The Roles of National Cancer Research Institutions in Evolving a Comprehensive Cancer Control Program in a Developing Country: Experience from Uganda

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\textbf{Abstract}

With the increasing global cancer burden, especially in the developing world, the World Health Organization made the Framework Convention on Tobacco Control and development of comprehensive national cancer control programs as key responses. Most countries in Africa lack the capacity to evolve a national cancer control program. This is mainly due to lack of resources. However, established cancer institutions could be used as resources for evolving a comprehensive national cancer program. Moreover, this has the appeal of presenting cancer control as an essential part of the public health response to disease. In Uganda, two cancer research institutions, the Uganda Cancer Institute and Kampala Cancer Registry, have contributed to initiation of a cancer control program. They have provided evidence on disease causation, burden and strategy for prevention, treatment and community involvement. Further, these institutions have created opportunities for international partnerships and collaborations in cancer research. Given the challenges of evolving a national cancer control program, each country should look internally for opportunities in existing cancer institutions as starting points for developing a national program. Evidence for feasibility should be provided to governments to help in formulating policies supportive of cancer control in these countries.

\textbf{Introduction}

In response to the looming global cancer crisis, the World Health Organization (WHO) prescribed prioritization of cancer control and prevention through the establishment of national cancer control programs and ratification of the Framework Convention on Tobacco Control \cite{1,2}. Uganda has ratified the framework convention on tobacco control as a key step in conforming with the WHO recommendation and the key practical step, the establishment of a national cancer control program, is the next to be taken.

This process has been slow partly because there is a need for strong evidence to guide it. However, unlike many other countries, Uganda is fortunate to have a rich history in cancer research, which has provided a framework for planning a national cancer control program. Cancer research institutions in Uganda such as the Kampala Cancer Registry and The Uganda Cancer Institute...
have evolved from the formative research era in the country and have a wealth of information that is proving instructive in guiding formulation of a comprehensive national cancer program [3, 4]. They have remained functional for the last 5 decades, producing seminal data which have been internationally acclaimed.

In this article, we provide an overview of these two key cancer research institutions in Uganda, looking at their roles in the last 50 years and currently towards guiding the formation of a functional comprehensive national cancer control program. It is hoped that this could be a model for using existing national cancer institutions as resources for evolving cancer control programs in countries with limited resources.

Global Cancer Burden

The WHO estimates that the global cancer burden will increase by 6,000,000 between 2000 and 2020, and that most of this increase will be in the developing countries, especially Sub-Saharan Africa [5]. Thirty percent of cancers in developing countries are related to infection, and most cancer patients are young and in their prime, as opposed to the elderly population of cancer patients in the developed world [6, 7].

HIV has emerged as a single major factor in the recent accelerated burden of cancer in Sub-Saharan Africa [8, 9]. It is the best example of the close relationship between infection, immune dysfunction and evolution of malignancies.

Burden of Cancer in Uganda

Uganda is one of the countries with very high morbidity and mortality due to cancer [10].

Early reports from the Kampala Cancer Registry and hospital records have shown that the pattern of cancer in Uganda is different from that observed in developed countries, with liver, penile, urinary bladder, esophagus and Kaposi’s sarcoma accounting for about 80% of all male cancers [8, 10]. In females, cervical cancer has been the commonest cancer since early periods, but the incidence has increased tremendously (fig. 1).

The current consensus is that there is an increasing burden of cancer in Uganda and that this is true of other countries in Sub-Saharan Africa. The trend for cancer
incidence over the last 4 decades has been upward [8]. The most dramatic increase in cancers in Uganda has been noted in cancers due to the HIV epidemic in the country [11, 12]. HIV/AIDS-related cancers common in the country include Kaposi’s sarcoma, non-Hodgkin’s lymphoma, carcinoma of the cervix and squamous cell carcinoma of the conjunctiva, which has increased greatly. The second group of factors responsible for the increase in cancer are lifestyle changes. Examples of cancers related to changes in lifestyle are lung cancer (strongly associated with tobacco) and hepatocellular carcinoma (related to consumption of alcohol, aflatoxin exposure due to poor storage of grains and infection with hepatitis viruses). Others are colon and esophageal carcinoma (which are associated with changing dietary habits), as well as breast cancer, which may be related in part to lifestyle choices such as diet and a decline in breast feeding. The third category of factors are nonspecific and possibly linked to environmental changes, which have led to an increase in cancers such as Hodgkin’s lymphoma, Burkitt’s lymphoma, leukemia, hepatocellular carcinoma and stomach cancer.

