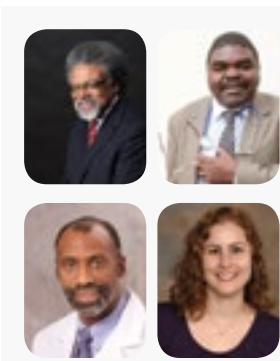


IMPLEMENTING A CERVICAL CANCER PREVENTION SERVICE PLATFORM IN ZAMBIA, FROM SCRATCH

GROESBECK PARHAM (TOP LEFT), CO-FOUNDER, CERVICAL CANCER PREVENTION PROGRAM, ZAMBIA, AND HONORARY CONSULTANT, UNIVERSITY OF ZAMBIA; **MULINDI MWANAHAMUNTU** (TOP RIGHT), CO-FOUNDER, CERVICAL CANCER PREVENTION PROGRAM, ZAMBIA AND CLINICAL HEAD AND DIRECTOR OF GYNECOLOGY ONCOLOGY, WOMEN AND NEWBORN HOSPITAL, LUSAKA, ZAMBIA; **MICHAEL HICKS** (BOTTOM LEFT), PROFESSOR OF OBSTETRICS AND GYNECOLOGY, UNIVERSITY OF NORTH CAROLINA, CHAPEL HILL, USA, AND FOUNDING DIRECTOR, CLINICAL TRAINING, CERVICAL CANCER PREVENTION PROGRAM, ZAMBIA AND **KRISTA PFAENDLER** (BOTTOM RIGHT), CLINICAL INSTRUCTOR, OBSTETRICS AND GYNECOLOGY AND FELLOW, GYNECOLOGIC ONCOLOGY, UNIVERSITY OF CALIFORNIA, IRVINE, USA



Through shared leadership, unyielding commitment and respect for local beliefs, we built – from scratch – a women-centric cervical cancer prevention infrastructure in Zambia. Startup financing was obtained by highlighting cervical cancer as an AIDS-defining disease and the importance of preventing deaths in women living longer with antiretroviral therapy. Myths were dispelled using culturally-informed community education. The human resource gap was narrowed and the cancer care pathway compressed using a platform of affordable technology and task shifting.

Cervical cancer is a major cause of cancer-related morbidity and death in low- and middle-income countries (LMICs). Although theoretically a preventable disease, implementation and scaling of effective prevention service platforms in these environments is difficult, due mostly to human resource, infrastructural and financial requirements (1). Overcoming these obstacles demands innovative approaches informed by knowledge of the overarching sociocultural context in which the disease occurs, an understanding of the operational nature of fragmented public healthcare systems, and an appreciation of how chronic economic depravity impacts human behaviour.

Background

In 2003, two United States gynaecologic oncologists (MH and GP) visited the University of Zambia Teaching Hospital, the nation's only state-run tertiary level healthcare facility, to assess the status of gynaecologic oncology care in general and the level of cervical cancer screening in particular. The visit was hosted by Friends of Africa, Inc., a non-profit United States-based organization (2), and the Center for Infectious Disease Research in Zambia (CIDRZ), a Zambian non-governmental organization led by a small group of American obstetricians/gynaecologists and Zambian nationals (3). Through a week-

long series of formal conferences, informal discussions, clinical ward rounds and social gatherings, we learned first-hand of the human devastation caused by cervical cancer in a large, high-risk, economically marginalized, unscreened population, and the effects of human immunodeficiency virus (HIV)-induced immunosuppression on the natural history of the disease and its outcomes (4, 5). A rapid assessment of the status of cervical cancer control activities in Zambia at that time revealed only 10,000 women had ever been screened by Pap smear since 1964. There were no facilities for radiation therapy, very limited access to chemotherapy, no formally trained oncologists, and woefully inadequate pathology services as there was only one cytology technician and one cytopathologist employed in the public sector, serving a population of 12 million people. Although Zambian colleagues enthusiastically embraced the idea of cervical cancer screening, its benefits in women with human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) were felt to be questionable, as their usual course was rapid death soon after diagnosis, long before cervical cancer could develop and progress (6).

