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Global Task Force on Expanded Access to Cancer Care and Control in Developing Countries



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About this publication

This publication is part of the Global Task Force on Expanded Access to Cancer Care and Control in Developing Countries (GTF.CCC) Working Paper and Background Note Series. It was produced as a background note in collaboration with partners at FHCRC, University of Washington and UCI for a database on cancer care and control programs in low- and middle-income countries (LMICs), and particularly to document examples of innovative delivery strategies.

This is a working background note and therefore represents research currently in progress that has not gone through a review process. Comments are welcomed at gtfcc@harvard.edu.

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Context

Cancer has emerged as one of the most significant threats to the health of persons worldwide. In 2010, it is expected that more than 7 million people across the globe will die from cancer, more than the number of deaths attributable to HIV, tuberculosis and malaria combined¹. Moreover, two-thirds of these deaths will occur in low- and middle-resource countries. New strategies for the prevention and treatment of cancer, effective in both low- and high-resource regions, are urgently needed.

Over the past several years, it has been recognized that infections cause approximately one-quarter of cancers²; in 2010, 3.3 million people will develop cancer directly as a consequence of a chronic infection. Cervical cancer, liver cancer, stomach cancer, lymphoma, bladder cancer, Kaposi sarcoma, and cancers of the head and neck can all be caused by chronic infections such as human papillomavirus, hepatitis B and C, *Helicobacter pylori*, Epstein Barr Virus, schistosomiasis, and human herpesvirus-8. These infection-related cancers may provide the best opportunity for short-term gains in the prevention and treatment of cancer, as illustrated in the following three examples. First, the deployment of a vaccine against human papillomavirus will likely prevent more than 95% of cases of cervical cancer and could potentially obviate the need to establish expensive and arduous screening programs in resource-limited regions³. Second, universal vaccination of young children against hepatitis B in Taiwan has nearly eradicated pediatric liver cancer, which previously was one of the most common cancers in Taiwanese children⁴. Third, the provision of cheap, non-toxic, oral antimicrobials can prevent or cure several infection related cancers, including stomach cancer⁵, liver cancer⁶, and lymphoma⁷. Taken together, it is apparent that the focus on infectious agents in the primary prevention and treatment of cancer may allow for enormous strides against these malignancies in the short-term.

It is notable that the proportion of cancers attributable to infections varies by geographic region. In the United States, it is estimated that infections cause up to 10% of cancers (or nearly 150,000 new cases annually), while in many regions of sub-Saharan Africa, nearly 50% of cancer cases are caused by infections⁸. In fact, seven of the ten most common cancers in Uganda are attributable to infectious diseases⁹. Therefore, to conduct the most efficient and impactful research in infection-related cancers,

scientists from the Fred Hutchinson Cancer Research Center (FHCRC) partnered with the Uganda Cancer Institute (UCI) in Kampala in 2004 to form the Uganda Program in Cancer and Infectious Diseases (UPCID).

Program objectives

UPCID has three core components to its activities: research, capacity building, and care delivery. These three foci are considered necessary in combination to make meaningful and sustained differences in infection-associated cancers, and the objects of each component are outlined below.

Research. UPCID research projects are aimed at elucidating the fundamental questions which could enable comprehensive cancer prevention and treatment strategies in infection-related malignancies. Examples of research questions currently being pursued are as follows. First, the program seeks to characterize the natural history of progression from primary acquisition of viral oncogens to the establishment of chronic infection and eventual development of malignancies. A striking feature of infection-related cancers is that more than 70% of persons throughout the world are infected with at least one pathogen which can cause cancer, but less than 0.1% will ever actually develop cancer. Collaborative research between scientists at the UCI and FHCRC is investigating both the pathophysiology of tumorigenesis and simultaneously discovering and validating blood- and saliva-based biomarkers to identify individuals at highest risk for developing cancer. Second, among individuals predicted to be at highest risk of developing cancer, UPCID is evaluating strategies to prevent the development of cancer. These approaches include increased application of traditional cancer screening methods, administration of antimicrobial therapy, and reduction of other risk factors established to increase the risk for developing cancer. As a final example, UPCID researchers are investigating novel therapies and care delivery methods specific to infection-associated cancers. These new therapeutics in particular will target the etiologic infectious agent, leading to reduced toxicity, increased efficacy, and lower cost. Each of the methods under evaluation would result in the establishment of prevention and treatment strategies utilizable in both resource-rich and resource-poor settings.

