

Access to Cancer Treatment in Low- and Middle-Income Countries

An Essential Part of Global Cancer Control

A CanTreat Position Paper



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Cancer is exacting severe costs from societies that are wholly unprepared to address it, and this toll will become even heavier in future years.

By 2020, cancer is expected to kill more than twice as many people worldwide as it did at the turn of the millennium. In low- and middle-income countries, however, the death rate will be more than five times greater than in the industrialized world. Already, more than half a million women in low- and middle-income countries die from breast or cervical cancer alone each year (Garcia et al., 2007). The poorer regions of the world also account for more than 90% of cervical cancer cases worldwide (WHO, 2006).

While global concern about health inequities is growing, very little attention has been focused on the rapidly increasing toll of cancer in developing countries. Today, an individual's odds of surviving cancer — or even of receiving any type of treatment, including basic palliative care — are strongly correlated with where that person lives. Whereas in the USA the five-year survival rate for patients with breast cancer is 84%, in The Gambia, a country where no cancer diagnosis has a five-year survival rate higher than 22%, breast cancer survival is just 12% (Sankaranarayanan R et al., 2010). Cure rates for childhood cancer hover around 75% in high-income countries, but fall to 10–15% in low-income countries. Each year, some 100,000 children die needlessly because they lack access to existing cancer treatments (Katikireddi, 2004).

Managing cancer requires a strategic and comprehensive approach across the entire cancer control spectrum that combines effective prevention with meaningful and timely access to cost-effective treatments, including palliative care, that can either cure the disease or significantly extend and/or improve quality of life. In high-income countries, new cancer-fighting tools and improved medical management strategies have resulted in notable declines in cancer mortality rates (Edwards et al., 2010). Gains in cancer survival do not always require expensive treatments. Increases in cancer survival have been achieved through the use of relatively low cost, often generic, cancer treatments or through radiotherapy. The treatments that have truly revolutionized cancer care and lowered cancer death rates in high-income countries, however, remain largely unavailable in many middle- and low-income settings.

This report proposes the launch of a long-term strategy to eliminate disparities in global cancer outcomes between rich and poor nations. Every patient — regardless of where he or she is born — deserves an equal chance at a long life and good health (Seffrin, 2008).

The Growing Cancer Threat in Low- and Middle-Income Countries

The magnitude of present and future cancer mortality will be directly related to the effectiveness of efforts to prevent, control and treat cancer, particularly in the developing world.

Today, cancer accounts for approximately one in every eight deaths globally (WHO, 2008) and more than half of the global cancer burden is found in low- and middle-income countries (Garcia et al., 2007). If the annual increase in cancer incidence continues at the present rate (depending on exposure to risk factors and access to treatment) it is predicted that by 2030 more than 26 million incident cancer cases will occur each year – more than double the 12.4 million new cancer cases in 2008 (WHO, 2008). Of these, some 70% will occur in low- and middle-income countries (Barton et al., 2006). By 2050, it is projected that low-income countries alone will account for up to three-quarters of all cancer deaths (Cavalli, 2006).

There are several reasons – many of them interrelated – why the long-term burdens associated with cancer and other chronic diseases in developing countries are certain to rise.

First, the world's population is projected to exceed 8 billion by 2030, with the sharpest increases projected in low- and middle-income countries (WHO, 2008). A growing population will inevitably lead to an increase in the cancer burden.

Secondly, a rapid ageing of national populations is also forecast, especially as countries continue to experience progress in combating diseases that have resulted in substantial premature death. In China alone, life expectancy has increased by two-thirds in the last 40 years (WHO, 2008). This demographic evolution will inevitably lead to increases in cancer, which is more commonly diagnosed among older people (Bray, Moller, 2006).

Thirdly, as developing economies grow, national populations become more susceptible to chronic diseases associated with affluence (WHO, 2009; Cavalli, 2006). In China and Latin America, parts of the world that have experienced notable economic advances in

recent decades, annual cancer incidence is increasing (WHO, 2008). Obesity is rising in all income strata in low- and middle-income countries, bringing with it increased risk of cancer, heart disease and other chronic diseases (Nugent, 2008). Experts foresee a marked increase in tobacco use in developing countries in coming decades (WHO, 2009b). Excessive alcohol intake, another risk factor for many cancers, is a particular problem in many developing regions, including sub-Saharan Africa and Eastern Europe.

Communicable diseases also contribute to the cancer burden in many developing countries. WHO reports that cancers related to seven infectious agents – including hepatitis, human papillomavirus, *h. pylori* and blood and liver flukes – together account for 18% of global cancer deaths, and disproportionately impact low- and middle-income countries (WHO, 2009b). In some countries, high prevalence of HIV is also driving increases in certain cancers such as Kaposi's sarcoma, non-Hodgkin lymphoma and invasive cervical cancer (Silverberg et al., 2009).

The urgency of addressing the rapidly growing cancer crisis in developing countries cannot be overstated. In addition to the extraordinary and rapidly growing human toll, cancer and other chronic diseases are an under-appreciated cause of poverty and an impediment to economic development (WHO, 2005). As the Commission on Macroeconomics and Health found: "Societies with a heavy burden of disease tend to experience a multiplicity of severe impediments to economic progress. Conversely, several of the great 'take-offs' in economic history . . . were supported by important breakthroughs in public health, disease control, and improved nutritional intake . . ." (Commission on Macroeconomics and Health, 2001). With cancer rates steadily rising in low- and middle-income countries, the disease will inevitably frustrate global development efforts unless urgent action is taken.

Cancer in Low- and Middle-Income Countries: A Diverse, Evolving Challenge

Lung cancer is the most commonly diagnosed cancer in low- and middle-income countries and the single most significant cause of cancer-related death (GLOBOCAN, 2008; Institutes of Medicine, 2007). After lung cancer, leading causes of cancer-related mortality in low- and middle-income countries are cancers of the liver, stomach, esophagus, colorectum and prostate (GLOBOCAN, 2008).

As in high-income countries, breast cancer is the most frequently diagnosed cancer in women in low- and middle-income countries (GLOBOCAN, 2008; Institutes of Medicine, 2007). The other leading causes of cancer-related mortality among women in developing countries are cancer of the cervix, lung, colorectum, stomach and liver (GLOBOCAN, 2008).

Particular cancers vary in their contribution to incident cancer diagnoses and cancer deaths.

For example, while the number of breast cancer diagnoses in low- and middle-income countries is roughly 50% greater each year than the number of cervical cancer cases, the two cancers cause roughly equivalent numbers of deaths (GLOBOCAN, 2008). Likewise, while more cases of stomach cancer are diagnosed each year in men than liver cancer, the latter is responsible for more deaths among men (GLOBOCAN, 2008).

Given the association of many cancers with environmental factors, the epidemiology of cancer varies considerably between regions. For example, whereas lung cancer is the leading cancer diagnosis among men in Southeast Asia, the Western Pacific and the Eastern Mediterranean, prostate cancer is the number one diagnosis among men in Africa, the Americas and Eastern Europe (GLOBOCAN, 2008)



A Timid Global Response to Cancer

Despite the urgency of the cancer crisis in developing countries, the international community has been slow to respond. Although low- and middle-income countries account for more than half of the global cancer burden, they attract a far lower proportion of global cancer spending.