Special mention should be made of childhood cancers, which have increased dramatically in the region without specific causes [8, 13]. The top 10 common neoplasms among children in Uganda are given in table 1.

The clinical course of disease in this age group is usually rapid, as these cancers tend to be more aggressive but otherwise treatable, with a good proportion being curable when diagnosed early and treated appropriately (fig. 2).

The high morbidity due to cancer in Uganda is attributed to late presentation of disease. This is also linked to high mortality, reflecting the lack of access to early diagnosis and treatment as a result of the poor status of the cancer care system in the country. This is further compounded by the high cost of treatment for cancer. The minimum cost of treating a patient with early breast cancer is 2,000,000 Uganda Shillings (approx. USD 1,000; per capita income in Uganda is USD 320).

Table 1. Childhood cancers in Uganda, 2000 (cancer registry data)

<table>
<thead>
<tr>
<th>No.</th>
<th>%</th>
</tr>
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<tbody>
<tr>
<td>Leukemia</td>
<td>24</td>
</tr>
<tr>
<td>Non-Hodgkin’s lymphoma</td>
<td>398</td>
</tr>
<tr>
<td>Hodgkin’s disease</td>
<td>9</td>
</tr>
<tr>
<td>CNS tumor</td>
<td>4</td>
</tr>
<tr>
<td>Retinoblastoma</td>
<td>20</td>
</tr>
<tr>
<td>Wilms’ tumor</td>
<td>18</td>
</tr>
<tr>
<td>Osteosarcoma</td>
<td>10</td>
</tr>
<tr>
<td>Kaposi’s sarcoma</td>
<td>127</td>
</tr>
<tr>
<td>Other sarcomas</td>
<td>141</td>
</tr>
<tr>
<td>Germ cell tumors</td>
<td>3</td>
</tr>
<tr>
<td>Other tumors</td>
<td>47</td>
</tr>
<tr>
<td>Total</td>
<td>801</td>
</tr>
</tbody>
</table>

Fig. 2. A young girl with early-stage Hodgkin’s lymphoma before and after treatment at the Uganda Cancer Institute.
Relevance of the Cancer Burden

Uganda, like many developing countries, has not been well prepared for the sudden burden of cancer it is now experiencing. This is recognized as a potential health threat of the same magnitude as infant mortality and infectious diseases. The majority of these cancer cases could be prevented or cured if detected early. Medications and infrastructure for treatment and disease management are not available. The inability to care for cancer patients has had a devastating effect on society and is manifested by the loss of productive members of the community and economy, the destruction of family structures and a squandering of precious family and national health resources on treating diseases at an incurable stage.

Historical Background of Cancer Research in Uganda

The history of cancer research in Uganda can be traced back to the pioneering work of missionary doctor Sir Albert Cook, who is regarded as the father of Western medicine in Uganda [14]. His meticulous case notes made between 1897 and 1904 were compiled and reviewed in 1954 by Dr. J.N. Davies [15]. From this review, it was concluded that a number of cases he saw were actually cancers, thus suggesting that cancer was present in the Ugandan population right at the outset of Western practice in the country, contrary to the view held at the time. To further substantiate this observation, the Kampala Cancer Registry was set up to collect systematic population data [16]. This is by far the oldest cancer registry in Africa. The operation of the registry required a well-developed pathology service, which was realized through the establishment and consolidation of the department of histopathology at the Makerere Medical School. The landmark description of Burkitt's lymphoma in 1958 by Denis Burkitt was an immediate beneficiary of the atmosphere of medical curiosity and descriptive research prevailing at the time [17]. The confirmation of Burkitt's lymphoma as a pathological entity in 1963 further confirmed the benefit of a well-established clinical research laboratory [18].