Preliminary activities

In the sphere of addressing the HIV/AIDS epidemic globally,

advocacy to increase access to antiretroviral therapy (ART) worldwide was crystallized with the inception of the Global Fund to Fight AIDS, Tuberculosis and Malaria in 2001 (7) and the United States President's Emergency Plan for AIDS Relief (PEPFAR) in 2003 (8). Both responses represented large political and financial commitments to the mitigation of HIV/AIDS worldwide through support of programmes targeting HIV and AIDS prevention, treatment, care and support, and health systems strengthening. In combination with the Doha Declaration in 2001 (9), which allowed developing countries to manufacture generic medications to combat public health crises like HIV, global access to ART was accelerated. However, despite longer lifespans as a result of ART, HIV-infected women continue to be at an elevated risk for the progression of human papillomavirus (HPV)-induced cervical cancer precursors to invasive cancer (10-13). There was no specific funding for cervical cancer prevention or treatment in these large global health initiatives as data was lacking on background disease prevalence, rates of progression, and accuracy of screening tests in this high-risk population, despite the fact that cervical cancer had been classified as an AIDS-defining disease by the United States CDC in 1993 (14). Neither were there clear cut guidelines for screening this subpopulation of women, particularly those who lived in resource-constrained nations, like Zambia.

In 2004, with the goals of developing and evaluating the appropriateness of cervical cancer screening protocols for HIV-infected women living in resource-constrained nations, and determining background disease prevalence, we undertook a pilot feasibility study among HIV-infected women attending the University of Zambia Teaching Hospital for HIV care and treatment. Under the auspices of a small (US\$ 25,000) grant from the University of Alabama in Birmingham Center for AIDS Research, we screened a cohort (n=150) of women using liquid-based monolayer cytology. The prevalence of squamous intraepithelial abnormalities on cytology was 76% (114/150), of which 32.6% (49/150) were high-grade lesions (HGSIL) and 20% (30/150) suspicious for squamous cell carcinoma (SCC) (15). At the time that these results were published they were among the highest abnormal cervical cytology rates ever reported in the literature (15). They were also some of the very first data demonstrating the need for routine cervical cancer screening of HIV-infected women, as a significant percentage of our cohort either had cancer or precursor lesions, and most (80%) were ART-naïve and seeking treatment for the first time. Data from the study was used to leverage financial support from PEPFAR, through the Centers for Disease Control (CDC), for routine cervical cancer screening of HIV-infected women in Zambia. Immediately after funding was granted (2005) we formed a partnership with the Zambian Ministry of Health, creating the Cervical Cancer Prevention Program in

Zambia (CCPPZ) utilizing a low-cost cervical cancer screening intervention called visual inspection with acetic acid (VIA) to be delivered by nurses in cervical cancer prevention clinics tightly linked to PEPFAR-supported public HIV/AIDS care and treatment infrastructures. CCPPZ was the first and largest PEPFAR-supported VIA-cryotherapy based "screen-and-treat" cervical cancer prevention initiative linked to HIV/AIDS care and support programmes in the developing world (16, 17). Inspired by the success of CCPPZ (16, 18) and other PEPFAR-supported initiatives, the United States State Department announced the launch of the Pink Ribbon Red Ribbon® campaign on September 2011 to expand "the availability of vital cervical cancer screening and treatment—especially for high-risk HIV-positive women—and also promoting breast cancer education" (19). Launched in Lusaka, CCPPZ was designated as PRRR's flagship programme. In subsequent years, multilateral support for cervical cancer prevention in LMICs has expanded to include support from World Bank and Global Fund and many others.

Reflections

A retrospective evaluation of CCPPZ's "ground-up" modus operandi and its activities, since its inception, suggests several critical aspects that contributed to the success of its initiation, scale-up and sustainability.

1. *We leveraged the momentum, infrastructure and capacity-building capabilities of a large and critical global health initiative.*

➔ By initially focusing programmatic activities on high risk HIV-infected women, we acquired the resources needed to initiate a programme to prevent a co-morbid condition – cervical cancer – and the time required to make programmatic adjustments and generate evidence of its value (17). Piggybacking cervical cancer prevention services on a pre-existing PEPFAR-supported HIV Care and Treatment infrastructure through CIDRZ provided an affordable opportunity to utilize the latter's administrative resources, information technology system, office space, management expertise, data management capabilities and approaches to problem solving, as well as its credibility in the larger healthcare space.