For other priority diseases that affect developing countries, the world has established concrete targets and used these goals to drive progress. In the case of HIV, for example, all countries have committed to achieve universal access to HIV prevention, treatment, care and support by 2010 (Political Declaration of Commitment on HIV/AIDS, 2006) and to reverse the global epidemic by 2015 (Millennium Development Goal 6). This has not been the case for cancer, which for many years has been largely overlooked in international commitments to health and development. No Millennium Development Goal currently addresses the growing toll from cancer and other chronic diseases in developing countries. And while encouraging steps have been taken more recently to increase attention to the urgent health needs of developing countries, the global pronouncements on cancer that do exist set forth few meaningful targets. Although the World Cancer Declaration reflects growing global recognition of the need to address the cancer threat in developing countries, the Declaration proposes merely that “appropriate” cancer treatments “will have improved for all patients worldwide” by 2020 (International Union Against Cancer. World Cancer Declaration. In <http://www.uicc.org/declaration>, <http://www.uicc.org/declaration>, last accessed July 14th, 2010).

Much more needs to be done. In September 2011, the United Nations will convene a summit meeting of heads of state to examine the looming challenges posed by non-communicable chronic diseases such as cancer, heart disease, diabetes and chronic respiratory disease. In the run-up to the meeting, organizers are working to develop chronic disease indicators for the Millennium Development Goals and their successor, and to jump-start a global movement to combat chronic diseases and strengthen health systems. One of the issues to be addressed at the meeting is access to essential medicines.

But these more hopeful efforts represent just the bare beginning of the kind of high-level, generations-long global mobilization that the cancer crisis merits. The global community must embark on a major long-term advocacy effort to equalize global cancer outcomes. A major step forward would involve immediate action to introduce affordable cancer treatment options and advocate for improved standards for cancer treatment in countries where these treatment options are currently unavailable.

Mobilizing Resources to Bring Cancer Treatments to Developing Countries

As in the case of AIDS, considerable financial outlays will be required to reverse the legacy of neglect of the cancer crisis in low- and middle-income countries. When considered against the scale and rapid growth of the crisis, however, the financial and technical resources that will be required to introduce cancer treatments in resource-limited settings are wholly manageable.

Placing the resource needs for cancer control in perspective is helpful. The US\$26 billion that would be required annually to equalize global outcomes for breast cancer (Breast cancer in developing countries, *Lancet*, 2009) would represent barely half the amount consumers spent in 2009 on video games (Wu, 2010) and less than 2% of annual global spending on armaments (Stockholm International Peace Research Institute, 2009).

Moreover, the costs of continued inaction are enormous. Without concerted efforts to address the growing cancer crisis, the rapidly increasing toll of cancer-related illness and death will continue to mount, placing unsustainable burdens on resource-limited countries. In the absence of effective action, global health disparities will widen, and low-income countries will be consigned to a future in which the fruits of globalization remain out of reach.

A Global Push For Cancer Control: Why Treatment Is Essential

Recent years have brought the beginnings of greater awareness of the cancer challenge (Moving cancer up the global health agenda, *Lancet*, 2010). With minimal resources devoted to cancer control and with effective treatments largely non-existent in many parts of the world, however, these steps are but the beginning.

The history of AIDS teaches that partial responses to complex health challenges are doomed to fail. In the case of cancer, only a comprehensive approach that combines public education including stigma reduction, early diagnosis and access to effective treatment and care will succeed.

Prevention is the first line of defense against cancer. A number of important global cancer prevention initiatives are beginning to take root. A worldwide push is underway to address rising tobacco use in low- and middle-income countries (WHO, 2009b). The Global Alliance for Vaccines and Immunization is scaling up efforts to deliver vaccines for hepatitis B and human papillomavirus, which in turn will help lower rates of liver and cervical cancer. These prevention efforts are critical, but they will not suffice on their own.

Scaling up cancer treatment is an essential pillar of a comprehensive response to rising cancer rates. Even with aggressive application of the best available prevention strategies, however, tens of millions of

new cancer cases will be diagnosed over the coming decades in low- and middle-income countries, making a prevention-only approach a recipe for failure. In the absence of treatment, individuals have little incentive to be screened or to seek health services. Without the prospect of treatment access, cancer will remain a stigmatized diagnosis, widely perceived as tantamount to a death sentence. Access to effective cancer treatment remains a significant missing piece in the puzzle.

As experience in AIDS has demonstrated, treatment can enable more effective prevention, and prevention makes treatment affordable (Salomon, 2005). Treatment is also essential to involving families, communities, religious groups, labor unions and employers in a common effort to promote good health (See text box on “Lessons from the global AIDS response.”). Given the low priority accorded cancer control to date in resource-limited settings, treatment access will be essential to build the strong, sustained awareness and public support that will be required to reverse the upward trend in cancer burdens in developing countries. To be effective, cancer treatment services must be comprehensive, encompassing preventive interventions to remove precancerous tissue, timely care in the early stages of cancer, effective treatment for more invasive cancer and palliative care whenever indicated and needed (Reeler et al., 2008).

Lessons from the Global AIDS Response

The global AIDS response provides an important precedent for the truly global campaign needed to combat cancer. While differences in the epidemiology, pathology and social context of cancer and AIDS mean that lessons from one disease are not automatically applicable to the other, many lessons of the AIDS epidemic are directly relevant to the global cancer challenge, and are worth heeding.

Advocates for global access to AIDS treatment demonstrated the feasibility of introducing complex chronic disease management strategies in resource-limited settings with weak health systems. By the end of 2008, 4 million people in low- and middle-income countries were receiving antiretroviral therapies — a 10-fold increase in only five years (WHO et al., 2009).

Several elements have driven the historic successes achieved on the AIDS front. First, international donors opened their pocketbooks, recognizing the epidemic's potential to erase decades of development gains. In 2008, US\$ 15.6 billion was available for AIDS programs in low- and middle-income countries — a 50-fold increase over amounts spent in 1996 (UNAIDS, 2009b). The leading provider of AIDS assistance is the U.S. government, with its President's Emergency Plan for AIDS Relief (PEPFAR) representing the largest health program ever enacted for a single disease.

The AIDS response also recognized treatment as an essential component of an effective long-term strategy to reduce the impact of the epidemic. Without treatment, individuals had little incentive to learn their HIV status or even take steps to reduce their risk. Following the advent of broad AIDS treatment access, the percentage of individuals in low-income countries reporting having ever been tested for HIV rose from 15% in 2005–2006 to 39% in 2007–2008 (WHO et al., 2009).