Three paths of research emerged. The first was the descriptive field of epidemiology, which looked at possible environmental causes, especially malaria and viruses. Linked to this was the involvement of laboratory sciences in the field of virology and immunology, strengthening the disease link with malaria which was key in the discovery of a viral cause of Burkitt’s lymphoma, namely the Epstein-Barr virus. The expertise at the then East African Virus Research Institute (now known as the Uganda Virus Research Institute) was instrumental in these discoveries. The third path of research development, thanks to the unending clinical curiosity of Denis Burkitt, was clinical research. Not only did Dr. Burkitt describe the tumor, he was the first to discover that this particular cancer could be cured through chemotherapy [19]. The discovery that one of Africa's most common cancers was potentially curable received the attention of cancer researchers throughout the world. The US National Cancer Institute saw it as an opportunity to collaborate with the Makerere University Medical School as a follow-up to the discovery of Burkitt’s lymphoma [20]. The establishment of the Uganda Cancer Institute (sometimes referred to below simply as 'the Institute') in 1967 was the climax of these achievements [21]. The initial landmark studies were on treatment of Burkitt’s lymphoma at the Uganda Cancer Institute's Lymphoma Treatment Centre [3]. This included the use of combination chemotherapy, treatment of central nervous system disease, the principle of tumor debulking and the pathogenesis of tumor lysis syndrome [22]. The Institute provided a base for clinical and investigative research collaboration between the National Cancer Institute and Makerere University, established a postgraduate training program in clinical and investigative oncology, provided a consultative oncology service for local and upcountry hospitals and lastly carried out multidisciplinary studies of common cancers in Uganda [3].

Apart from Burkitt’s lymphoma, other tumors were also studied. The first report of the efficacy of chemotherapy alone in childhood Hodgkin’s disease came from the Institute, at a time when radiotherapy was the main modality in resource-rich countries for management of early-stage disease [23, 24]. A comprehensive description of adult and childhood endemic Kaposi’s sarcoma, response to treatment and early observation of an epidemic form of the disease in Africa came out of the Institute [25–32]. The initial attempt at objective staging of hepatocellular carcinoma was the Kampala Staging Scheme, which was devised at the Institute and presented at the international symposium on liver cancer held in Kampala in 1971 [33, 34]. This was to be followed by the landmark report on the efficacy of adriamycin as a single agent in hepatocellular carcinoma [35]. Given the challenge of the availability of chemotherapy in developing countries noted at the onset, the Institute proposed the concept of an essential drug list for cancer therapy which has since been accepted and adopted by the WHO as a key component of the global cancer control effort [36, 37].
Barriers to Implementation of National Cancer Control Programs in Africa

Cancer control is aimed at reducing cancer incidence, morbidity and mortality and to improve the quality of life of patients in a defined population through the systematic implementation of evidence-based interventions for prevention, early detection, diagnosis, treatment and palliative care. A comprehensive program addresses the whole population by responding to the needs of different subgroups at risk within the population.

There are several barriers to effective implementation of cancer control programs in Africa and other developing countries [38]. These have been well highlighted recently and include:

- Low political priority and lack of funding from government and donor agencies
- The large increase in cancers due to lifestyle changes following modernization and urbanization
- An outdated health care system aimed primarily at communicable diseases
- Low cancer awareness in the population
- Lack of trained cancer specialists and health workers
- Lack of diagnostic and treatment capacity
- Scarce and expensive cancer medicines
- Few functional cancer registries.

For there to be an effective national cancer control program, different components need to be in place and functional. There is a need to gather information, determine priorities and implement appropriate initiatives. The schematic outline of Mellstedt [39] elegantly describes the flow of activities towards implementation of a comprehensive program and highlights the prominent role of research.

Current Roles of Cancer Research Institutions in Uganda: The Kampala Cancer Registry

The Kampala Cancer Registry is a population-based cancer registry that registers cancer cases from Kyadondo County, which comprises the Kampala district, the capital of Uganda, with its surrounding peri-urban areas. The registry data are computerized using the CANREG program. Since its inception, the Kampala Cancer Registry has published its data in the WHO series Cancer Incidence in Five Continents, volumes I, VII, VIII and IX [40].