Capacity Building. The delivery of effective cancer care requires a multidisciplinary team with unique specialty training. It is far too easy to dismiss the ability to deliver impactful cancer care in resource-poor regions on account of the complexity of the disease; similar arguments were made against the expansion of HIV and TB care programs, and have been proven wrong the world over. However, the acute shortage of trained cancer care teams in the areas with the greatest cancer burden accentuates the need for expanded training activities. Until recently, the country of Uganda had a single full-time physician and a single full-time nurse with formal training in oncology practicing at the country's sole cancer center. Ancillary and supportive services essential for cancer care delivery, including pharmacy, laboratory medicine, and pathology are similarly lacking cancer-specific expertise in Uganda. At the same time, few health care providers, researchers, and policy-makers in the United States have developed a sufficient understanding of the issues unique to cancer in low-resource regions which would allow them to effectively collaborate with peers in these areas to make meaningful improvements. Thus a central mission of UPCID is to provide a series of bidirectional training activities to build the human capacity for cancer care and research in resource-limited regions.

Care Delivery: Cancer is a complex and chronic disease, and the reduction of morbidity and mortality in resource-limited areas will only be realized through a multimodal approach. Access to both care providers and medications is currently an important limitation, and UPCID is developing novel approaches to expand access. These include: identifying and eliminating barriers to presenting for cancer care, as over 70% of new cancer diagnoses in Uganda are among persons with extremely advanced disease¹⁰; implementation of guideline-driven cancer care to reduce the inappropriate use of chemotherapy, assuring access to those who could benefit from its administration; and increasing the efficiency of cancer care delivery in resource-poor regions through the creation of care-delivery teams. Another factor which results in poor outcomes after cancer diagnoses in resource-limited areas is the loss to follow-up. Cancer treatment can be both expensive and prolonged, making the receipt of a full course of treatment elusive for those either without resources or who must travel long distances to obtain cancer care. UPCID is investigating methods of increasing community awareness of cancer and empowering localized healthcare advocates in cancer who can assist community members in reaching and remaining connected with remote cancer treatment centers. Finally, no model currently exists of a cancer treatment facility in low-resource regions which would allow for the efficient and impactful delivery of care in this setting. UPCID has worked with an international team of architects to design the first cancer clinic, training center and laboratories in a resource-limited region as a collaboration between a US National Comprehensive Cancer Center and a local cancer institute, which may offer such a model in similarly challenged settings.

Outcomes and Impact

Over the first five years of UPCID, substantial progress has been made in each programmatic area. Over a dozen research projects are currently under way at the research clinic, with work to date elucidating the pathogenesis, diagnosis and treatment of the two most common cancers in sub-Saharan Africa, Kaposi sarcoma¹¹⁻¹⁵ and lymphoma¹⁰. The training program has expanded the capacity to treat cancer in Uganda several fold. To date, five Ugandan physicians have been trained in cancer care through a 13-month fellowship at FHCRC in a program which provides the foundations of cancer care tailored to resource-limited settings. To date, an additional 101 Ugandans and Americans have trained with the program in a variety of disciplines, including pharmacy, nursing care, infectious disease medicine, epidemiology, laboratory sciences, research coordination, regulatory management, and program administration. These people will greatly expand the international capacity to improve cancer care and research around the globe. Finally, the work to improve clinical care will allow UPCID to implement and evaluate cancer care guidelines in the coming year, measure the impact of increasing access to care, and break ground on the new cancer center in October 2011.

Challenges and lessons

Great challenges remain in reducing the morbidity and mortality of cancer around the globe. Cancer remains low on the list of health priorities of policymakers in resource-poor regions, and is still not seen as an important global health issue for many donor agencies¹⁶. This creates challenges in funding new initiatives and reduces the perceived urgency to make large changes in healthcare delivery systems. The lack of personnel trained in cancer research, care delivery, or education is among the greatest challenges faced by UPCID as the few persons with expertise are required to simultaneously provide patient care, conduct cutting-edge research, and administrative leadership. Finally, the lack of cancer

literacy in the general population of many low- and middle-resource countries leads to ignorance about the burden of cancer in these settings, as well as contributes to an absence of cancer advocacy and a complacency with current systems. Despite these challenges, the experience of UPCID has shown that a collaborative, multidisciplinary approach to global cancer focused on research, capacity building and care delivery can make many meaningful and sustainable improvements in resource-limited settings.

