



Risk factors for cervical cancer among distinct populations in low-resource countries: feasibility of cervical cancer screen-and-treat program on ukerewe island of lake victoria, Tanzania

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Purpose of review

A mass cervical cancer screening using World Health Organization-endorsed visual inspection with acetic acid (VIA) and cryotherapy triage was conducted over 5 days at Nansio District Hospital on Ukerewe Island, Tanzania in Lake Victoria. The aim was to evaluate the feasibility of a pilot screen-and-treat on a lower resource island and compare the results to previously held screen-and-treats in higher resource mainland settings.

Recent findings

Two hundred and eight-two women underwent VIA on Ukerewe Island during July 2017. The frequency of abnormal VIA screens was nearly twice that observed on the mainland in 2016 (18.4% vs 10.7%, respectively; $P=0.0091$). Island women had lower rates of grand multiparity (19.8% vs 26.8%, $P=0.02$) and more island women did not know their HIV status (80% vs 50%, $P<0.0001$). Overall, 31% of abnormal VIA screens occurred among women under 30 years between the two sites. Due to the cost of transporting CO₂ tanks, cryotherapy was nearly twice as expensive on the island as compared to the mainland.

Summary

Although transfer of an entire pilot screen-and-treat program to Ukerewe Island is feasible and well-received, expenses associated with ferrying equipment may be prohibitive to long-term sustainability. Higher VIA positivity rates were observed on the island.

Keywords

colposcopy, global health, mass screening, Tanzania, uterine cervical neoplasms

INTRODUCTION

Cervical cancer is the fourth most common cancer in women worldwide, with 569,847 new cases and 311,394 cancer-specific deaths having occurred in 2018 [1]. A staggering 90% of the disease burden is found in the developing world [2,3]. The death toll is highest in East Africa where approximately 50,000 women die each year [3]. Although mortality rates can be decreased with prevention and early diagnosis, screening modalities are not widely accessible in Sub-Saharan Africa [4,5].

In developed countries such as the United States, the availability of cytology screening with high-risk human papillomavirus (HPV) DNA testing has reduced incidence and mortality rates significantly [6]. However, pathologic evaluation of

cervical cytology is not widely available in East Africa because of the exorbitant costs and lack of gynecology trained pathologists making it difficult to implement traditional screening programs. Tanzania started widely dispersing the HPV vaccine in 2018 among school-aged girls between 9 and 14 years old but there is currently no reported data for the country-wide vaccination rate [4,5,7,8].

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KEY POINTS

- Two cervical cancer screen and treat campaigns were held successfully on mainland Tanzania and Ukerewe Island in 2016 and 2017.
- The VIA positivity rates on Ukerewe Island were higher than mainland Tanzania; this is likely secondary to the prevalence of higher risk factors in more rural settings.
- Although the WHO recommends screening to start at age 30, exceptions should be made in regions with risk factors such as high HIV positivity rates and early sexual debut.

Concurrent human immunodeficiency virus (HIV) infection may expedite the progression of HPV-mediated neoplastic transformation [9]. In Tanzania, the HIV prevalence is 4.5% and in 2018, 1.6 million people were living with HIV [10,11]. Furthermore, there is a lack of physicians trained in radical surgery for early stage cervical cancer, limited radiotherapy units for locally advanced tumors, and unavailability of antiangiogenesis and immunotherapy agents for recurrent or metastatic disease in Sub-Saharan Africa making it impertinent to focus on prevention since treatment for disease is more costly and harder to find [5^{***},12^{*},13,14].

The World Health Organization (WHO) has endorsed guidelines for visual inspection with acetic acid (VIA) with appropriate triage to immediate cryotherapy to eradicate dysplastic lesions [12^{*},15]. VIA screening has been shown to reduce disease-specific mortality by 31% in India, and in recent years, government-supported programs provide VIA free of charge in every district of Zambia [16–18]. Building on this work, we recognize that even within low-resource settings, a spectrum exists; the more remote a settlement is, the more lacking are effective screening programs. Our main objective was to evaluate the feasibility of bringing mass screening to a remote island in Lake Victoria and compare the island screening results to a previously held screening in a higher resource mainland setting performed the year before.