The Registry has contributed greatly to the understanding of cancer in Uganda by providing summary data on the burden of cancer in Uganda. It has provided information on the changes in cancer trends, the outcome of cancers and the etiology of cancers in the country; this has been most noticeable in the era of HIV [8, 11, 40, 41].

Based on information from the Registry, 2 cancers have been prioritized for immediate control, namely cancer of the cervix and breast cancer. In males, cancer of the prostate and esophagus are being considered for control action.

It is hoped that the Registry will play a key role in evaluating the success of this intervention program, as well as providing information on factors influencing disease presentation and prognosis. The registry has recently also provided information on factors influencing survival of patients with cervical cancer and the role of treatment in outcome, especially among HIV-infected patients with cervical cancer [41]. The commonest subtypes of human papillomavirus in the country are 16, 18 and 45, which comprise over 80%, and this is the basis for the current pilot human papillomavirus vaccine project [42, 43].

The expansion of cancer registration in the country is being prioritized, though the biggest bottleneck has been lack of funds. As early as the 1960s, 2 population-based registries were opened in Kuluva in the West Nile district and at Ishaka Hospital, but both have closed down due to lack of funds. There is a need to reactivate these registries and to open new ones to increase national coverage.

Current Roles of Cancer Research Institutions in Uganda: The Uganda Cancer Institute

Overview

The mission of the Uganda Cancer Institute since its inception has been three-pronged: research into the treatment of commonly occurring malignancies in the region, provision of optimal clinical care guided by the results of treatment research and provision of training in cancer care for a broad range of health care professionals using as models cancers prevalent in Uganda as an entry point into understanding oncology in general. Because of the increase in cancers related to HIV, the need to provide care has become more urgent due to the high patient load.

Current Opportunities for Research Collaborations and Relevance to Local Disease Patterns

The Institute is re-emerging as an important cancer research institute once more, as there is a critical need to
develop capacity to handle the whole range of cancers emerging in the country [21]. There are great opportunities to study cancers related to HIV, both AIDS defining and associated [44, 45]. Other areas of research available to the Institute include the role of various pathogens in the causation of cancers, which is becoming a very important area in cancer research [46]. This is potentially the starting point for the pursuit of new therapies and vaccines, especially for cancers associated with viruses, such as hepatitis B and C viruses, which can cause hepatocellular cancer. Human papillomavirus subtypes, which cause cervical cancer, Kaposi's sarcoma-associated herpesvirus, which causes Kaposi's sarcoma, and Epstein-Barr virus, which causes Burkitt's lymphoma, are also well characterized. A number of joint research projects and shared facilities exist with premiere HIV research institutions such as the Joint Clinical Research Center, the Infectious Disease Institute and the Uganda Virus Research Institute.

**Research Training through International Research Collaborations**

With a strong local research capacity, collaborative research with international colleagues becomes more engaging, rewarding and mutual. We are focusing on training highly qualified and motivated homegrown health care professionals who can undertake the challenge of both research and care which combines research skills and clinical care as a complementary measure [44]. The goals of this institutional research capacity development will be to create a unique research training program in cancers commonly seen in Uganda and to improve care for patients with malignant diseases in Uganda. This will support research on cancer epidemiology, pathogenesis, treatment and prevention, providing a reservoir of continued leadership in good research skills at the Uganda Cancer Institute, which are key for an eventual national cancer control program.

Several US-based institutions such as Case Western Reserve University, University of California, San Francisco, University of Washington and the Fred Hutchison Cancer Research Center are already engaging with the Uganda Cancer Institute to build capacity for research along these lines.

**Provision of Care**

The main focus of research at present is provision of care in a socioeconomically deprived setting with limited capacity for cancer care provision [44, 45]. This is against the backdrop of the AIDS pandemic and the impact of antecedent HIV-related malignancies.

