



## Review article

## Evidence-based improvisation: Facing the challenges of cervical cancer care in Uganda

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## A B S T R A C T

There is significant disparity in the prevalence of cervical cancer globally, with low- and middle-income countries (LMICs) shouldering a disproportionate share of disease incidence and an even greater proportion of morbidity and mortality. Available resources for diagnosis, treatment and palliation of cervical cancer are inversely related to per capita income. While prevention and screening remain public health priorities, given the large number of women affected by cervical cancer, expanding treatment capacity should be included in any evidence-based intervention plan. Uganda, a country with a high incidence of cervical cancer, serves as a representative case study in terms of the challenges of diagnosis and access to treatment in sub-Saharan Africa. Providers and patients in Uganda are challenged by late presentation to care, limited training opportunities, cost-prohibitive diagnostic studies, insufficient access to gold-standard treatment, and under-utilized palliative care services. This review highlights the ways in which Uganda's experience is typical of the continent at large, as well as areas where Uganda is unique. We describe the ways in which a small but dedicated group of gynecologists carefully use limited evidence and available resources creatively to provide the best possible care for their patients. We show that improvisation, albeit evidence-based, is central to the nature and success of oncology care in Africa (Livingston, 2012). We argue that a “recalibrated global response” (Farmer et al., 2010), particularly stressing the expansion of radiotherapy capabilities, could dramatically improve cancer care and outcomes for women in Uganda as well as in LMICs globally.

## 1. Introduction

Worldwide, there is great disparity in access to cancer treatment and outcomes. Despite the fact that low- and middle-income countries (LMICs) experience 78% of years of life lost (YLL) and 77% of disability-adjusted life years (DALYs) due to cancer, these less-developed countries account for just 6% of total resources spent on cancer care globally (Beaulieu et al., 2009; Institute of Medicine Committee on Cancer Control in L, Middle-Income C, 2007). This gross funding discrepancy severely limits available treatment, which, together with typically advanced disease at diagnosis, contributes to the high mortality rates in LMICs.

Cervical cancer is the fourth most-common cancer among women worldwide with 528,000 new cases and 265,700 deaths estimated in 2012. Cervical cancer is over-represented in LMICs, where 84% of new

cases and 87% of the deaths occur (Torre et al., 2015). Incidence in East Africa is among the highest in the world. In Uganda, cervical cancer is the most common malignancy and responsible for the greatest cancer-related mortality among women with 3915 new cases and 2275 deaths annually (MOH, 2010; Bruni et al., 2016).

While incidence has decreased in developed countries secondary to widespread uptake of screening and vaccination, incidence of cervical cancer in Uganda, as well as in neighboring countries, has increased. Less than 10% of Ugandan women have ever been screened for cervical cancer (MOH, 2010; Ndejo et al., 2016). Lack of screening is at least in part responsible for the magnitude of the cervical cancer epidemic in sub-Saharan Africa.

Although prevention is vital for cervical cancer control, treatment is also an essential part of any strategic intervention package (Gelband et al., 2016). Although comprehensive vaccination of pre-teen girls is

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projected to be cost effective and lifesaving, incidence of cervical cancer would not be expected to drop for two decades, with maximal effect realized 50 years following comprehensive vaccination (Jit et al., 2014). Meanwhile, cervical dysplasia and early cancers will remain common and treatable. In those two decades before a benefit would be expected, approximately 11 million women in low-income countries will be diagnosed with cervical cancer (Atun et al., 2015). Treating these cancers improves survival and local control (Yap et al., 2017), palliates symptoms cost-effectively (Barton et al., 2003), and could even be cost-saving if scaled up to meet demand (Atun et al., 2015).

In Uganda, at least 80% of cervical tumors are diagnosed in an advanced stage (MOH, 2010). As a result, five-year overall survival (reported at a time when external beam radiation was available), for all cases is approximately 18% (Gondos et al., 2005). Lack of record keeping, attrition and the lack of systematized follow-up (MOH, 2010; Maranga et al., 2013; Mutyaba et al., 2009), all limit the accuracy of this estimate.

This paper gives an overview of the challenges providers and patients face when treating cervical cancer in Uganda. We will show how providers rely on evidence-based improvisation to design best-available treatment plans for their patients. Cervical cancer research is concentrated in high-income countries (Ginsburg et al., 2017); thus, findings must be extrapolated and adapted for use in low-resource settings. We will show the ways in which such improvisation can effectively solve problems as well as the ways in which it is limited. We will argue for expanding radiation in LMICs.

## 2. Training

In the United States, patients with gynecologic cancers have better outcomes when treated by gynecologic oncology subspecialists (Dahm-Kahler et al., 2016), but there is a dearth of specialty-trained surgical and medical gynecologic oncologists in Africa, including Uganda (MOH, 2010). Formal gynecologic oncology training opportunities in sub-Saharan Africa are limited: three fellowships in Ethiopia, one in Ghana, one in Kenya, one in Zambia and several in South Africa (Johnston et al., 2017). The entire sub-Saharan portion of the continent has the capacity to train roughly as many fellows per year as the state of California. Funding for individual fellows is variable; as these programs are considered post-graduate degrees in East Africa, trainees must pay tuition averaging \$3500 US dollars (USD) per year (Dubowitz et al., 2010), three-times Uganda's average national annual income (UBOS, 2014).