Increased access to AIDS treatment was made possible by dramatic declines in the prices of standard antiretroviral drugs in low- and middle-income countries. Numerous factors contributed to these unprecedented price declines. Through the Accelerating Access Initiative, major pharmaceutical companies agreed to tiered pricing for their patented AIDS medicines, permitting low-income countries to obtain drugs at significantly reduced prices. Generic manufacturers began supplying countries with high-quality, low-cost antiretroviral compounds. And where particular shortages existed — such as with antiretroviral formulations suitable for paediatric treatment — influential stakeholders such as the William J. Clinton Foundation and UNITAID stepped in to facilitate access to affordable products.

The AIDS response also recognized that access to treatment was not likely to be sustainable without long-term efforts to buttress health systems. Accordingly, international partners have worked with countries to build robust national systems for strategic information, introduced task-shifting to expand human capacity in clinical settings and undertaken focused training, mentorship programs, institutional twinning and other strategies to build the capacity of local clinicians to manage HIV disease.

Another important feature of the AIDS response is the transformative role of advocacy and activism, including the involvement of people directly affected by the disease. Eschewing a top-down approach, the global AIDS response actively involved and empowered affected communities, faith-based groups and, in many cases, individuals diagnosed with the disease and their families. Especially in high-burden settings, AIDS has become a fight embraced by people from every walk of life.

Key Elements of a Comprehensive Response to Cancer

It is time for a historic push to address the looming cancer crisis. The remainder of this report outlines elements of a proposed comprehensive response to cancer that includes:

- National planning based on quality epidemiology and strategic information;
- Health systems strengthening and improved provider training;
- Improved education of health professionals and the public to enable early cancer detection and increase positive treatment outcomes;
- A focus on early diagnosis, which greatly increases the benefits of treatment and reduces treatment costs;
- Access to traditional treatment approaches including chemotherapy, hormonal therapy, radiotherapy and surgery, as well as to quality palliative care;
- Access to newer, targeted therapies made possible by creative strategies to lower treatment costs and increase treatment access.

Improving Strategic Information

Knowledge is power. Unfortunately, when it comes to cancer control in low- and middle-income countries, knowledge is shockingly scarce.

As recently as 2000, less than 20% of the world's population lived in a country with a cancer registry, and only 35% resided in a jurisdiction that systematically monitored the cause of deaths (WHO, 2008). Among 56 African countries, fewer than ten routinely track cancer incidence, cancer mortality or cancer patient survival (Kanovos, 2006). The picture is only marginally brighter in Asia, where fewer than one in three countries collect data on cancer incidence, and only about one in six monitor cancer mortality (Kanovos, 2006).

These deficits undermine efforts to improve cancer outcomes in developing countries. Lacking strategic information on national cancer burden, policy-makers often remain unaware of the cancer toll in their country. Unable to identify priority cancers or problematic survival patterns, public health agencies lack the means to develop evidence-based prevention and treatment programs for cancer.

Assembled in Cape Town in 2006 to examine the cancer toll in the region, African leaders acknowledged the need to establish cancer registries in all countries.

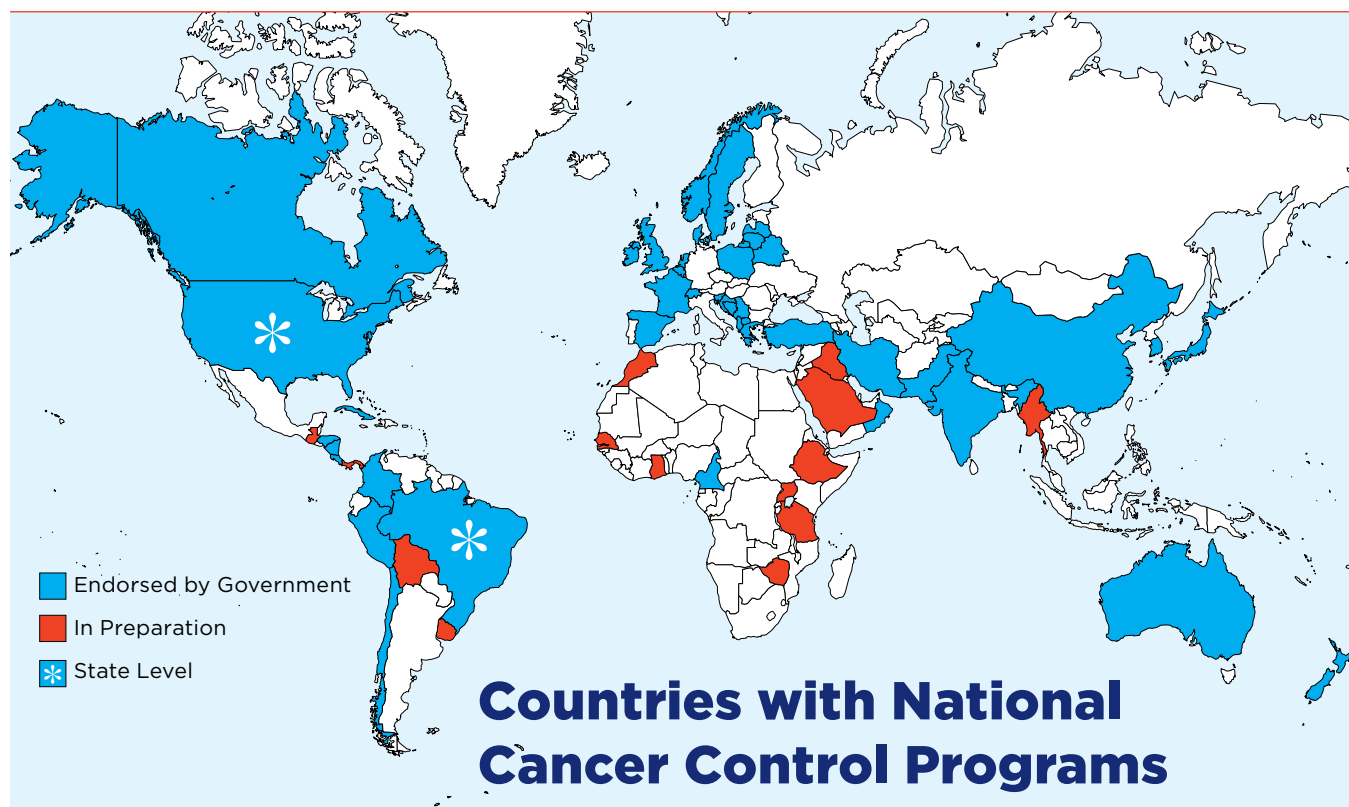
Regional leaders pledged to work collaboratively with WHO's International Agency for Research on Cancer to establish cancer registries in strategic locations.

Follow-through on such pledges is essential. International donors and technical agencies should intensify assistance to help countries plan and implement cancer information systems. And focused training programs are needed to equip country staff with the data collection and analytic skills needed to put cancer data to effective use.

National Planning for Cancer Control

A critical first step in strengthening cancer control efforts is to ensure that every country has a national strategic plan to address cancer. To date, most countries have failed to develop such a plan. As of December 2006, only two African countries had national cancer control plans in place (Cape Town Declaration, 2006).

