

Scaling up cancer diagnosis and treatment in developing countries: what can we learn from the HIV/AIDS epidemic?

Cancer is a bigger problem in developing countries than human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS).

The cancer burden in developing countries is reaching pandemic proportions. More than half of the 12.4 million estimated new cases of cancer in 2008 and two-thirds of the estimated 7.6 million cancer deaths, occurred in low- and middle-income countries (LMICs) [1]. Globally, cancer kills more people each year than AIDS, tuberculosis and malaria combined [2], and the number of deaths is growing rapidly. Health systems of developing countries, which are already struggling to cope with the AIDS epidemic, are ill-prepared to deal with this new and rapidly growing challenge.

Changing lifestyles, chronic infection and increasing life spans lie at the root of the global growth in cancer. As more and more countries urbanize, changes in reproductive patterns and diet, insufficient exercise, smoking, drinking and obesity combine to increase cancer risk. In addition, around 1 in 4 cancers in developing countries, as opposed to only 1 in 10 in the developed world, are linked to infection. Individual risk of cancer also increases dramatically with age, and the average age of populations is increasing more rapidly in LMICs than in the richer world.

Despite this, cancer remains a low priority for LMIC health spending, as well as for donor nations. Only 5% of global resources devoted to cancer are spent in developing countries [3], and cancer control is conspicuously absent from the internationally agreed Millennium Development Goals [4].

Yet, the knowledge and tools to make a major impact on these diseases exist today. Cervical cancer can be effectively prevented through vaccination or screening coupled with treatment of precancerous lesions. Cervical and breast cancers have a generally good prognosis if detected early. But there are currently few facilities for cancer prevention and treatment in developing countries, few plans for scaling up and few vocal cancer activists to influence policy makers and funding agencies. Cancer drugs are largely inaccessible, and access to diagnostics is often limited to one or two hospitals in the capital of an LMIC. Pain control (including morphine) is inaccessible for >80% of the world population. It is urgent to promote actions to ensure that effective pain control measures will be available to cancer patients in pain [5]. Radiotherapy facilities, which are an essential part of treatment of most common cancers, are scarce and nonexistent in over most Asian and African countries [6]. Health staff and the general

population are largely unaware of the need to screen for cancer or of the improved treatment outcomes if cancer is detected early. Referral systems are weak and staff inexperienced in cancer detection and diagnosis. Human resources for health care may be attracted by better paying jobs in cities or in well-funded HIV/AIDS programs and leave rural screening/early detection programs. The few qualified health professionals, who have been trained in more advanced cancer diagnosis and treatment, are often offered better paying jobs abroad and leave health services in their home countries [7]. Access to cancer drugs is still limited or nonexistent for most cancer patients in developing countries and cancer is thus a death sentence for most people in these countries.

What have we learned from HIV/AIDS?

What has the public health community learned from over 25 years of experience with HIV/AIDS that will enable us to address cancer in developing countries in a more effective way? How can we do things differently and more effectively, save lives and prevent premature death from cancer?

1. Access to cancer treatment is mandatory

Between 2003 and 2008, access to antiretroviral therapy for people living with HIV in LMICs increased 10-fold. This has driven a dramatic decline in HIV-related mortality, which previously was thought by many groups including World Health Organization (WHO) to be an unachievable goal [8]. Evidence also suggests that the availability of treatment helps reduce HIV infection rates, in part not only because it reduces viral load at the individual and community levels but also because it creates increased demand for testing and counseling. As the Brazilian experience with antiretroviral treatment showed in the late 1980s, the promise of treatment is an incentive for testing [9]. Without the hope of treatment, people will not come forward to test or screen. This is an important lesson for cancer in LMICs.

Today, both treatment and diagnostics for cancer are expensive and difficult to obtain in LMICs. The costs of many targeted therapy drugs are very high [10]. In Hong Kong the monthly cost of Gefitinib and Erlotinib, both used for non-small-cell lung carcinoma, is HKD 14 000 (US\$ 1806) and HKD 18 000 (US\$ 2322), respectively, per month per patient [11]. In the United States, multidrug therapy for colorectal cancer costs up to US\$ 30 790 for 8 weeks of treatment [12]. The prices of these and other therapies put them beyond the reach of public health systems in the vast majority of countries.

As a first step cancer drugs on the WHO list of essential drugs, which are low cost but effective cancer drugs, should be

made available in developing countries based on public health priorities. In addition, there are now new initiatives to make more expensive life-saving cancer therapies available in developing countries. Access strategies that adapt the cost of medicines in nonreimbursed markets to what patients can actually afford to pay [13] are showing sustainable results. In addition, new clinical trials have shown that it is possible to determine early on whether a patient is responding to treatment, thereby allowing interruption or changes in treatment approaches to be made expeditiously and cost-effectively. The implementation of these and other models that draw on innovative approaches and look to the lessons from other diseases must be explored, expanded and made affordable if we are to effectively address the cancer epidemic in the developing world.