In response to the high unmet need for surgeons trained to perform oncologic pelvic surgeries, one group of Canadian gynecologic oncologists, in partnership with the Society of Gynecologic Oncology of Canada and with local colleagues, has developed a focused high-intensity hands-on curriculum designed to train gynecologists in complex surgery including radical hysterectomy and lymphadenectomy (Elit et al., 2010). The program was piloted in Mongolia and implemented in Kenya, consisting of a 2-week course combining seven online teaching modules with hands-on surgical training in-country. Similar recurring 1-week training opportunities for a core group of gynecologists in radical hysterectomy and lymphadenectomy at publically-funded tertiary care hospitals in Kampala, Uganda have been offered by dedicated US-based gynecologic oncologists for several years.

Under the leadership of local senior gynecologists, Uganda is developing a fellowship program in gynecologic oncology. The fellowship will be a joint effort between the Uganda Cancer Institute and Mulago National Teaching and Referral Hospital with financial support from the African Development Bank (ADB). The ADB has recently designated Uganda as the regional Center of Excellence for oncology and has created funding opportunities for training through the newly-established East African Oncology Institute (East Africa Centers of Excellence Uganda, 2014). The fellowship will also draw support, mentorship and recurring hands-on in-country training from gynecologic oncologists

stationed abroad. Organizations like the Society of Gynecologic Oncology and the International Gynecologic Cancer Society are recognizing the importance of formal training opportunities in LMICs and are investigating strategies to facilitate access to hands-on training.

## 3. Diagnostic challenges

### 3.1. Imaging

In addition to the lack of trained gynecologic oncologists, accurate diagnosis is limited by imaging capabilities. Despite the clinical-staging paradigm, diagnostic work-up in more-developed countries usually includes Computed Tomography (CT), Magnetic Resonance Imaging (MRI) and/or Positron Emission Tomography (PET) scans. These advanced imaging technologies can help detect lymph node metastases, frequently missed by clinical staging, which can significantly impact treatment planning (Bourgioti et al., 2016; Hansen et al., 2015). However, access to CT, MRI and PET technology is limited by costs and availability of machines in LMICs. While medical care has been offered free of charge at public facilities in Uganda since 2001, nearly half of the country's healthcare financing continues to come from out-of-pocket expenditures (Orem and Zikusooka, 2010). Patients must self-pay for some labs and all imaging and pathology studies. CT scans, costing at least as much as the average monthly national income (300,000 Ugandan Shillings, about \$80), are not feasible for most patients in Uganda.

By contrast, a pelvic ultrasound in Uganda is a more feasible expenditure (about 20,000 shillings or \$5). There are data to suggest that ultrasound can compare favorably to MRI in their ability to characterize tumor size, depth of invasion and parametrial infiltration (Epstein et al., 2013; Fischerova and Cibula, 2015; Fischerova et al., 2008). Thus, Ugandan gynecologists use physical exam, biopsy and ultrasound to inform staging and treatment planning for their patients.

### 3.2. Pathology

Pathology services are essential for diagnosis and treatment, as well as for accurate registries. However, service coverage in sub-Saharan Africa is, at best, one-tenth of the coverage of high-income countries (Adesina et al., 2013). While Uganda has a rich history of strong pathology scholarship, contributing to formative research on pathogenesis of Burkitt's Lymphoma (Walusansa et al., 2012), services are insufficient, with an estimated 1 pathologist for 1.5 million people (Nelson et al., 2016). Laboratories, equipment and staffing must increase to significantly improve capacity. While costs are substantial, a professional pathology group has devised a three-tiered laboratory system to standardize and streamline resources to provide full-spectrum oncology care in low resource settings: tier one lab start-up costs would be at least \$25,000, tier two \$240,000 and tier three \$412,000 (Warner, 2017).

Registries, which are essential for understanding the epidemiologic magnitude of disease in order to mobilize response, are not common in sub-Saharan Africa. Uganda has one of the only registries considered to be comprehensive on the continent, yet, nearly half (48%) of cervical cancer cases captured by the Kampala Cancer Registry do not report a stage (Wabinga et al., 2003). Gynecology and pathology faculty at the Uganda Cancer Institute (UCI) and Mulago Hospital are creating new processes to standardize and improve two-way reporting.

As pathology services at government hospitals are congested, a network of private pathology labs have emerged in Kampala, Uganda. Quicker specimen processing and good-quality reporting come at a higher cost to patients. These private labs are variable in their commitment to reporting to the Kampala Cancer Registry. As with imaging and laboratory reports, patients serve as their own mobile medical record, transporting their own formalin-laden specimens to labs and then couriering reports to their treating physicians.

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