2. *We chose a prevention intervention that was contextually appropriate and patient-centred.*

➔ The choice of VIA as the primary screening test was a practical decision, based on prevailing circumstances. Although World Health Organization (WHO) endorsement of this screening modality for resource-constrained environments was not to come until 2013, observational studies and field demonstration projects in LMICs had already shown that it was safe, feasible, acceptable, and

could reduce cervical cancer incidence and mortality rates (20-22). Two of us (GP, MH) were experienced colposcopists and thus very familiar with the application of acetic acid to the cervix as a step in the evaluation of abnormal Pap smears. The severe shortage of physicians in Zambia and the fact that VIA could be readily mastered by non-physician providers, prompted us to task-shift the prevention activities from doctors to nurses, the latter of which were much more abundant in number. As a screening test VIA results are rendered in two-three minutes, facilitating immediate treatment (cryotherapy, cold coagulation, LEEP), thereby reducing the need for multiple visits and the subsequent possibility of loss to follow prior to definitive treatment, in a relatively low-cost single-visit “see-and-treat” approach.

- ➔ Naked-eye VIA lacks the ability to evaluate certain vascular changes in cervical lesions that may reflect malignant transformation (e.g., coarse punctations or/and mosaicism), yet colposcopy equipment was too expensive. As an alternative we taught screening nurses how to use a commercially available digital camera to capture images of the cervix (digital cervicography) during the screening examination, project and magnify them on a bedside monitor/ television screen located in the clinic. Digital images were discussed with each client for purposes of education and to help dispel prevalent myths and misconceptions about the origin and nature of cervical neoplasia (23). If nurses needed expert consultation to help interpret the findings they could download the images and email them through a locally produced web-based consultation portal, to one of several gynaecologic experts, for immediate distance consultation. This provided nurses with expert back-up and prevented patients from having to make subsequent visits to the clinic prior to receiving a definitive assessment. Each week all digital images were reviewed by the CCPZ team. Harnessing the power of mobile technology (digital cervicography, web-based consultation) to facilitate communication between nurses in the field and physician-consultants at the university improved the accuracy and efficiency of clinical decision-making. It also facilitated the scale of standardized, quality-assured, cervical cancer screening and real-time distance consultation to all provincial and large district hospitals across Zambia, where it would never have been possible before (24, 25).

3. We overcame the inertia associated with taking the “first step” and strengthened the existing healthcare delivery system along the way.

- ➔ The CCPZ leadership team made a joint decision to start the Program with meagre resources and build as we proceeded, rather than wait until we had developed all of the necessary systems, human capacity and financing. Some of the major problems we confronted and the home grown solutions we developed are demonstrated in a table entitled “Critical Problems and Practical Local Solutions in the Cervical Cancer Prevention Program in Zambia” (26). These approaches to problem-solving provide valuable practical examples for implementing similar programmes in resource-constrained settings. They reflect the product of critical thinking by a very close knit team of pragmatic clinicians (doctors, nurses, public health practitioners), consisting of Zambian nationals and an expatriate United States board-certified gynaecologic oncologist (GP) living within the country, representing the creative process involved in the development of local solutions for local problems instead of transplanting ideas effective in different environments but locally inappropriate.

4. We integrated the Program within preexisting government-operated healthcare infrastructures.

- ➔ A significant proportion of the female population in Zambia receive their healthcare through government-operated clinics in which most services are delivered free of charge to patients. Although chronically plagued with inefficiencies due to shortages of mid/high-level personnel and underfinancing, these facilities provide access to the target population and their involvement is critical as a bridge to the eventual institutionalization of cervical cancer screening as a routine healthcare service. After gaining permission from appropriate Ministry of Health officials at the national and local levels, we personally visited each clinic in Lusaka in which we implemented the first sets of “screen and treat services”, accompanied by the Director of Lusaka Public Health Services (Dr Moses Sinkala, deceased). During these visits we consulted with the nurse-in-charge of each facility and explained the Program and its purpose in detail, after which arrangements for implementation were made. Improvements to the infrastructure of clinics from our programme’s funds benefited the general healthcare infrastructure. Using this approach gave the Program access to physical space, utilities, maintenance, waste disposal and medical/pharmacy services for patients, and ease of referral to and from other departments within the health facilities. It also aided significantly in the transition of our activities from “special project” to “routine service”, eventually paving the way for government takeover and ownership which occurred in 2015.