METHODS

A week-long pilot cervical cancer screen-and-treat workshop was planned at Nansio District Hospital on the island of Ukerewe in Tanzania in July 2017 after IRB approval at UC Irvine for retrospective data analysis with written consent waived. The primary objective was to evaluate the feasibility of a pilot screening on the island. Secondary objectives included the collection of demographic information

from the participants, training of healthcare providers, comparing VIA results to a previous year's screening on the mainland, and a cost analysis.

Campaign sponsorship

This pilot program was spearheaded through a partnership between the University of California, Irvine School of Medicine and the nongovernmental organization, CureCervicalCancer (CCC). Fundraising was conducted from December 2016 through June 2017, with all raised monies used to purchase necessary medical supplies, transfer instruments and accessory equipment to Mwanza, Tanzania, facilitate workshop advertising, arrange for transportation of team members, and recruitment of Swahili-English interpreters.

On the ground advertising and participant recruitment

In order to recruit patients for the pilot 'screen-and-treat' campaign, fliers and banners in Swahili were distributed in churches, schools, and hospitals. Local television and radio ads were played in Swahili. A truck with a loudspeaker was also driven around villages during the week of the workshop advertising the campaign.

Participant eligibility and exclusion criteria

Female participants were between ages 18 and 70 years and had to be currently or previously sexually active. Exclusion criteria for *screening* with VIA included women who were younger than 21 years who had never been sexually active. Exclusion criteria for *treatment* with cryotherapy included those with an acetowhite lesion covering greater than 75% of their cervix, lesions and/or other physical examination findings concerning for invasive cancer, concomitant pelvic inflammatory disease, or concurrent pregnancy.

Clinical procedures

Women who volunteered to participate in the pilot cervical cancer screen-and-treat workshop were registered, asked to provide their age, parity, and HIV status. Voluntary HIV testing was available on-site if a patient did not know her status. All data was recorded without subject identifiers.

Clinical procedures taught to onsite healthcare workers included:

- (1) Vaginal speculum placement with satisfactory visualization of the cervix.

- (2) Visual inspection of the cervix with 5% acetic acid, recognition of abnormal vascular markings (i.e. punctuation, mosaicism, atypical vessels), and acetowhite staining indicative of cervical neoplasia
- (3) Cryotherapy procedures employing standardized protocols.

Although awaiting VIA screening, participants were provided with leaflets in Swahili describing HPV and cervical cancer. VIA screening took 10 min and an additional 20 min if followed by cryotherapy. Condoms were offered to all women. Pregnancy tests were performed on all women requiring cryotherapy. Women with acetowhite lesions encompassing greater than 75% of the cervix as well as those with findings suspicious for invasive cervical cancer were referred to Bugando Medical Center (BMC) on mainland Mwanza to receive a free consultation and proceed with further treatment. No healthcare worker performed any of the above listed procedures without direct supervision from trained personnel. The screen-and-treat program was performed exactly the same way on Ukerewe Island as it had been conducted the year prior at Buzuruga Hospital in mainland Mwanza.

Regional notes

Ukerewe is the largest inland island in Africa (Fig. 1, [19]) and can be reached by a 4-h ferry ride on Lake



FIGURE 1. Map of Ukerewe Island. Map of East Africa highlighting Northern Tanzania including Ukerewe Island in Lake Victoria and mainland Mwanza [19].

Victoria. The population of approximately 345,000 is transient with many fishermen coming in and out of the community [20]. Nansio District Hospital is the only hospital on the island and has obstetrics, pediatrics, and surgery. Radical surgery, chemotherapy, and radiation are not available on the island and blood products are very limited.

