic.

The relation between globalization and the changing role of government must also not be underestimated. In previous decades, the ‘reform’ of health systems in developing countries often meant less accessibility and downsizing constraints. While it can be argued that global markets will benefit health locally through economic growth, the reality is more complex. With globalization, the inequities of health in developing countries have not been reversed. Many of the poorest countries with the
research initiatives

Equitable and beneficial collaborations between researchers in the developed and developing world can often foster studies leading to increased knowledge and may improve well-being of local and global populations struggling against cancer. Similarly, appropriate technology transfer initiatives can benefit resource-limited settings and should be encouraged when supported by private and public governmental and non-governmental agencies [12]. Finally, mutually beneficial collaborations between practitioners from different regions can assist in the implementation of control services such as screening and pathology as well as palliative care.

priorities moving forward

While the social and economic burdens of cancer will continue to accumulate in developing countries, there are promising efforts underway in the scientific, medical, economic, and policy arenas that will likely have a positive impact on the availability and effectiveness of care and the quality of life for individuals with cancer. Goals for the future to address the growing need should remain clearly in focus.

Globally and nationally, there is a continuing need for awareness and communication about the disparities in care and appropriate ways to address them. Raising awareness of the growing burden of chronic diseases – including cancer – is an important aim for professional organizations, governmental and non-governmental agencies and foundations, and public health professionals [1]. Education is needed, not only in technical areas, but to foster better-informed decision making on the part of governments and health ministries. Much of economic and policy decision-making remains in the control of politicians and government officials. They may need detailed information and broad-based support to make sound decisions about cancer prevention and control [6]. This also includes information and support to address some of the causes of cancer in individual communities. Training for epidemiological research is another important educational goal [12].

Locally, there is a significant material and infrastructure need that includes basic diagnostic services, surgical and radiotherapy facilities, and expanded palliative care. Greater resources are needed for cancer surveillance and information as well as to provide adequate detection, prevention, diagnosis, and continuing care. Early detection, particularly for breast and cervical cancer, and control of risk factors such as tobacco and alcohol should be the cornerstone of preventative strategies [54]. Indeed, it is estimated that over one-third of cancers are preventable and another one-third are potentially curable provided they are detected early in their course [55].

Much of that early detection also points in the direction of communicable disease. Yet, in studies of impact and burden of disease, it is not always easy to distinguish between communicable and non-communicable diseases. More generally, evaluation of disease burden is complicated by overlapping between different diseases and conditions. For instance, it is estimated that 26% of cancers in developing countries can be attributed to infectious agents. Liver, cervical, bladder and stomach cancers are particularly linked to...
infections [11]. Consequently, it appears that preventing infection could have a significant downward impact on the prevalence and incidence of particular types of cancer. As evidence from developed countries suggests, to a certain extent, the cancer burden is unnecessary if barriers to cancer screening can be removed, resistance to physician visits overcome, and if culturally competent interventions to reduce smoking, unhealthy diet, and increasing proper exercise can be instituted [56].

The investment of capital in cancer-related intensive areas to develop resources should be a priority and progress accordingly with the growing need. At the same time, improved health care finance and better access to health services are needed in many countries facing the most severe burden of cancer incidence and mortality. The role of international initiatives could be substantial and could lead to targeted initiatives that would have significant impact at the local level. This would imply mobilization of resources at international level and the potential establishment of a Global Partnership for cancer to mirror the effect that similar initiatives have achieved in polio, malaria, tuberculosis and HIV/AIDS, among others.

concluding remark

Many cancer causes in developing countries are preventable, yet the burden of cancer incidence and death is rapidly and dramatically expanding. A number of factors are thought to be responsible for the shift toward increasing rates of malignancy in developing nations, including a transition to some of the lifestyle, diet, and environmental risks previously associated with highly developed societies. While the needs are many, the international community has coalesced around some key strategies for addressing the prevention and treatment of cancer by setting forth a clear and realistic vision for the future. There remain many sobering obstacles to the tremendous effort represented by this undertaking. Extensive investment at the global and local level will be needed to mount adequate responses to the growing pandemic of cancer.

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