References

1. World Health Organization. Cancer. In: World Health Organization, editor. Fact Sheets. Number 297 ed. Geneva, Switzerland; 2009.
2. Parkin DM. The global health burden of infection-associated cancers in the year 2002. *International Journal of Cancer*. 2006;118(12):3030-44.
3. Garland SM, Hernandez-Avila M, Wheeler CM, Perez G, Harper DM, Leodolter S, et al. Quadrivalent vaccine against human papillomavirus to prevent anogenital diseases. *N Engl J Med*. 2007 May 10;356(19):1928-43.
4. Chang M-H, Chen C-J, Lai M-S, Hsu H-M, Wu T-C, Kong M-S, et al. Universal Hepatitis B Vaccination in Taiwan and the Incidence of Hepatocellular Carcinoma in Children. *N Engl J Med*. 1997 June 26, 1997;336(26):1855-9.
5. Steinbach G, Ford R, Globler G, Sample D, Hagemester FB, Lynch PM, et al. Antibiotic treatment of gastric lymphoma of mucosa-associated lymphoid tissue. An uncontrolled trial. *Ann Intern Med*. 1999 Jul 20;131(2):88-95.
6. Liaw Y-F, Sung JY, Chow WC, Farrell G, Lee C-Z, Yuen H, et al. Lamivudine for Patients with Chronic Hepatitis B and Advanced Liver Disease. *N Engl J Med*. 2004 October 7, 2004;351(15):1521-31.
7. Casper C, Nichols WG, Huang ML, Corey L, Wald A. Remission of HHV-8 and HIV-associated multicentric Castleman disease with ganciclovir treatment. *Blood*. 2004 Mar 1;103(5):1632-4.
8. Boyle P, Levin B, International Agency for Research on Cancer. World cancer report 2008. Lyon: IARC Press; 2008.
9. Cancer incidence in five continents. Volume VIII. IARC Sci Publ. 2002;155:1-781.
10. Bateganya MH, Stanaway J, Brentlinger PE, Magaret AS, Wald A, Orem J, et al. Predictors of Survival After a Diagnosis of Non-Hodgkin Lymphoma in a Resource-Limited Setting: A Retrospective Study on the Impact of HIV Infection and Its Treatment. *J Acquir Immune Defic Syndr*. 2011 Apr;56(4):312-9.
11. Johnston C, Orem J, Okuku F, Kalinaki M, Saracino M, Katongole-Mbidde E, et al. Impact of HIV Infection and Kaposi Sarcoma on Human Herpesvirus-8 Mucosal Replication and Dissemination in Uganda. *PLoS ONE*. 2009;4(1):e4222.
12. Nguyen H, Okuku F, Ssewankambo F, Magaret A, Johnston C, Wald A, et al. AIDS-associated Kaposi sarcoma in Uganda: response to treatment with highly active antiretroviral therapy and chemotherapy. *Infectious Agents and Cancer*. 2009;4(Suppl 2):O5.
13. Casper C. The Increasing Burden of HIV-Associated Malignancies in Resource-Limited Regions. *Annu Rev Med*. 2010 Jan 27.
14. Gantt S, Kakuru A, Wald A, Walusansa V, Corey L, Casper C, et al. Clinical presentation and outcome of epidemic Kaposi sarcoma in Ugandan children. *Pediatr Blood Cancer*. 2010 Mar 4;54(5):670-4.
15. Phipps W, Ssewankambo F, Nguyen H, Saracino M, Wald A, Corey L, et al. Gender Differences in Clinical Presentation and Outcomes of Epidemic Kaposi Sarcoma in Uganda. *PLoS ONE*. 2010;5(11):e13936.
16. Boyle P. The globalisation of cancer. *Lancet*. 2006 Aug 19;368(9536):629-30.



The Global Task Force – convened in November 2009 by the Harvard Global Equity Initiative, Harvard Medical School, Harvard School of Public Health, and the Fana-Farber Cancer Institute – is comprised of leaders from the global health and cancer care communities, and is dedicated to the development, implementation and evaluation of strategies to advance the agenda of **Expanded Access to Cancer Care and Control in Developing Countries**

The Harvard Global Equity Initiative (HGEI) is an interfaculty research program at Harvard University devoted to promoting equitable development with a particular focus on the dimension of health and serves as the **Secretariat of the GTF.CCC**

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