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2. Cancer must be mainstreamed in health systems

The few health facilities in LMIC that are capable of cancer diagnosis and treatment are usually inaccessible to poor, rural populations. As a result, most people receive little or no medical attention. We need a public health approach that is tailored to local conditions, an approach that integrates early detection, earlier diagnosis of cancer, effective treatment and palliative care with other services in ways that strengthen health systems as at all levels.

It is now recognized that the impact of the AIDS response is higher where HIV programs are integrated with other health and social welfare services. In some countries, HIV services have been shown to strengthen chronic care as a whole [14] and to have a positive impact on primary care [15]. The same approach is needed for cancer. At each level of the health care system—in dispensaries and health centers and in district, regional and specialized hospitals in capitals—we need to identify what can be done to detect and address cancer effectively while ensuring a high quality of care.

Low-cost, low-technology approaches have been proven effective and feasible in many resource-constrained environments. For example, evidence has shown that cervical cancer can be detected through visual inspection and premalignant lesions can be treated with cryotherapy [16]. While the method may have limitations such as the difficulty of quality control, these procedures can be carried out by trained nurses even in the most basic primary health care settings [17, 18] and a recent trial in India showed the procedure to be quite effective [19]. While another trial in India showed the new human papillomavirus (HPV) test to be more effective in reducing mortality than visual inspection [20], the HPV test is not yet available or affordable in developing countries. Until the HPV test is available and affordable for developing countries, visual inspection is the best option as it would build the infrastructure and human resources required for screening. Once the HPV test becomes available and affordable, this test should be the primary screening tool while visual inspection with acetic acid (VIA)

could be used for triaging HPV-positive women. The vaccines that protect against certain subtypes of the HPV, the principal cause of cervical cancer, can be effectively delivered at primary health care levels, as has been documented through early experience with the Gardasil Access Program (Gardasil Access Program Progress Reports, unpublished data). However, these vaccines are not available or affordable in developing countries, and they would not replace the need for continued screening given that vaccinated girls may have other virus strains than those prevented by the vaccine and that many girls may already have been exposed at the time of vaccination.

Early detection is critical to improving breast cancer survival. A pilot program in Malaysia [21] succeeded in reducing the number of breast cancers presented in stages 3 and 4 from 77% to 37% as a result of community public awareness campaigns and the training of health staff in clinical breast cancer examination. The authors estimate that the public awareness was probably more effective than the staff training as the staff never stayed long in the area before getting transferred. However, other programs have lost women to follow-up possibly due to lack of trust in the health system or a cure indicating the importance of public education on cancer including that it often can be cured if diagnosed early on [22].

Other research has shown that resource-sparing, cost-effective treatment could be achieved in breast cancer treatment—as a model for other cancers—via various scientific approaches including better evidence-based indications for cost-effective therapy, modifying modes of administration, shorter—but still effective—courses or doses, innovation of more ways of combinations or indications of less expensive drugs and the use of generics after testing bioequivalence [23], through a direct measure of the individual patient's cells response to therapy [24], and the use of biomarkers that help identify when treatment will be effective. However, some of the methods are very expensive and will not be available in developing countries for the foreseeable future. In the mean time, approaches such as use of mobile phone for follow-up could make a major difference.

3. Advocacy and education is a must

Much more can be done to save lives. It starts with defining public health priorities on the basis of prevalence and incidence of cancers as well as identification of what cancers can be effectively treated within the limitations of the health system of each developing country. Greatly increased health education, information and communication are needed to educate communities that cancer is not necessarily a death sentence, that risks can be reduced through healthy life styles, that screening can increase chances of successful treatment, in particular for cancers with a good prognosis, and that there are now vaccines that protect against some types of cancers. People also need to have access to good quality care, otherwise they will not want to screen. Also required now is the political will to act, and activists and advocates who can mobilize the funding to mainstream cancer prevention and treatment in poorer countries.

we know enough to make a start

The knowledge and experience exist today to take effective action and to make a significant difference to cancer outcomes in LMIC [25]. Cancer control is a human right [26]. The challenge is to apply that knowledge through a public health framework to maximize the benefits for as many as possible, while keeping costs at a manageable level for poorer countries and donors alike. Pilot programs are good but they are insufficient. We now need to go to scale with what we know to be cost-effective interventions.