Opportunities exist for a new paradigm of care, taking advantage of existing social factors in the community [47, 48]. Family support is still very strong in Uganda as it is...
Close family relationships and community can be engaged in care support and awareness programs [48]. Social science research will be key in understanding some of these societal factors and the important issue of how they may be integrated into standard care for cancer patients. These are areas vital for providing comprehensive and holistic care.

**Community Programs and Initiatives**

A mobile screening program for breast cancer and potentially other cancers such as cervical and prostate cancer is being piloted in partnership with colleagues from Yale University and the Dana-Farber Cancer Institute (fig. 3). The overall objective of this project is to find ways of improving the outcome of Ugandan women with breast cancer through early detection by a community mobile mammography service. We are assessing the utility of this method in delivering this service to women in the community without access to screening and diagnostic services for breast cancer, one of the commonest cancers in Ugandan women. If this program is successful, it will most likely lead to the development of similar interventions for other common cancers in the community. A community early detection program using a mobile service in low-resource settings is innovative, especially in eliminating disparity in access and hence equity.

In partnership with our community of patients and relatives, the Uganda Cancer Institute has formed the Uganda Child Cancer Foundation, a child cancer awareness and advocacy group. The rights of children with cancer in Uganda and Africa in general have never been highlighted. Children with cancer are entitled to access to a good quality of care as with any other childhood illnesses. Moreover, most childhood cancers here could be treated with curative intent [49]. The Uganda Child Cancer Foundation has been assisting children with cancer to access good care in addition to mobilizing social support for their families and leading in child cancer prevention efforts.

We have also encouraged the formation of cancer survivor groups such as the Uganda Women Cancer Support Organization, which is very active in highlighting breast and cervical cancer. Community awareness and sensitization programs in partnership with the media have increased the level of awareness of cancer tremendously. We provide technical support to antitobacco groups such as the Uganda National Association of Community and Occupational Health, an environmental action network. The result of this has been the ratification by Uganda of the Framework Convention on Tobacco Control.

**Influencing the National Cancer Agenda**

We recently held the first strategic workshop on cancer in Uganda together with the Ministry of Health. The objective of the workshop was to identify bottlenecks and key areas for intervention in prevention, surveillance and provision of cancer care in the country. It was also meant to identify major stakeholders with capacities for research, training and care. Three major obstacles to implementation of a national cancer control program were identified: lack of a policy framework (regulatory authority and legislation), lack of capacity (fiscal and human) and lack of a coordinating mechanism.

Solutions to address these obstacles were proposed, and the Ugandan Ministry of Health and the WHO country office have committed to provide leadership in formulation and implementation of a national cancer policy to guide and regulate cancer activities, increase resources for cancer control and establish a coordinating mechanism for a national cancer control program.

**Summary and Implications**

Elements of all the public health priorities for a national cancer control program are discernable in Uganda, through the evidence available from research institutions and their leadership. The infrastructure for training and research is in place through international collaborations. Mechanisms for continual evaluation and quality monitoring, including effectiveness, are available. Evidence has been presented to the government and WHO at the country level and there is commitment to establishing a comprehensive national cancer control program for Uganda.

The key lesson from this is that each country has unique opportunities within existing activities which can be creatively used as a starting point for initiating a cancer control program. Evidence from this existing set-up should be identified and provided to governments to help in formulating national cancer policies and programs.

**Conclusion**

With the increasing global cancer burden, especially in the developing world, the WHO has made the Framework Convention on Tobacco Control and the development of comprehensive national cancer control programs as key responses. However, most countries in Africa lack
the capacity to establish such a program. They lack institutional and human resources to set this into motion. The approach of creatively using available designated cancer institutions as focal points for evolving a comprehensive national cancer control program would be opportune. This has the potential of making cancer control an essential part of the public health response in a particular country, with the appeal of a comprehensive approach encompassing prevention, early detection, early treatment and palliative care. In Uganda, the opportunities provided by the already existing cancer research institutions were made use of through objectiveness, creativity, community involvement, international partnerships and finally approaching government with the evidence of functionality. Each country should look at its unique background to approaching the problem of cancer and crafting responses, as a starting point for initiating a national cancer control program.

Acknowledgements

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References