5. We designed the programmatic infrastructure in accordance with the natural history of the target disease.

➔ Implementation of services for the early detection of cervical cancer, particularly among populations of previously unscreened women in high HIV prevalence environments, uncovers cervical abnormalities ranging from simple and complex precancerous (cervical intraepithelial neoplasia) lesions to advanced stage invasive cancer. From the outset we trained nurses to treat simple precancerous lesions with cervical ablation (cryosurgery and thermocoagulation) and complex ones with surgical excision (loop electrosurgical excision procedure – LEEP) (27), both in outpatient settings. In doing this, we ensured treatment of the full spectrum of precancerous lesions was feasible within the context of a “screen and treat” algorithm. Screening nurses were also trained to perform punch biopsy on lesions that were suspicious for invasive cancer and refer them for appropriate treatment. During the early phase of the Program the vast majority of cervical cancers detected were advanced stage, but as the years progressed and more women accessed screening earlier, the percentage of early stage cancers shifted from 24% to 42%, many of which could be treated and cured with radical surgery alone, if properly performed (26). In response to this change we (GP, MH, MM) implemented a training programme for the surgical treatment of early stage invasive cervical cancer in the Department of Obstetrics and Gynaecology at the University of Zambia Teaching Hospital. Additionally, the leadership of the hospital’s Department of Obstetrics and Gynaecology created a Gynaecologic Oncology Unit (headed by MM) to improve the care of women with gynecologic malignancies and the surgical training of registrars. We formed tight linkages with the government’s newly established (2006) national cancer centre in Lusaka (Cancer Diseases Hospital) for referral and treatment of women with advanced stage invasive cervical cancer for treatment with chemoradiotherapy.

6. We constantly refined Program operations.

➔ From the inception of CAPPZ, community education was a centrepiece, as cervical cancer and its prevention/treatment methods are surrounded by myths and misconceptions. We assessed local perceptions of cervical cancer, screening and treatment in a door-to-door community-based initiative (21) and used them to shape the content of the messages delivered by peer educators to improve uptake of services. As our appreciation of the impact of “folk beliefs” deepened we opened up a collaboration with the newly formed Ministry of Chiefs and Traditional Affairs to engage local traditional tribal chiefs,

traditional marriage counsellors and traditional healers as primary advocates for screening (28). We also employed street-theatre skits throughout Lusaka to disseminate messages about the importance of cervical cancer screening and to challenge the common belief that cancer has spiritual origins.

- ➔ When informed by screening nurses and peer educators of the growing demand for screening services by non-HIV infected women, we rapidly extended them to the general population of women in the community, regardless of HIV status. We offered HIV counselling and testing to all women attending screening clinics. These policy changes had the collateral effect of transitioning a service platform built initially for a small but important sector of the population, to a general population-based cervical cancer prevention programme.
- ➔ As our need for histopathology services increased we supported public sector pathology services through bulk purchases of supplies (wax, stains, glass slides, ethanol, etc.) and equipment (microscopes, microtomes, etc.). We also negotiated discounted pricing for private sector histopathology services.
- ➔ We established a data collection system that allowed us to constantly assess all programmatic phases through a rigorous process of monitoring and evaluation of interim outcomes. Our use of routine programmatic indicators (e.g., screening uptake rates by age and HIV status, rates of cryotherapy-ineligible lesions, screening positivity and CIN2+ detection rates by age and HIV status, rates of “same-day services” and “appropriate referrals”) provided ongoing evidence on the role of improvements in the quality of screening and treatment services over time (29). We utilized programmatic data and modeling techniques to learn, for instance, that one case of high-grade cervical intraepithelial neoplasia (CIN 2/3) was detected for every 100 women screened; one case of cervical cancer was detected for every 145 women screened; one case of cervical cancer was prevented per 46 HIV-infected women screened (26, 30). These process and outcomes indicators were among the only clinical effectiveness metrics in the absence of a well-functioning population-based cancer registry and/or a widely-used national-level citizen identification system to measure declines in cancer incidence over time.

