Structural Barriers to Diagnosis and Treatment of Cancer in Low- and Middle-Income Countries: The Urgent Need for Scaling Up

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ABSTRACT

Noncommunicable diseases are now recognized by the United Nations and WHO as a major public health crisis. Cancer is a main part of this problem, and health care systems are facing a great challenge to improve cancer care, control costs, and increase systems efficiency. The disparity in access to care and outcomes between high-income countries and low- and middle-income countries is staggering. The reasons for this disparity include cost, access to care, manpower and training deficits, and a lack of awareness in the lay and medical communities. Diagnosis and treatment play an important role in this complex environment. In different regions and countries of the world, a variety of health care systems are in place, but most of them are fragmented or poorly coordinated. The need to scale up cancer care in the low- and middle-income countries is urgent, and this article reviews many of the structural mechanisms of the problem, describes the current situation, and proposes ways for improvement. The organization of cancer services is also included in the analysis.

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INTRODUCTION

Noncommunicable diseases are now recognized by the United Nations and WHO as a major public health crisis, and cancer care in low- and middle-income countries (LMICs) is now acknowledged as a global health priority.¹ As urbanization and conversion of the low-income populations to a Western style of life continues, the cancer rate continues to increase and will need to be matched by strengthening of the health systems of the low-income countries (LICs). In middle-income countries (MICs), cancer treatment centers exist, but most of them are located in urban areas. The disparity in access to care and outcomes between countries is staggering (Fig 1). The reasons for this disparity include cost, access to care, manpower and training deficits, and a lack of awareness in the lay and medical communities.² Many people have little understanding of cancer, and in some cultural environments, women are loath to admit to their husbands that they have noticed a lump in the breast or vaginal bleeding. This, coupled with the cost of transportation and treatment and, frequently, the failure of the primary health care provider to recognize the possibility of cancer, results in an unknown fraction of patients with cancer dying before reaching a treatment facility. Because of these barriers, diagnosis is usually late

(80% of patients are diagnosed at stage III and IV), such that the assumption that cancer is almost invariably fatal becomes a self-fulfilling prophecy.³ Before developing strategies to improve cancer care, however, it is essential to first establish what cancer health services exist on a country-by-country basis.

There are two important initial steps to begin to scale up cancer care in LMICs. One is to determine that adequate systems exist to evaluate the cancer burden, and the second is determining whether the resources are available to address the identified burden. The data from these two steps can be analyzed to determine specific barriers to care that need to be overcome when scaling up cancer control programs. Evaluating the existing cancer burden is challenging in most LMICs because of a paucity of cancer registries, and only recently has the International Agency for Research in Cancer attempted to change this. The Global Initiative for Cancer Registry Development is a project that intends to develop and improve cancer registries around the world.⁴ Most cancer burden data in LMICs are comprised of a series of summary statistics, such as those provided by Globocan.⁵ However, these statistics are averages that may be generated by registries in a handful of countries that are used to predict the cancer burden for an entire continent. Because of these reasons, policies may be directed toward a spurious average population that does not allow for potentially large

Fig 1. Global Human Development Index (HDI). Reproduced with permission from the International Agency for Research on Cancer, Wild CP: Cancer in the global NCD agenda: Is it enough? World Cancer Leaders' Summit, Cape Town, South Africa, November 18-19, 2013.

geographic differences in cancer incidence. The importance of equity has been underlined by the United Nations Development Program, which, for the first time, has incorporated a Coefficient of Inequality (IHDI) into its Human Development Index (HDI; Fig 2).⁶ The HDI and the IHDI are the same in circumstances of absolute equality, but the IHDI is reduced as inequality increases. The difference between the HDI and IHDI is known as the loss to human development as a result of inequality. The IHDI can lead to a better understanding of the inequalities across populations and inform policies designed to reduce inequalities.

There are several stages in the care of patients with cancer, including diagnosis, staging, treatment, follow-up, and palliation. In many LMICs, there are no physicians who specialize in any aspects of these stages of care. Data are of low quality because, in the poorer countries, there are few pathologists, and in some countries, regulation of pathology is weak such that unqualified people make many diagnoses. It is important to improve pathology resources and build capacities for better diagnosis at the technical and diagnostic level. There is also a need in some countries for not only population-based but also

hospital-based registries. This will provide a link between data collection, better diagnosis, and proper care. Naturally, all efforts for better diagnosis must have the necessary coordination with adequate access to care. Sometimes treatment is provided by a physician with little experience in cancer care, and it is common to have a surgeon both perform the surgery and prescribe chemotherapy. This paradigm is quite different from that in high-income countries (HICs), where medical oncologists administer chemotherapy.