In order to implement, what we know, on a large scale, much greater resources are needed. Professional organizations, multilateral organizations, advocates, activists and governments of LMIC must come together to advocate for action against cancer and for the funding to do what we know is right [5, 27]. The longer we wait, the greater the challenges will be.

The time for action on cancer in developing countries is now.

CanTreat International

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references

1. International Agency for Research on Cancer. World Cancer Report. 2008; Lyon: International Agency for Research on Cancer, 25–26.
2. American Cancer Society. Global Cancer Facts and Figures. 2007; Atlanta, GA: American Cancer Society, 1.
3. Ngoma T. World Health Organization cancer priorities in developing countries. *Ann Oncol* 2006; 17 (Supplement 8): viii9–viii14.
4. Huerta E, Grey N. Cancer control opportunities in low-middle income countries. *CA Cancer J Clin* 2007; 57: 72–74.
5. The World Cancer Declaration 2008: A call to action from the global cancer community. Geneva: International Union Against Cancer (UICC) 2008.
6. Samei M, Rosenthal MD, Kinley III D et al. No time to loose. *IAEA Bull* 47: 1.
7. The World Health Report 2006: Working together for Health. Geneva: WHO 2006.
8. Report on the Global HIV/AIDS Epidemic. Geneva: UNAIDS 2008.
9. Berkman A, Garcia J, Muñoz-Laboy M et al. A critical analysis of the Brazilian response to HIV/AIDS: lessons learned for controlling and mitigating the epidemic in developing countries. *Am J Public Health* 2005; 95: 1162–1172.
10. Access to cancer drugs. A UICC Position Paper, Revision 2008/2009. International Union Against Cancer (UICC), Geneva, 2008/2009. http://www.uicc.org/templates/uicc/pdf/special20reports/access_to_cancer_drugs_uicc.pdf (3 March 2010, date last accessed).
11. Sing-hung LO. Hormonal therapy and targeted therapy in palliative cancer care. *Palliative Care 4th Hong Kong Symposium, HKSPM Newslett* 2007: 14–17.
12. Gerber D. Targeted therapies: a new generation of cancer treatments. *Am Fam Physician* 2008: 1–10.
13. Reeler AV, Saba J. Developing strategies for developing countries. *Pharm Exec Europe* 2007: 28–30.
14. Janssens B, Van Damme W, Raleigh B et al. Offering integrated care for HIV/AIDS, diabetes and hypertension within chronic disease clinics in Cambodia. *Bull World Health Organ* 2007; 85: 880–885.
15. Walton DA, Farmer P, Lambert W et al. Integrated HIV prevention and care strengthens primary health care: lessons from rural Haiti. *J Public Health Policy* 2004; 25: 137–158.
16. World Health Organization. Comprehensive Cervical Cancer Control: A Guide to Essential Practice. Geneva: World Health Organization 2006.
17. Bradley J et al. Delivering cervical cancer prevention services in low resource settings. *Int J Gynecol Obstet* 2005; 89: S21–S29.
18. Agurto I et al. Involving the community in cervical cancer prevention programs. *Int J Gynecol Obstet* 2005; 89: S38–S45.
19. Sankaranarayanan R et al. Effect of visual screening on cervical cancer incidence and mortality in Tamil Nadu, India: a cluster-randomised trial. *Lancet* 2007; 370: 398–406.
20. Sankaranarayanan R et al. HPV screening for cervical cancer in rural India. *New Engl J Med* 2009; 360: 1385–1394.
21. Devi BCR, Tang TS, Corbex M. Reducing by half the percentage of late-stage presentation for breast and cervix cancer over 4 years: a pilot study of clinical downstaging in Sarawak, Malaysia. *Ann Oncol* 2007; 18: 1172–1176.
22. Pisani et al. Outcome of screening by clinical examination of the breast in a trial in the Philippines. *Int J Cancer* 2006; 118: 149–154.
23. Elzawawy A. The 'win-win' initiative: a global, scientifically based approach to resource sparing treatment for systemic breast cancer therapy. *World J Surg Oncol* 2009; 7: 44.
24. Pachmann et al. Monitoring the response of circulating epithelial tumor cells to adjuvant chemotherapy in breast cancer allows detection of patients at risk of early relapse. *J Clin Oncol* 2008; 26: 1208–1215.
25. Reeler AV, Qiao Y et al. Women's cancers in developing countries: from research to an integrated health systems approach. *Asian Pacific J Cancer Prev* 2009; 10: 519–526.
26. Seffrin J. Cancer control as a human right. *Lancet Oncol* 2008; 9: 409–411.
27. London declaration on cancer control in Africa. Presented during the African Cancer Reform Convention, London, May 2007.