National cancer plans play a pivotal role in strengthening cancer control efforts, increasing accountability, building national policies and programs and coordinating the efforts of diverse stakeholders. Again experience in the AIDS response is instructive.



Source: Sepulveda,WHO; International Cancer Control Congress 2009: "National Cancer Control Programmes Capacity Assessment" presentation

Virtually every low- and middle-income country now has a national strategic plan in place to guide responses to HIV/AIDS (UNAIDS, 2008). The World Bank has established a dedicated technical service to aid countries in reviewing and strengthening their national AIDS strategies. More than 100 countries have adopted specific outcome targets for AIDS prevention and treatment (UNAIDS, 2009a). And every two years, countries are required to report on their progress toward these national targets.

Of course, no plan is likely to be effective if it is not adequately funded and implemented. Yet experience in the AIDS epidemic suggests that the development of a national strategy is an important sign of political support. The existence of a sound national plan also provides an ideal platform for mobilizing domestic and international resources.

A similar effort is needed for cancer, which causes far more deaths each year than AIDS. The World Health Organization advises all countries to develop national cancer diagnostic and treatment guidelines that provide for a minimum standard of care and promote equity in treatment access (WHO, 2002). The Institute of Medicine recommends that national cancer plans be reviewed

and updated every three to five years, taking account of new research developments and emerging opportunities to introduce effective preventive or therapeutic interventions that may previously have been unavailable (Institute of Medicine, 2007).

In their 2007 report, the IOM observes that the causes of and outcomes for cancer in developing countries are different from conditions in affluent, economically developed countries such that a "one-size-fits-all" solution for national cancer control plans is impractical for the developing world (IOM, 2007). Instead, IOM recommends that resource-appropriate strategies be employed to combat and control cancer, profiling the evidence-based, expert consensus guidelines of the Breast Health Global Initiative (BHGI) as a paradigm for developing comprehensive resource-sensitive, evidence-based clinical guidelines for the management of major treatable cancers (Anderson, 2006). As an ongoing public-private global health alliance devoted to address the healthcare needs of medically underserved women, the BHGI has pioneered the development of expert consensus guidelines to outline realistic approaches for breast cancer early detection, diagnosis, and treatment in low and middle income countries (LMCs) to assist ministers of health, policy makers, health care

institutions and others to prioritize resource allocation in breast care programs in LMIC (Anderson, 2009). Since then, guidelines following the BHGI resource-stratified methodology have been developed for other solid cancers including head and neck cancer (Wee, 2009), hepatocellular carcinoma (Poon, 2009), non-small cell lung cancer (Soo, 2009) and endometrial cancer (Tangjitgamol, 2009).

Strengthening Health Systems to Deliver Life-Saving Cancer Treatments

A robust, flexible, well-functioning health system is the *sine qua non* of cancer control. Especially for chronic diseases that affect broad swathes of the population, mainstream health systems must be prepared to deliver timely, high-quality preventive, diagnostic and therapeutic services for cancer. In a comparative study of 12 countries in Africa, Asia and Central America, disparities in cancer outcomes correlated with the level of development of health services (Sankaranarayanan R. et al., 2010).

Poorly developed technical infrastructure and an insufficient number of clinicians trained in the delivery of cancer treatment impede the ability of many low- and middle-income countries to improve medical outcomes for cancer patients (Anderson et al., 2008). Though the picture varies considerably from one country to another, many people in low- and middle-income countries have limited access to clinics, and the number of doctors and nurses to serve populations is often severely inadequate. In every low- to middle-income region, pathologists able to provide accurate diagnoses and staging of cancers are in short supply. Laboratory facilities, equipment and technicians to provide screening programs and radiotherapy services for treating cancers fall far short of need, with some African countries lacking such services altogether (Kavanos P., 2006).

Increased medical training is key. Recommended strategies to improve the availability of medical training programs include the creation of regional cancer training networks to build capacity for the delivery of cancer care in low-income countries (Cape Town Declaration, 2006) and the establishment of cancer “centers of excellence” (Institute of Medicine, 2007).



In Recife, Brazil, for example, the establishment in 1994 of a multi-disciplinary paediatric oncology program led to a steady improvement in clinical outcomes for children with cancer. Compared to the 1980s, five-year survival rates for children treated at the Recife hospital rose from 32% to 63% in 1997–2002 (Howard et al., 2004). Institutional “twinning,” in which networks of referral, information and support are established between institutions with well-developed cancer capacities and those without, has also proved successful in expanding clinical capacity to treat childhood cancer (Ribeiro, Rigo, 2006). Another example of a timely initiative to build capacity for cancer treatment is the Virtual University and regional Training Network Initiative of the International Atomic Energy Agency’s Programme of Action for Cancer Therapy (IAEA/PACT), which uses a virtual university approach to provide training for cancer control in Africa. The vuccnet

program will combine on-line virtual education with on-the-ground training targeting the specific educational requirements of low-resource countries.

In Ghana, the Breast Health Global Initiative (BHGI) has implemented the BHGI resource-stratified guidelines (Anderson, 2008) through the creation of collaborative “Learning Laboratories” that concentrate on the strategic establishment or expansion of breast cancer care programs in LMCs (www.bhgi.info). Working with HopeXchange, the Ghana Breast Cancer Alliance, the Komfo Anokye Teaching Hospital in Kumasi and the Korle-Bu Teaching Hospital in Accra, BHGI is now operating breast cancer specialty training courses in the major cities of Ghana. Through these courses, BHGI has developed a specialized resource-appropriate curriculum targeting the educational needs of healthcare professionals and civil society NGOs regarding the early detection, diagnosis and treatment of breast cancer. IAEA/PACT is now collaborating with BHGI to expand the reach, progress and outcomes of the BHGI Learning Laboratories by adopting the BHGI Ghana curriculum onto VUCCnet. The curriculum currently in use on a pilot project basis in Ghana will soon be accessible in three additional African countries, now in pilot phase for VUCCnet: Tanzania, Uganda and Zambia.

At the same time that these and other educational efforts are made to extend existing human resources as far as possible, another important concern is the so-called ‘brain drain’ of skilled workers who migrate to take better paid jobs outside their home countries. In developing health workforce plans, action must be taken to minimize the potentially negative impact of this phenomenon on countries with already limited resources (World Health Organization, 2006b).

While the need to expand specialist capacity is critical, evidence has also shown that a number of low-technology interventions that can be carried out by trained health staff in primary health care settings significantly contribute to improving cancer survival. For example, a pilot program in Malaysia reduced the percentage of late-stage presentations of breast cancers from 77% to 37% through public awareness campaigns and the training of health staff in clinical breast cancer examination (Devi et al, 2007). Cervical cancer can be effectively prevented through vaccination and diagnosed through simple screening techniques, although even such simple techniques can be challenging in a resource-

constrained developing country environment. Screening a woman once only between the ages of 35 and 40 reduces her lifetime risk of cervical cancer by 25–36% (Goldie et al., 2005). If detected early, cervical cancer can also be treated in a primary healthcare facility by cryotherapy, a procedure that freezes and destroys diseased tissue. Cryotherapy is simple and inexpensive, does not require electricity, can be successfully administered by nurses and is more than 90% effective for cancer diagnosed at early pre-malignant stages (Luciani, et al., 2010; Sankaranarayanan R et al., 2007).