The year prior, our collaborative effort held a similar mass screening at metropolitan Buzuruga District Hospital in mainland Mwanza. The second most populous city in Tanzania, Mwanza is home to 2.8 million residents and Buzuruga Hospital is in the municipality of Ilemela with a population of 343,001. Mid-level providers treat most patients with physician administrators available for consultation on most days. Except for Cesarean section, surgery is rarely performed at this site. Radical oncologic surgery, chemotherapy, radiation, and imaging beyond ultrasonography are not available.

Cost analysis

The elements analyzed focused on the costs (in US dollars with conversion to Tanzanian shillings) of the screening materials purchased and that of CO₂ tanks rented. The costs required to bring the mass screening equipment to Ukerewe Island via ferry were also considered. Physician time and that of other health-care providers' times were not factored into these analyses.

Statistical analysis

Demographic data and VIA results from Ukerewe Island were analyzed and compared with demographic and clinical material collected during the mass screening workshop at Buzuruga Hospital (28). Statistical tests included the Chi-squared test, Fisher's exact test, Mann-Whitney, and Kruskal-Wallis tests as indicated. A descriptive cost analysis was also performed.

RESULTS

Demographics

A total of 841 women (282 on Ukerewe Island and 559 at Buzuruga the year prior) registered to take part in the cervical cancer screen-and-treat workshops. The median age was 37 years on Ukerewe Island and 35.4 years in Buzuruga ($P=0.01$). Although there were no significant differences in the average number of children in each cohort, grand multiparity (i.e., >5 children) was significantly less prevalent among patients screened on the island ($P=0.02$). Overall, the majority of women

Table 1. Demographics of women who participated at the two cervical cancer screen-and-treat workshops

Workshop	Median age (range)	Average parity (range)	Grand multiparity (%)	Unknown HIV status (%)
Buzuruga (2016)	35.4 (18–83)	3.3 (0–16)	150 (26.8%)	283 (50%)
Ukerewe (2017)	37 (18–72)	3.5 (0–15)	56 (19.8%)	249 (88%)
<i>P</i> value	0.01	0.81	0.02	<0.00001

HIV, human immunodeficiency virus.

Buzuruga (mainland, metropolitan site); Ukerewe (island, rural site).

Grand multiparity: >5 children.

did not know their HIV status, with island women being less likely to have undergone prior testing compared to women on the mainland ($P < 0.00001$). These data appear in Table 1. The majority of women screened were between the ages of 30 and 50 at both sites.

Visual inspection with acetic acid screening results and cryotherapy disposition

Significantly more women on Ukerewe Island had VIA positive screening results compared to Buzuruga (18.4% Ukerewe, 10.7% Buzuruga, $P = 0.0091$) (Fig. 2 and Table 2). In total, 40% of women on the island who were VIA positive were younger than 30 in comparison to 33% of VIA positive women at Buzuruga were younger than 30 ($P = 0.25$). Combining both sites, 31% of VIA positive screens occurred among women under 30 years of age. There were no significant differences between the two sites among the VIA positive women and known HIV infection (4% Ukerewe, 8% Buzuruga, $P = 0.327$).

Thirty-seven women on Ukerewe Island underwent immediate cryotherapy, as compared to 48 patients at Buzuruga (Fig. 2). Fifteen women on the island were not treated due to concurrent pregnancy, clinical evidence of pelvic inflammatory disease, patient refusal, or acetowhite lesions greater

than 75% of the cervix and/or concern for carcinoma ($n = 6$). These women were advised to come back after resolution of PID or pregnancy or referred to BMC, a tertiary cancer center, on the mainland for further care. Twelve women on the mainland were not treated for similar reasons, including nine with acetowhite changes and/or lesions concerning for carcinoma. Any woman with invasive disease or lesions larger than 75% of their cervix was referred to BMC. Although the majority of women referred for invasive cancer were over age 50, one patient was under age 30 (Table 2). Finally, a total of five women were not treated due to unanticipated exhaustion of CO₂ supply on Ukerewe Island. These women were requested to come back the following week for treatment once CO₂ tanks were replenished.