In essentially all cancers, patients with localized disease have a better outcome, because in such circumstances, surgical removal or radiation therapy may well be sufficient to cure the patient, whereas with more advanced cancer, surgery and/or radiation therapy can be adjunctive at best. For this reason, early detection programs should be developed in close conjunction with improving treatment options so that patients diagnosed with a cancer may be treated with intent to cure. For specific cancers where low-technology techniques such as breast examination or visual inspection of the cervix are possible, early detection for those cancers should be built into cancer control plans. However, even when the tumor is locally advanced, a combination of chemotherapy and/or radiation or surgical therapy may still be able to achieve prolongation of survival or cure.

The development of national cancer control plans was recommended by the World Health Assembly in Resolution 58.22 and adopted in 2005.⁷ Ideally, most elements of cancer control, including prevention, screening, and early detection followed by prompt and accurate diagnosis and treatment (including palliative care), should be included. However, cancer treatment, the focus of the planned high-level meeting, is much more complex than prevention, requiring the development and delivery of treatment and assessment of response and survival, whereas prevention may require little or no disruption of daily life, and much can be accomplished by education of the public and health care providers.

Fig 2. Cancer burden by Human Development Index (HDI). Data compiled from Bray F, Jemal A, Grey N, et al: Global cancer transitions according to the Human Development Index (2008-2030): A population based study. *Lancet Oncol* 13:790-801, 2012.

THE NEED TO SCALE UP CANCER CARE IN LMICs

As countries develop, the all-cause mortality rate decreases rapidly, but cancer mortality increases because of increased exposure to carcinogens and the impact of common risk factors. However, this is a complex equation; as countries develop and introduce health

systems and screening, the incidence of cancer increases, but often of early cancers.

Globocan estimated that in 2012 there were 14.1 million new cancer cases and 8.2 million deaths in the world,³ and it predicts that the world cancer burden will increase by approximately 50%. In 2012, 57% (8 million) of the new cancer cases and 65% (5.3 million) of the cancer deaths occurred in the less developed regions where 85% of the world's population lives. The high mortality rate in LMICs compared with HICs and the increasing incidence of cancer demonstrate the need for upscaling. To overcome the three general barriers to cancer care (cost, education, and access), financial support must be organized by governments, whether in the form of insurance systems or government-subsidized hospitals capable of providing an appropriate level of care. The term capacity building may also be used in this context, identifying obstacles to achieve goals and testing potential solutions. Capacity building implies sufficient expertise available to undertake both tasks and to measure the outcomes of the implemented solutions. Capacity building also implies that upscaling is associated with a significant amount of research into which treatment approaches are optimal in a given setting and also research to identify the optimal approach to the implementation of the proposed solutions for obstacles identified. Data capture systems with both hospital-based data and data derived from clinical trials are needed.

UPSCALING

Scaling up cancer care requires first that a survey or a situation analysis be undertaken to determine the resources available for all aspects of cancer care, including facilities, equipment, systemic therapy, cancer experts, and infrastructural support. Particularly important is the number of oncologists, specialty surgeons, and radiotherapy centers who treat patients with malignancies relating to their specialty (eg, gynecology, orthopedics, ophthalmology). The issues and barriers that can be identified as relevant to upscaling include the following.

Affordability and Access to Care

Affordability and access to care are relevant to improving both cancer and general health care and necessary to ensure that a given population is able to access health care. Access can be improved by developing specific referral guidelines, educating the public, addressing the issue of traditional medicine, creating an ambulance service, and developing hospital/clinic networks. This is particularly important in many countries where big cities have highly developed health care structures while small cities or communities in the country have limited availability of services.^{8,9} In LICs, the first need is to have in place basic elements for better cancer control, whereas in MICs, the challenge is affordability, access to care, and fragmentation of services. According to Margaret Chan, WHO Director General, one of the priority goals is to promote universal health coverage worldwide to ensure that all people obtain the health services they need without suffering financial hardship. We consider it a vital role of governments and funding agencies to overcome these barriers.¹⁰