Addressing the cancer epidemic in low- and middle-income countries will require a public health approach that identifies what can be done to diagnose and treat cancers more effectively at each level of the health system. Experience in the response to diseases such as HIV has shown that such interventions should be integrated with other health and social welfare services in order to maximize their benefits and the number of people who can access them. Lessons learned from these experiences can help define country-specific plans that mainstream cancer services in ways that also strengthen health systems overall.

Timely Diagnosis of Cancer in Low- and Middle-Income Countries

On average, cancer is diagnosed much later in resource-limited settings than in high-income countries. It is estimated that up to 80% of cancers in low- and middle-income countries may be incurable by the time they are diagnosed (Institute of Medicine, 2007). Comparative international studies indicate that late diagnosis accounts for a substantial share of sub-optimal cancer outcomes in developing countries (Sankaranarayanan R et al., 2010), although it is far from the only barrier to better cancer outcomes. According to studies in Latin America, timely diagnosis alone cannot make up for the negative impact of the limited availability of cancer prevention interventions in the first place (Cazap et al., 2008).

Early diagnosis of cancer is critical to improving medical outcomes, especially in settings where expensive, state-of-the-art interventions may not be available to treat late-stage cancers. To generate population-level improvements in cancer outcomes, programs should include appropriate education to drive awareness and

interest among people at risk, and should achieve high coverage by using the mainstream health care system to provide information and education. Screening programs, where relevant, should rely on high quality screening tests and be linked to timely follow-up care (WHO, 2006). Not all screening programs, (i.e. mammography screening or breast self-exam) have been validated as efficient and cost-effective. More evidence needs to be collected and analyzed before scarce resources in developing countries are allocated to such efforts.

Ethiopia's efforts to improve breast cancer outcomes offer valuable insights regarding promotion of earlier cancer diagnosis. A recent study found that low levels of cancer awareness and late diagnosis in Ethiopia contribute to suboptimal health outcomes, underscoring the importance of coupling technical initiatives to build diagnostic capacity with public education campaigns to reduce stigma, help individuals avoid cancer risks and motivate them to seek diagnostic screening. The study also highlights the need for careful system planning and streamlining to avoid delays in cancer diagnosis and linkage to care. In Ethiopia – where health service delivery is often fragmented and where many patients first consult traditional healers – cancer patients typically go through three or more care channels before they reach the hospital they need (Dye, 2010).

Other studies suggest that some screening techniques for certain treatable cancers – such as colorectal or cervical cancer – may meet recognized cost-effectiveness criteria in low- and middle-income countries (Brown et al., 2006). In a number of cases, low-tech, more affordable alternatives exist to expensive, state-of-the-art screening methods routinely used in high-income countries. Advances in affordable screening options for cervical cancer, for example, include direct visualization of precancerous lesions (either with coloration with acetic acid or with Lugol's iodine), as well as screening for chronic HPV infection (Institute of Medicine, 2007). This approach to cervical cancer screening is now being put to use in numerous programs throughout the world.* The new rapid HPV test also seems promising. Trials conducted in India showed that the HPV test was more effective in reducing

mortality than the traditional visual inspection (Sankaranarayanan R. et al., 2009). For colorectal cancer screening, fecal occult blood tests may be a suitable alternative to more complicated sigmoidoscopy or colonoscopy (Ginsburg et al., 2010).

Especially at the earlier stages of efforts to bring cancer care to developing countries, initial work to expand diagnostic capacity should focus on high-prevalence settings where such initiatives will be most cost-effective. For example, in many developing countries it appears that urban-dwelling women tend to be at greater risk for breast cancer than women living in rural areas, presumably because of differences in lifestyle and exposure to potential carcinogens (Dey et al., 2009; Kruger, Appfelstaedt, 2007). In light of higher population density in urban areas and their relatively better developed service infrastructure, the epidemiology of breast cancer in such settings strongly suggests that an early focus on scaling up diagnostic services in urban settings will be most cost-effective and have the greatest public health impact.

The benefits of establishing services first in urban areas may also extend to cancer registries. Because of low population density and other issues, cancer registries in rural areas can be many times as expensive as those in urban settings, and may produce only marginal gains in knowledge of how cancer is developing in a particular country (Institute of Medicine, 2007). Of course, any strategy that relied exclusively or principally on registries in urban settings would need to account for differences between rural and urban patterns of cancer in a particular country.

* For a summary of programs that are effectively using visualization to improve cancer outcomes, see <http://www.rho.org/screening.htm>.

Increasing Access to Quality Cancer Surgery and Radiotherapy

Medical management of most cancers typically requires some combination of surgery and radiotherapy, often complemented by systemic chemotherapy.

Half or more of cancer patients need radiotherapy (IAEA, 2003). Yet although developing countries account for 85% of the global disease burden, they have only about one-third of the world's radiotherapy machines (IAEA, 2003). In Indonesia, the world's fourth most populous country, available radiotherapy services represent less than 10% of national need (Barton et al., 2006).

Limited access to radiotherapy results in needless deaths in low- and middle-income countries. Conversely, for advanced cervical cancer, the second most commonly diagnosed cancer among women in developing countries, cure rates range from 30% to 75% when radical radiotherapy is available (IAEA 2006).

Even where radiotherapy is not available, many lives can be saved through timely surgery. The Breast Health Global Initiative (BHGI) has been a leader in developing, implementing and studying evidence-based, economically feasible and culturally appropriate "Guidelines for International Breast Health and Cancer Control" for low- and middle-income countries to improve breast health outcomes. In the BHGI guidelines for Stage I and II breast cancer, modified radical mastectomy rather than breast-conserving surgery is the recommended course of treatment in low resource settings when radiation therapy is unavailable (Eniu et al., 2008). Where resources are available, complementary interventions such as breast-conserving surgery with post-operative radiotherapy, sentinel lymph node biopsy and breast reconstruction are recommended (Eniu et al., 2008). Available evidence indicates that initial surgical treatment is likely to be cost-effective in low- and middle-income countries for treatable cancers such as breast, cervical and colorectal cancer when detected early (Brown et al., 2006).

Access to Cancer Drugs: Addressing a Critical Shortcoming in Cancer Control

Cancer therapies represent one of the great "missing links" in cancer control efforts in low- and middle-income countries. Currently, and despite the many research advances of recent years that have significantly elevated the role of systemic therapy in the management of many priority cancers, little or no international funding is available for cancer treatment. As the chart on page 14 illustrates, non-communicable diseases (NCDs) such as cancer are largely absent from the billions spent on global health.