Cost analysis

The total cost of funding the five-day workshop at Buzuruga on the mainland was \$11,218.72 USD or 23,850,998.00 Tshs (Table 3). By comparison, the total cost of the pilot screen-and-treat campaign held on rural Ukerewe Island was \$11,418.04 USD or 24,982,662.00 Tshs (Table 3). During this period, the median per capita household monthly income in Mwanza was approximately 11,400.00 Tshs. When comparing the cost between the island and

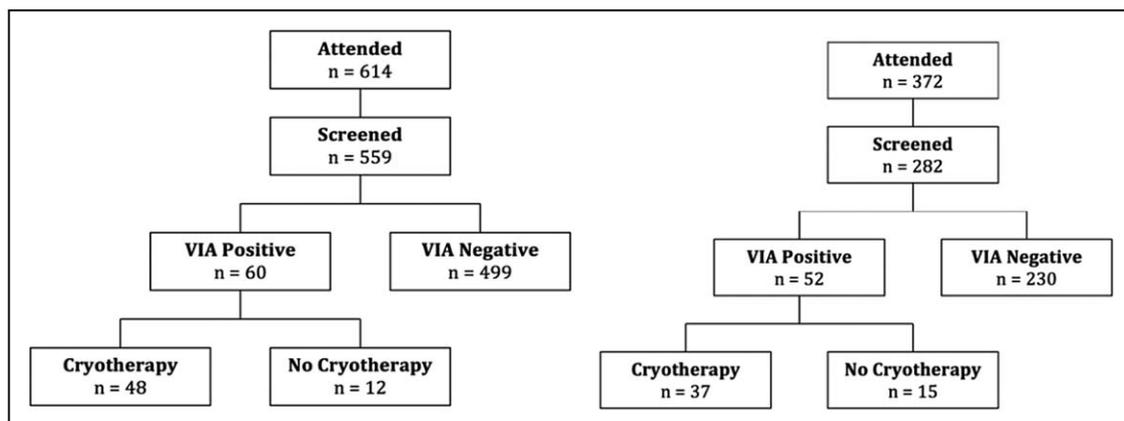


FIGURE 2. CONSORT Flow Diagram from Screening Sites. CONSORT diagrams for workshops in mainland Buzuruga (left) and Ukerewe Island (right).

Table 2. Age breakdowns according to VIA outcomes at both screening sites

	Buzuruga % (n)	Ukerewe % (n)	Total
Age of women screened (years)	559 total	282 total	841
<30	29% (164)	34% (97)	261
30–50	63% (353)	51% (145)	498
>50	7.5% (42)	14.2 (40)	82
VIA positive	60 total	52 total	112
<30	30% (18)	40% (21)	39
30–50	65% (39)	54% (28)	67
>50	5% (3)	6% (3)	6
VIA negative	499 total	230 total	729
<30	29% (146)	33% (76)	222
30–50	63% (314)	51% (117)	431
>50	8% (39)	16% (37)	76
Cryotherapy	48 total	36 total	84
<30	33% (16)	44% (16)	32
30–50	65% (31)	50% (18)	49
>50	2% (1)	6% (2)	3
Referred for higher level of care	9 total	7 total	16
<30	0	14% (1)	1
30–50	78% (7)	86% (6)	13
>50	22% (2)	0	2

VIA, visual inspection with acetic acid.