7. We emphasized the importance of personal sacrifice for the benefit of the enterprise.

➔ Building a cohesive team of individuals committed to improving cancer care, from the ground up, in an environment of very limited resources and low financial

remuneration required a remodelling of their outlook to embrace the belief that personal sacrifices in the present can fuel expansive development of the enterprise in the future. We used our weekly digital image review team meetings to emphasize the importance of patient-centred care, efficiency, teamwork, transparency, quality, reliability, personal responsibility, and, most of all, personal sacrifice as investments for future growth of the enterprise, from which each individual would eventually benefit.

Summary

Like any small business startup, we had a vision of the enterprise (women-centric “screen and treat cervical cancer prevention services”), where we wanted to establish it (Zambia), and the customer base (marginalized, unscreened HIV-infected women). Accordingly, we designed the product (digital cervicography, web-based consultation, immediate treatment with outpatient ablation/excision and referral for surgery or chemoradiation) to facilitate efficiency, quality control, monitoring and evaluation. We determined how the product should be marketed (nurse-led service platform to prevent cervical cancer in HIV-infected women, offered in government-operated public health clinics in Lusaka) in accordance with the overarching sociocultural and economic context. After securing a financial investor (PEPFAR) we piloted the enterprise in a few sites, utilizing a culturally-informed marketing strategy (peer educators, traditional chiefs, marriage counselors, healers) to dispel misconceptions about its intent and increase uptake. Through routine feedback from customers and employees, we refined the product as we went along (extended services to all women regardless of HIV status). We added value to the general healthcare environment in which we worked by sharing resources when appropriate (support for pathology services). As a result of our successes and progress, a larger investor (Pink Ribbon Red Ribbon) invested heavily in the enterprise by leveraging even more funding from the initial investor (PEPFAR), thereby facilitating scale-up to all of the country’s provincial and large district hospitals, and global recognition of the enterprise and its product. As often happens, an even larger entity (Zambian Government) eventually absorbed the enterprise, leading to its institutionalization and thereby improving the chances of long-term sustainability. ■

Dr Groesback Parham is a United States board-certified gynaecologic oncologist and Professor of Obstetrics and Gynaecology at the University of North Carolina, Chapel Hill. He co-founded the Cervical Cancer Prevention Program in Zambia with Dr Mulindi Mwanahamuntu in 2005. Dr Parham has lived

in Lusaka since 2005 and designs novel early detection service platforms for women’s cancers (cervix and breast) in resource-constrained African environments, evaluates innovative cancer prevention and educational medical technologies and teaches gynaecologic oncology surgery in his position as Honorary Consultant at the University of Zambia.

Dr Mulindi Mwanahmauntu is a Consultant Obstetrician/Gynaecologist who currently serves as Clinical Head and Director of Gynaecology Oncology at the Women and Newborn Hospital in Lusaka. He co-founded the Cervical Cancer Prevention Program in Zambia with Dr Parham in 2005.

Dr Michael Hicks is a United State board-certified gynaecologic oncologist, Professor of Obstetrics and Gynaecology at the University of North Carolina, Chapel Hill, and served as the Founding Director of Clinical Training for the Cervical Cancer Prevention Program in Zambia in 2006. He continues to interact with the programme through continuing medical education activities, surgical training and clinical research.

Dr Krista Pfaendler is a United States board-certified obstetrician/gynaecologist and serves as a Clinical Instructor of Obstetrics and Gynaecology and a Fellow in Gynaecologic Oncology at the University of California, Irvine. Dr Pfaendler initially worked with CCPPZ as a Fogarty International Clinical Research Scholar during which time she developed the LEEP referral clinic, participated in clinical research, designed clinical algorithms and assisted in the development of the programmatic data base. She continues to interact with the programme through a project studying quality of life among cervical cancer survivors.

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