Cancer Specialists/Service Provision

One important issue is the creation or expansion of a health workforce dedicated to cancer. Ideally, cancer services should be delivered by a team of pharmacists, oncology nurses, junior doctors,

medical assistants, social workers, and specialist cancer doctors. It can be difficult to create such teams when there are no medical or surgical oncologists to take a leading role. A European Society for Medical Oncology survey (2006) reported that only 22 countries of the 39 respondents were able to state how many oncologists there were in the country. Of those countries that could provide figures, the number of oncologists varied markedly, with up to 3,000 new patients with cancer per year per oncologist.¹¹ If cancer treatment is to be improved, training more medical and surgical oncologists must be one of the priorities. If the number of oncologists is small or nonexistent, there is no alternative but to send suitable candidates to train in another country or to invite oncologists to train a number of oncologists locally. This is not always possible and is associated with the risk of migration, although technology now allows for online courses (eg, VUCCnet by International Atomic Energy Association [IAEA]).¹² The University of Lund has developed an online training course for radiation therapists,¹³ and this, supplemented by visits from other countries could well be enough to establish a radiation center, assuming the government, IAEA, and/or nongovernmental organizations have been able to provide the necessary equipment. Generalists, however, whether surgical or medical, could learn relatively easily how to manage some types of cancer. Job shifting, where nursing staff or volunteers take on a much larger role, can also be a great help in terms of ensuring the best use of the few oncologists' time. Another possible option is to train primary care physicians, establish a network of community doctors working in small local facilities, and implement a referral system to regional hospitals and reference cancer centers, according to each patient. This is the model of Plan Esperanza (Hope Plan) in Peru.¹⁴

Hands-On Training and Licensing

In low-resource countries, a partial solution for training is the apprenticeship system, whereby a trainee works with a recognized oncologist. In addition to an oncologist willing to train others, another option would be the creation of one or more national or regional organizations (colleges, academies, or boards) involved in cancer care but that are outside the university system. The academy/board may serve as an entity for developing examinations that must be passed to be recognized/licensed as an oncologist. In fact, the main systems of local education and training remain, with some exceptions, the universities, institutes, and local bodies that give an attendance certificate rather than certification in a specialty. This might be overcome by accepting certification by an international organization, such as the African Organization for Research and Treatment in Cancer,¹⁵ the Latin American and Caribbean Society of Medical Oncology,¹⁶ the Middle East Cancer Consortium,¹⁷ and the South and East Mediterranean College of Oncology.¹⁸ In MICs, training and licensing are performed by universities, scientific societies, and governmental bodies.

Migration of Health Workers

Health worker migration (eg, to private settings, from rural regions to urban, from one country to another) means that the workforce is often too small to provide effective care. Some countries at a midlevel of development may lose a high fraction of all of their trainees. Although the Organization for Economic Cooperation and Development and WHO have provided recommendations relating to

migration, they are not always followed.¹⁹ Improving working conditions and salaries is one way to prevent, lessen, or reverse worker migration. Of course, some workers only leave to acquire additional skills, attend meetings, learn through the observation of skilled professionals, or acquire new techniques.

Early Detection

It is critical to diagnose cancer as soon as possible. Optimally, this is before a patient develops symptoms or at least soon after the patient becomes symptomatic. This requires education of the public and primary caregivers with respect to the signs and symptoms of cancer. These investigations usually include biopsy of abnormal tissue and establishing a pathologic diagnosis. Early detection is important because when localized cancer is identified, treatment is generally less intensive, less toxic, and less expensive; requires fewer medical, nursing, and pharmacologic services; and results in an improved outcome. In addition, there is a higher likelihood of cure with an early diagnosis, and this creates a cadre of survivors of cancer who can become patient advocates.

Advanced Stage at Presentation

Most patients present with stage III or IV disease. Late detection is defined here as patients with disease that is beyond localized. To address this issue, the obstacles to early diagnosis must be identified. Economic obstacles may include the cost of transportation, cost of diagnosis, and loss of income. However, if patients are allowed to leave the treatment facility, they may fail to return to complete treatment.²⁰ Economic issues may be resolved by developing a program of training in a task that provides patients with income while away from home and sometimes when they return. Also, free accommodation close to the hospital may be a possible option.

In countries where health coverage exists, reasons for late diagnosis may be fear of the disease, delay in diagnosis as a result of system disruptions, lack of information, or complicated bureaucratic steps and complex or delayed referral mechanisms.

Accurate Diagnosis

One important aspect of accurate diagnosis is the availability of pathologists skilled in diagnosing cancers. This starts with adequate handling of tissues so that appropriate slides can be examined. Modern techniques use immunohistochemistry and often various molecular techniques because it may be difficult or impossible to diagnose some tumors without these methods. These techniques may be accessible only at some specialized referral centers. A major problem in LICs is the paucity of pathologists and the need to physically transport specimens, which causes delays and possible loss of specimens. Other challenges of obtaining high-quality functional pathology laboratory data in low-resource settings are availability of trained technicians and supplies maintenance. One action that may help is to establish algorithms for diagnostic approaches; this minimizes waste and cost and allows centers to decide which reagents and monoclonal antibodies they will keep in stock. Another possibility is to develop relationships between pathologists in country, and external universities or organizations can be of considerable help in improving techniques, training, and so on. Use of telepathology, such as iPath²¹ used by the International Network for Cancer Treatment and Research, may make consultations at a distance possible both within and between countries.