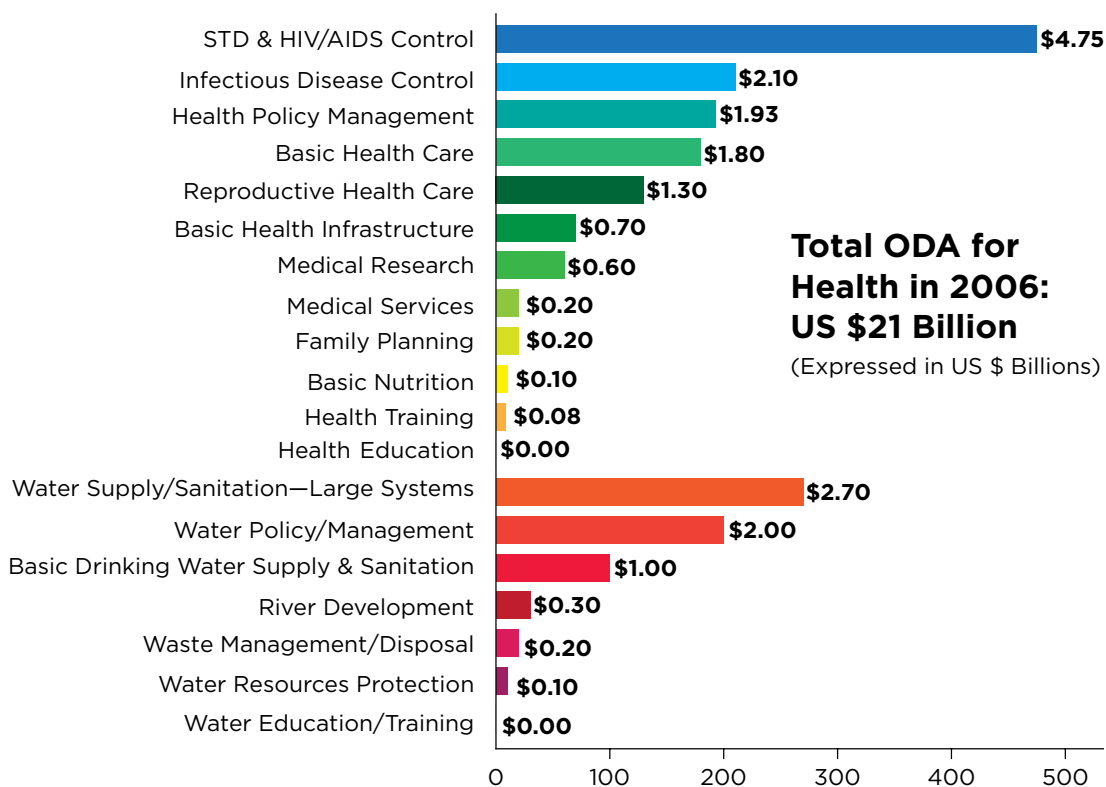
While calls for improved screening and preventive interventions are rightly greeted with broad agreement, there is often a disturbing silence when it comes to introducing cancer treatments in resource-limited settings. Such an undertaking, it is assumed, is cost-prohibitive and unfeasible in countries where doctors lack the ability to administer sophisticated treatments, clinics are overburdened, laboratories are unable to provide clinical monitoring and patients are perceived to be unlikely to adhere to prescribed therapy.

Interestingly, this was precisely the response when activists began demanding increased access to HIV antiretroviral drugs in low-income countries. Yet, ten years later the results have been astonishing. The evidence has shown that sharply tiered pricing and other innovative pricing options are possible for sophisticated therapies. Laboratory capacity can be built, and in the meantime low-tech, less expensive alternatives to laboratory monitoring can be adopted. And patients in low-income settings have proved just as determined to fight for their health as patients in high-income countries, often achieving adherence rates superior to those reported in Europe and North America.

As in the case of AIDS, excellent medical outcomes are achievable with available cancer treatments, even in the world's most resource-limited settings. Admittedly, cancer treatment is more complex than HIV treatment as it often requires surgery, radiation and chemo/hormonal therapy as well as specialized medical care. Still, affordable drugs are already available for a number of priority cancers.

For breast cancer, for example, experts recommend tamoxifen for patients with ER-positive tumors in low- and middle-income countries (Anderson et al., 2008). Endocrine therapy does not typically require especially

NCDs Not Appearing in the \$21 Billion Spent on ODA Health



Source: WHO NCDnet

sophisticated technology, but clinicians must be able to determine a patient's hormone receptor status to know whether she would benefit (Anderson et al., 2008). Recent analyses also suggest that basic treatment for colorectal cancer is cost-effective in low-income countries (Ginsburg et al., 2010). Other therapies are highly efficacious and would be recommended for widespread use in resource-limited settings if their cost could be reduced.

More cost effective benefit can sometimes be achieved by using better evidence-based indications for therapy, modifying modes of administration, using shorter-but still effective-courses or doses, finding new combinations or indications of less expensive drugs or the use of generics after testing bioequivalence (Elzawawy, 2009; Elzawawy, 2008), or through a direct measure of the individual patient's cell response to therapy and the use of biomarkers that help identify when treatment will be effective (Pachmann et al. 2008).

Partners in Health — a pioneer in introducing complex HIV treatments in developing countries — is similarly paving the way for greater access to cancer treatments in resource-limited settings, definitively demonstrating that what has been accomplished with respect to AIDS is achievable for cancer control as well. In Haiti, where Partners in Health first demonstrated the feasibility of antiretroviral therapy in a resource-limited setting, the organization is working with specialists from the Dana Farber Cancer Institute to deliver life-preserving cancer services, including LEEP surgery, hysterectomies, lumpectomies, mastectomies and other oncologic surgeries, as well as chemotherapy. The organization is also providing therapeutic services to cancer patients in Malawi and Rwanda.

A number of efforts are already underway to increase access to cancer therapies in resource-limited settings. For example, WHO analyzes cancer drugs for inclusion in its essential medicines list, which countries use to prioritize drug procurement and distribution in the health sector. IAEA assists countries in purchasing radiotherapy machines and other technologies to treat leading cancers. Through the Global Task Force

on Expanded Access to Cancer Care and Control in Developing Countries (GTF.CCC), Harvard University and the Dana Farber Cancer Institute are working to design, implement and evaluate therapeutic and other cancer control interventions in developing countries (see <http://isites.harvard.edu/icb/icb.do?keyword=k69586&pageid=icb.page345335>).

Some pharmaceutical industry leaders are also participating in partnerships to expand access to cancer treatments. With funding from AstraZeneca, Axios is collaborating with Tikur Anbessa, the main referral hospital in Addis Ababa, to bring breast cancer treatments to scale in Ethiopia. The initiative includes the development of clinical breast cancer guidelines, capacity-building assistance, support for the development of cancer control policies and planning for long-term sustainability. In a 32-month period in 2006–2008, more than 1,200 patients were provided with high-quality treatment and follow-up for breast cancer, with the number of newly enrolled patients nearly doubling in the last 12 months of this period (<http://www.axios-group.com/x/File/Ethiopia%20project%20fact%20sheet%20Feb%20EN.pdf>).