Table 3. Cost breakdown of screen and treat components for 2016 and 2017

Item	2016: Buzuruga				2017: Ukerewe			
	No. of needed	Per Item Cost – Tz	Cost – Tz	Cost – USD (exchange rate = 2126Tsh/1USD)	No. of needed	Per Item Cost – Tz	Cost – Tz	Cost – USD (exchange rate = 2188Tsh/1USD)
Acetic acid	15	1,333	20,000	9.41	15	1,333	20,000	9.14
Bleach	15	3,533	53,000	24.93	15	3,533	53,000	24.22
Plastic buckets	30	7,065	212,000	99.72	30	7,065	212,000	96.89
1L H ₂ O	20	1200	24,000	11.28	20	1200	24,000	10.97
Paper towels	10	18500	185000	87.01	10	18500	185000	84.55
CO ₂ tank	2	107,700	215,400	101.32	2	165,200	330,400	151.00
Plastic speculums	50		Donated		50		Donated	
Gloves	800		Donated		500		Donated	
Head lamps	8		Donated		5		Donated	
Cryo gun/tips	1	22,806,998	22,806,998	10,727.65	1	22,806,998	22,806,998	10,423.67
Cotton swabs	1000		Donated		800		Donated	
Lubricant	N/A	N/A	N/A	0.00	N/A	N/A	N/A	0.00
Drapes	N/A	N/A	N/A	0.00	N/A	N/A	N/A	0.00
Speaker announcements	1	310000	310000	145.81	1	310000	275,000	125.69
Flyers/ advertisement	N/A	N/A	24,600	11.57	N/A	N/A	24,600	11.24
Translators	N/A	N/A	N/A	0.00	1		7000	3.20
Total USD:			Total USD:	11,218.72			Total USD:	11,418.04
Total Shillings:			Total Shillings:	23,850,998.00			Total Shillings:	24,982,662.90

mainland mass screenings, the island campaign was more expensive. The same amount of supplies purchased for Buzuruga was also purchased for Ukerewe Island so these costs were the same. The costs that differed between the two years was the price of CO₂ tanks. The cost of CO₂ tanks for Buzuruga was 215,400 shillings and the cost of CO₂ tanks for Ukerewe Island was 330,400 shillings. The cost of the CO₂ tanks was greater for the island screening because there was an additional cost for transportation and rental given the distance the tanks had to be taken. This amounts to 4,487 shillings per woman treated in 2016 vs 8,929 shillings per woman treated in 2017.

DISCUSSION

Screen and treat campaigns have been successfully implemented around the world including on mainland Tanzania but we wanted to assess the ability to set up such a program in one of the most rural and remote locations in Tanzania. Through this pilot project, we were able to successfully transport a pilot screen and treat program to Ukerewe Island. Although feasible, there are many barriers to sustain the availability of screening on the island. Ukerewe is isolated from the resources available to populations on the mainland. The island is approximately 4 h by ferry from Mwanza. Resources such as CO₂ tanks for cryotherapy are hard to transport across the lake making the provision of preventive healthcare more challenging. A subset of patients who were VIA positive were unable to be treated because CO₂ gas ran out during the week and were referred to other sites for treatment or asked to return the following week for treatment once the CO₂ had been replaced. Healthcare access is more limited on Ukerewe with only one district hospital that serves all of the islands in Lake Victoria. Ukerewe has many transient fishermen who report having multiple sexual partners which, in turn, increases the risk of exposure of women to oncogenic HPV. Accordingly, higher rates of VIA positive screens were noted on the island compared to mainland screening from the year before. Furthermore, those screened on the island were less likely to have undergone prior HIV testing.

Similar to what is observed in the US, the available evidence in sub-Saharan Africa indicates that differences in cervical cancer incidence and mortality exist due to social inequality and lack of economic development [21,22]. A 2018 study examining cervical cancer awareness among women in Tanzania specifically noted that women who were least likely to be aware of cervical cancer and its risk factors were located in rural areas [11].

Increased burden of disease is related to the higher poverty rate, lower level of urbanization, low literacy rates, gender inequality, and poor access to healthcare services [5²²,23]. These factors can be applied on a regional level and attributed to the higher incidence of cervical dysplasia on Ukerewe Island in comparison to the relatively more developed metropolitan district on the mainland.