Staging

A fundamental component of proper cancer treatment is to evaluate the extent of disease. A standard staging system exists, the TNM system developed and updated by the International Union Against Cancer. However, many cancers are staged by systems designed specifically for them. Depending on equipment and resources, optimal staging can include ultrasound, x-rays, computed tomography, magnetic resonance imaging, positron emission tomography, and surgical procedures. Such staging systems may or may not be feasible in LMICs or may be only partly feasible or used only in a small number of institutions. Tiered staging recommendations are important to adapt staging strategies to resource-appropriate levels. Inadequate staging may lead to the wrong treatment and also make comparisons between treatment centers difficult.

Treatment

Multiple approaches to treatment exist, including all modalities (surgery, radiation, systemic therapy, or combinations). In the least developed countries, access to care, whether radiation, surgery, or systemic therapy, may be nonexistent (only 10% of Africans have access to radiation according to IAEA). Naturally, there are important differences with respect to treatment between LICs (lack of basic treatment modalities) and MICs (where resources and facilities exist and the usual problem is access to care). Most cancer centers in LMICs use modified treatment regimens derived from those used in HICs, but they often have not been studied in LMICs. When multiple modalities are used, multidisciplinary committees should determine therapy. Ideally, there should be a standard therapy in use in the country to ensure that all patients, even if treated by a nononcologist, receive acceptable, standard therapy. This implies collaboration among hospital networks and availability of all required modalities and anticancer drugs at all facilities where patients will be treated.

Surgery is often not considered a component of global health. This is beginning to change as studies have shown that surgery is cost effective and there is a large unmet burden of surgical disease.²² In many LMICs, surgeons are the only physicians patients with a tumor will meet. With cancers of the breast, cervix, stomach, colon/rectum, and prostate, for example, it is often a general surgeon, gynecologist, or urologist who provides all surgical and nonsurgical treatments, including chemotherapy. This is quite different than the treatment paradigm in HICs. Building a cancer control policy or cancer centers without parallel development of surgical capacity can create an imbalanced system of access to cancer care. Although one goal of upscaling cancer care should focus on establishing medical oncologists in LMICs, it is imperative that surgeons are also involved in cancer control planning and training efforts.

Supportive Care

Cancer treatment centers must be able to prevent or treat acute or chronic complications of cancer or its treatment. Supportive care may include antiemetics, hydration fluids, access to blood products for transfusion, antibiotics, analgesics, and a range of medications for the control of other symptoms.²³ Psychosocial and spiritual support is an important element of the overall support required by patients undergoing therapy for cancer. Social support may also entail economic support.

Palliative Care

Many experts now consider palliative care to begin with the diagnosis of cancer and to include symptom control before and after treatment as well as end-of-life care. An attempt should be made to develop pain-free hospitals and to provide adequate opiate access and integration of palliative care into the health care system.

Pharmacist

Anticancer drugs can be dangerous to the person making up the doses for patients, and laminar flow or sufficient ventilation conditions that protect the individual preparing unit dosages should be available. Good records are essential for drug use so that ordering can be timely to avoid inappropriate gaps in treatment. Pharmacists can also maximize use of multidose vials.

Essential Drug List for Cancer

The WHO Essential Medicines List is composed of a set of medicines that “satisfy the priority health care needs of the population.”²⁴ Drug prices may vary enormously between countries; some pharmaceutical companies in LMICs charge higher prices than in HICs, and corruption within the system is common. The method of identifying essential drugs may also need to be considered. In the poorest countries, most drugs must be imported, and their value may be, to some extent, determined by who orders the drugs and who pays for them.

Data Capture

With respect to observational or research studies, it is important to collect data about late presentation or diagnosis, infrastructure of cancer hospitals or units, toxicity, and efficacy of therapy, as well as late effects, rehabilitation, adherence to treatment protocols, and so on. Today, this type of information is not readily available in many countries. Similarly, the existence of local data is important for planning and organization of cancer care and health services. Good and useful data can be obtained from hospital databases, if available.