In addition, the Harvard Global Equity Initiative, working under the GTF.CCC umbrella, has announced plans to help purchase cancer drugs at affordable prices for use in developing countries (Kmietowicz, 2009). In India, the Cancer Patients Aid Association, a charitable non-

governmental organization, works with 60 doctors to deliver cancer treatments to patients who would otherwise lack access (Cancer Patients Aid Association, <http://www.cpaaindia.org/aboutus/index.htm>). The IEAA/PACT Initiative is a collaborative initiative between a number of international and technical organizations aimed at helping low-and middle-income countries mobilize funding for cancer prevention, cure and care as well as develop national cancer control programs following WHO guidelines.

A number of countries have taken steps to negotiate lower prices for cancer-related preventive and therapeutic compounds. For example, efforts by the Mexican government resulted in a sharp price reduction for vaccines to prevent HPV, the primary cause of cervical cancer. In addition, some countries are taking steps to use the flexibilities allowed in international trade rules to lower the cost of cancer drugs. In 2007, the government of Thailand issued compulsory licenses for the generic manufacture of four anti-cancer drugs – Docotexel to treat lung and breast cancer, Letrozole for breast cancer, Erlotinib for lung cancer and Imatinib to treat chronic myeloid leukemia and gastrointestinal stromal tumor (Ministry of Public Health, 2008). Borrowing a page from national AIDS responses, Thailand cited Article 31(b) of the Agreement on Trade-Related Aspects of Intellectual Property Rights under the World Trade Organization to permit the public, non-commercial use of priority medicines. The public health benefits of this approach are



evident from a review of pricing data for the breast cancer drug Letrozole, which costs 30 times more as a patented medicine than when generically manufactured (Ministry of Public Health, 2008).

There are other potential strategies to reduce per-patient costs for cancer treatment. For example, decreasing treatment times or prescribing intermittent therapy may be options in settings where adherence to clinical guidelines applicable in high-income settings may not be financially feasible (Bines, Eniu, 2008). These and similar strategies urgently merit focused research to build the evidence base for action.

In addition to cost issues, there are also bureaucratic hurdles to increasing access to cancer treatment. Even when cancer drugs are donated, it sometimes takes up to a year to make them available in developing countries due to issues with drug registration, customs requirements (and the occasional lack of cooperation from customs agents), forecasting and the like. Actors such as the International Network for Cancer Treatment and Research (INCTR) have been active in working to overcome these hurdles.

Access to Palliative Care

Access to palliative care is also emerging as a major issue in providing humane and effective cancer care. In many cases, national policies established to discourage drug abuse and the diversion of pain drugs into illicit markets have the unintended impact of severely limiting access to essential pain drugs for patients with cancer. A study released by the European Society for Medical Oncology (ESMO) and the European Association for Palliative Care found that patients in 41 European countries frequently do not receive the drugs they need to manage strong pain, even though these drugs are included on cancer treatment formularies, because of excessive or ill-managed policies to discourage abuse of these essential drugs. Similar restrictions in opioid use exist in many low- and middle-income countries (Cherney, 2010).

The report recommended revising opioid formulary restrictions to comply with the WHO essential medicines list as a minimal standard; government review and repeal of excessive restrictions that impede good clinical care of cancer pain; the establishment of alternative, emergency prescription systems to provide opioids for patients in severe pain who cannot obtain a paper prescription; the

Alleviating Stigma and Empowering Patients

Cancer-associated stigma associated is one of principal barriers to effective action to bring cancer under control in many countries (Walsh, 2009). Where a disease is highly stigmatized, many individuals avoid screening and other services and patient activism to demand greater public attention is slow to develop.

Investing in treatment programs is perhaps the most effective strategy for alleviating the stigma associated with cancer. This has been amply demonstrated by experience in the AIDS epidemic, where treatment scale-up has led to dramatic increases in HIV testing in many countries (WHO et al., 2009).

Additional steps to combat stigma should accompany efforts to expand access to cancer treatment. These should include strong political leadership and support for national awareness campaigns. Networks of cancer survivors and their family members can also play a critical role in removing the silence and invisibility surrounding cancer.

ready availability of special opioid prescription forms to physicians; and ensuring that pharmacists have the authority to correct technical errors in opioid prescriptions in consultation with the prescribing physician.

Initiatives such as the International Union Against Cancer (UICC)* Global Access to Pain Relief Initiative (GAPRI) are working at the international level, including with relevant UN agencies, as well as at a national level in key countries to ensure that effective pain control measures will be available universally to all cancer patients in pain (<http://www.uicc.org/node/94>). Likewise, the Pain and Policy Studies Group of University of Wisconsin Carbone Cancer Center works with national authorities to promote sound use of accessible opioid analgesics to relieve the pain and suffering associated with cancer and its treatment (www.painpolicy.wisc.edu). The Group collaborates closely with the WHO Cancer Control Program and the International Narcotics Control Board and has projects in Romania and India.

*UICC is in the process of changing its English name to the Union of International Cancer Control.

The Role of Pharmaceutical Companies in Expanding Cancer Treatment Options in Low- and Middle-Income Countries

Private industry must also play a vital role in accelerating access to essential cancer treatments in developing countries. With the rise of new economic powers such as Brazil, China, India and Russia and the transition to a more multi-polar world, emerging markets represent the best hopes for future profitability for major pharmaceutical companies, many of which are now confronting the expiration of blockbuster patents. Companies such as GlaxoSmithKline are actively exploring ways to expand market presence in resource-limited settings as a long-term corporate strategy.

As an immediate step, private industry can implement sharply tiered or no-profit pricing of cancer drugs in low- and middle-income countries. This approach has proven essential to recent treatment breakthroughs in the global AIDS response. As a result of the combination

of tiered pricing, generic manufacturing and targeted negotiations, the average price of HIV antiretroviral regimens has continued to fall, declining by 48% in low-income countries between 2004 and 2008 (WHO et al., 2009).

A similar approach is feasible as a first step to increase access to cancer treatments, as well. For example, Axios currently partners with four pharmaceutical companies to facilitate the donation or tiered pricing of cancer drugs. This strategy to facilitate expanded treatment access relies on three steps (Reeler, Saba, 2007). First, a model is developed to calculate the percentage of a setting's population that would have the means to access a given drug at different price levels, taking into account strategic information regarding national income, disease epidemiology, public health principles

Research to Develop Affordable New Tools to Treat Cancer

In many respects, we are living in a golden era of biomedical research advances. The mapping of the human genome points the way toward promising avenues of research. And the combined potential of publicly funded basic research and applied research conducted by pharmaceutical companies has repeatedly generated critical advances in treating diseases such as AIDS, multiple sclerosis and diabetes.

However, commercial considerations rather than public health priorities tend to drive industry research efforts. The economic incentive is a powerful driver of new therapeutics for diseases in high-income countries, but the fruits of such research tend to be unaffordable for patients in low-resource settings. Not only do major pharmaceutical companies often perceive no economic incentive to develop low-cost treatments for primary use in resource-limited settings, but they also recognize little financial motive in conducting other focused research, such as studies to ascertain whether intermittent therapy or shorter duration of treatment could achieve satisfactory health outcomes while reducing costs.