VIA screening and treatment with cryotherapy in low resource settings has been shown to be a reliable and a cost-effective method for screening for cervical cancer. When compared to other methods, including cytology and HPV screening, VIA performed at 5-year intervals with immediate treatment in the setting of abnormal screening results is the least expensive option and saves the greatest number of lives [6,24]. VIA with cryotherapy allows training of local mid-level health providers with certification made possible during mass screen-and-treat campaigns [15]. This ensures sustainability of screening programs following US-led interventions.

However, when comparing the cost between the mainland and island workshops, the island campaign was more expensive. The cost of CO₂ tanks for the island program was nearly two-thirds greater than the cost of CO₂ tanks for the mainland due primarily to the additional cost of transportation and increased cost of the tanks from the distributor since we had to carry them further away. Overall, this translates to 4,487 shillings for each woman treated on the mainland Buzuruga and 8,929 shillings per woman treated on Ukerewe Island. The cost for the CO₂ treatment was almost double for the island population than it was for the mainland. It was also logistically difficult to get CO₂ tanks to the island given that they had to be transported on a ferry. The ferry tickets also have to be taken into consideration and this proves to be another barrier to care and screening on the island. Moving forward, it will be important to consider alternative strategies to treat VIA positive patients that are not dependent on CO₂ tanks. Recent evidence suggests similar efficacy between cryotherapy and thermocoagulation and thermocoagulation is easier to transport and has an unlimited number of uses [25]. It would also be important to research more cost-effective ways of examining cytology or HPV tests in low resource settings [4,6].

Although the WHO guidelines recommend screening with VIA only between the ages of 30–50, our screening campaigns demonstrated relatively high rates of VIA+ screens in patients under 30. Lesions most concerning for microinvasion or frankly invasive carcinoma were observed more frequently in patients greater than 50 years. An

argument against expanding cervical cancer screening to a wider age group is that HPV transformation is relatively slow and younger patients can clear the virus. However, these data arise predominantly from industrialized nations. Concurrent HIV infection in women under 30 years may lead to severe dysplasia more rapidly [7]. Furthermore, patients are at higher risk of developing dysplasia where the access to medicine is lower; Tanzania has one of the lowest patient-to-doctor ratio in the world (1:50,000) [5[■]]. Some patients were observationally using intravaginal tobacco for gynecologic complaints prescribed by local healers. Given the known carcinogenic effects of tobacco, vaginal tobacco may represent a unique risk factor for cervical cancer in these subpopulations. Additional factors such as polygamy and grand multiparity may also have negative attributable risk. A 2012 study evaluating age of sexual debut in Tanzanian adolescents demonstrated a mean age of sexual debut of approximately 14.6 years, with 57.8% of participants having sex before turning 15 [26]. Reported condom use was low and females were more likely to endorse sexual partners of older ages [27]. For these patients, 'catch-up' screen-and-treat after age 30 years may be too late for local therapy to render any benefit. Based on the prevalence of novel risk factors, it may be important to adjust the WHO recommendations as to what age to start screening based on region.

In summary, we were successfully able to run a screen and treat campaign even in a rural setting on Ukerewe Island. Our data demonstrate that even in a country with a high cervical cancer burden, regional differences in risk factors exist and may contribute to the prevalence of VIA positivity. By virtue of its remote location and unique population, patients here likely have a higher risk of developing cervical cancer. This is underscored by the fact that prevention through screening is more expensive to provide on the island. This lends to expanding WHO age guidelines for screening in remote areas. Despite inroads into gaining some measure of sustainability on the mainland, our program represents one of the only opportunities for women in Ukerewe to have undergone cervical cancer screening. For some of the island women, our pilot workshop was the first pelvic exam in their life. Our experience suggests that screen-and-treat is possible even in a remote, rural area such as Ukerewe Island where we were able to transfer a functional workshop to serve a receptive community. Continued training of local healthcare providers and a viable alternative to cryotherapy would support the sustainability of screen-and-treat programs in Ukerewe Island and other remote regions commonly found in the developing world.

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Conflicts of interest

There are no conflicts of interest.

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