Follow-Up

Patient follow-up has two main functions. First, after completing treatment, many patients may be at risk for recurrent disease. Follow-up allows for continued care and also for determination of recurrence and survival rates. In many of the LMICs, follow-up is haphazard, and patients often fail to return for appointments. Depending on the disease, follow-up can lead to earlier detection of recurrent disease, although there is limited, if any, formal evidence that detecting recurrent disease early has any advantages. Because some diseases may relapse late, decisions have to be made regarding the intervals between follow-up visits. Second, follow-up is also used to detect late effects.

Fertility may be impaired with many chemotherapy regimens, and in young people who develop cancer before having a family, measures may be taken to assist patients to have families (eg, sperm banking in males). Without follow-up, late effects from therapy (eg, low fertility, second malignancy, physical disability, psychological or CNS effects) may not be recognized, and regimens associated with severe late toxicity will not be identified. Noting the late effects that occur (that may strongly influence both survival and quality of life) becomes increasingly important to treatment design as the survival rate increases.

Research

Research is a basic element of the primary goals of an oncology program in any country. Various types of research may be required (eg, epidemiologic, basic, implementation), but central to all is clinical research, which is designed to increase the survival rate and reduce toxicity. Clinical research requires that oncologists have some training in research and for data managers to be available. Research can answer important questions regarding treatment effectiveness compared with toxicity, modification of treatment regimens, and the implementation of treatment guidelines or protocols. Ethical approval for clinical research is essential. The extent to which this is directed by the government or cancer control committee or is left to universities or independent groups and cancer centers to decide is likely to differ from country to country, particularly relating to resources.²⁵⁻²⁷ It becomes of major importance to search for how to get best value from cancer care (ie, the best total outcome of care in relation to costs). Such research would be beneficial not only for LMICs but all countries. Hence, it would be a win-win scientific approach. The usual model for clinical research in developed countries has pharmaceutical companies playing a mayor role. Publicly funded, nongovernmental source, private sector, university, and hybrid models are innovative options in low-resource settings.²⁷

Economic Issues

Economic issues are important to all aspects of cancer treatment including cost of diagnosis, hospitalization, anticancer drugs, other medicines required, transportation, and other facilities such as radiotherapy centers. Governments may weigh the cost of treatment of patients with cancer against economic loss, as well as the effect of financial support on the fraction of potentially curable patients who complete all required treatment. Health insurance that includes cancer may cost less than might be expected because of the lower incidence of cancer in LMICs and the fact that the cost of many anticancer drugs may not be as high as anticipated because, today, many are generics. In addition, maximizing the cure rate may lead to less economic loss from patients leaving the workforce. Early diagnosis may mean that patients require much less therapy, which is cheaper, less toxic, and more successful, in localized cancer than when cancer is diagnosed later and the tumor is more advanced (where treatment costs are higher and outcome worse).²⁸

ORGANIZATION OF CANCER SERVICES

At present, in many LMICs, cancer services are unorganized or fragmented, as in the case of Latin American countries.²⁹ There may be no cancer institute and often no specialists or experts (or only a small and insufficient number). As part of the cancer control plan, the structuring and coordination of cancer services should be addressed. The first question is how patients with cancer will be identified, and the answer should be via primary health care services. In many LMICs, primary care doctors are key in the structure of the health care system. Some secondary-level hospitals may have cancer units capable of providing treatment to a significant proportion of patients with limited-stage cancer. Patients diagnosed with cancer who cannot be treated at the secondary level are referred to a treatment center.

If there is a major cancer center in the region, it is important to establish referral patterns and possibly systems that enable transportation from a noncancer hospital to the cancer hospital. Major cancer centers, as discussed earlier, may also provide training for oncologists and other health workers involved in cancer care. Where there are no medical oncologists, major regional hospitals may endeavor to treat at least some cancers. Within the country, it may be possible to provide additional training to specialists and general surgeons such that they are able to treat patients with cancer. The government may require centers to meet certain requirements to be designated as a cancer center. In addition to the treatment centers, an institute may be designated as the national cancer institute, which is given authority by the government to develop the cancer program for the entire country and works with regional centers to audit, coordinate, and monitor the delivery of care at a national level. The institute may or may not deliver patient care and may be a primary location of basic research relating to cancer, depending on available resources.

As the need for improved cancer care rapidly expands in LMICs, it is vital that countries develop methods for scaling up cancer care.

This requires accurate estimates of the burden of cancer, identification of available cancer treatment resources, and plans to overcome burdens to cancer care. This will require a coordinated global effort to address the financial, medical, and social obstacles that face patients with cancer in LMICs.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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