The certainty that emerging markets will represent the greatest share of future growth in consumption of pharmaceuticals suggests that a different approach is merited. Pharmaceutical companies should recognize the long-term economic importance of low- and middle-income countries to the industry's bottom line, and prioritize studies that specifically address health challenges in resource-limited settings.

Other options worthy of exploration include the channeling of public funds through innovative models that unite public and private sectors (Trimble et al., 2009). For neglected diseases that primarily affect poor countries, an array of public-private product development partnerships have arisen to spur new research. Focus areas for these innovative partnerships are diverse and include development of new TB diagnostics, development of microbicides to reduce women's risk of contracting HIV during sexual intercourse and fortification of staple foods in regions where malnutrition is prevalent.

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and health infrastructure capacity. Next, strategies are developed to maximize access to key drugs for different income groups of patients. Finally, Axios works with pharmaceutical partners to reach out to governments and key stakeholders, with the aim of increasing public awareness, building national capacity and addressing

requirements for wide coverage in the country. This approach to creative access facilitates public health strategies that involve bilateral agreements with research-based companies and countries, institutions and patients in resource-limited settings, and represents one way to close existing access gaps.



The Way Forward: A Blueprint to Revolutionize the World's Approach to Cancer Treatment

Building meaningful and sustainable access to cancer treatment in developing countries requires action towards five overarching goals:

1. Improve health system responses in low- and middle-income countries to address cancer, chronic diseases and other long-term health challenges. International donors and technical agencies should intensify technical support to low- and middle-income countries to strengthen the strategic cancer information systems needed to inform programmatic responses. International players should support countries in establishing and maintaining national cancer programs. Guided by a milestone-driven strategic plan, each national cancer program should address key challenges to the delivery of cancer prevention, diagnosis and treatment in resource-limited settings. National programs should strengthen human resources for cancer care through focused clinical training, implementation of task-shifting to stretch available resources and increased investments in medical education. Strategies to strengthen health systems should include plans for the procurement and implementation of needed laboratory services. With particular focus on high-priority cancers, national programs should undertake efforts to implement affordable screening programs, build surgical capacity and establish accessible radiotherapy services to accelerate treatment access. Care services should be guided by national cancer treatment guidelines and supported by targeted research initiatives to fill gaps in the evidence base for cancer treatment. Well-designed, strategically-located cancer registries should be established to provide strategic information for policy development, programmatic planning, and monitoring and evaluation.

2. Expand creative strategies to build access to cancer treatment. Intensive advocacy and standard-setting at the global, regional and national levels should build a consensus that recognizes treatment as essential to the cancer response. Cost-effectiveness studies should be conducted that take into account countries' capacities to identify optimal strategies for early detection and treatment of locally prevalent cancers. Creative access strategies — such as sharply tiered pricing or bilateral agreements between industry and developing countries — should be implemented to facilitate increased treatment access. International technical agencies and health researchers should rigorously document and promote local cancer treatment initiatives and pilot projects to demonstrate the feasibility of cancer treatment in resource-limited settings and identify best practices. Increased support is needed to target research to develop affordable, cost-effective diagnostic and therapeutic tools specifically for use in developing countries. Donors should support intensified advocacy by non-governmental organizations to build support for the generic manufacture of essential off-patent treatments, and key philanthropies and technical experts should work actively with generic manufacturers to increase their involvement in the production of affordable, effective, high-quality cancer treatments and access to radiotherapy.

3. Improve financing for comprehensive cancer responses in low- and middle-income countries. It has been demonstrated that investments in public health are directly linked to a country's potential for economic growth. If developing nations are to become productive and economically self-sufficient, investments in the health of these countries' populations are essential (Sachs, 2001). Cancer constitutes a major and growing public health burden in developing countries, one that demands that international donors and global opinion leaders actively explore innovative financing strategies to underwrite the long-term costs associated with scaling up cancer

treatment in resource-limited settings. These include the so-called Tobin Tax on currency transactions to increase and sustain financial flows for priority global undertakings, such as addressing the looming cancer crisis in developing countries. In addition, donors should significantly increase financing for state-of-the-art management of cancer and other chronic diseases. To build support for this global undertaking, advocates should target key decision-making groups such as the G20, the BRIC countries (e.g., Brazil, Russia, India and China), the United Nations, WHO and the World Health Assembly, the World Economic Forum, and the U.S. Congress and other parliamentary bodies.

4. Build an advocacy movement to support these objectives.

Grassroots energy on cancer must increase by several orders of magnitude. Robust advocacy efforts should target key constituencies such as the G20, WHO and other multilateral organizations, the pharmaceutical industry, national governments, opinion leaders and influential non-governmental organizations. To integrate cancer control into broader health initiatives, cancer and other non-communicable diseases should be included in mid-term development goals. Intensified efforts should promote strong national leadership to endorse the scale-up of cancer treatment, embrace specific national targets for cancer control, implement public awareness campaigns and improve

national cancer surveillance systems. Above all, national publics must be persuaded that the fight to improve access to cancer treatment is both critical and winnable.

5. Urgently develop and implement targeted initiatives to expedite the introduction and scale-up of preventive and therapeutic interventions for priority cancers, guided by milestone-driven health outcome targets.

Urgent efforts are needed to accelerate control and management strategies for key cancers where medical advances have made rapid progress possible. For instance, nearly 90% of children with cancer can be effectively treated; survival rates for breast cancer patients can be raised from their current low levels in developing countries to more than 80%; and dramatic improvements in medical outcomes for women with cervical cancer are also achievable. With support from the international community and private industry, all countries should devise and urgently implement focused national plans to harness these biomedical advances for the benefit of their populations. At the same time and while national plans are conceived and implemented, every sound local initiative or pilot project should be encouraged, as they help assess the effectiveness of local strategies; increase local awareness and build local momentum and grass root response.

Ensuring access to cancer treatments in developing countries is entirely feasible. This has been demonstrated not only by the historic achievements made in expanding AIDS treatment access, but also by the growing number of programs in resource-limited settings that are effectively piloting cutting-edge diagnostic and therapeutic interventions for priority cancers.

To achieve this vision, substantial new resources and strong political leadership will be needed. *A Call to Action on Cancer in Developing Countries* has just been published in the *Lancet* and the authors of this issue paper hope that it will serve to galvanize international action and funding for the fight against cancer in developing countries. Donors should support this Call to Action and the work of CanTreat the Global Task Force on Expanded Access to Cancer Care and Control in Developing Countries and other groups that are already engaged in supporting comprehensive cancer control initiatives in resource-limited settings. But additional partners will also be needed to support this long-term undertaking.

Whether global health disparities grow or diminish in coming decades will be determined, in large measure, by the world's approach to cancer and other chronic diseases. This new frontier in global health awaits, demanding concerted efforts to ensure a healthier, fairer world.

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