

Use of thermo-coagulation as an alternative treatment modality in a 'screen-and-treat' programme of cervical screening in rural Malawi

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The incidence of cervical cancer in Malawi is the highest in the world and projected to increase in the absence of interventions. Although government policy supports screening using visual inspection with acetic acid (VIA), screening provision is limited due to lack of infrastructure, trained personnel, and the cost and availability of gas for cryotherapy. Recently, thermo-coagulation has been acknowledged as a safe and acceptable procedure suitable for low-resource settings. We introduced thermo-coagulation for treatment of VIA-positive lesions as an alternative to cryotherapy within a cervical screening service based on VIA, coupled with appropriate, sustainable pathways of care for women with high-grade lesions and cancers. Detailed planning was undertaken for VIA clinics, and approvals were obtained from the Ministry of Health, Regional and Village Chiefs. Educational resources were developed. Thermo-coagulators were introduced into hospital and health centre settings, with theoretical and practical training in safe use and maintenance of equipment. A total of 7,088 previously unscreened women attended VIA clinics between October 2013 and March 2015. Screening clinics were held daily in the hospital and weekly in the health centres. Overall, VIA positivity was 6.1%. Almost 90% received same day treatment in the hospital setting, and 3- to 6-month cure rates of more than 90% are observed. Thermo-coagulation proved feasible and acceptable in this setting. Effective implementation requires comprehensive training and provider support, ongoing competency assessment, quality assurance and improvement audit. Thermo-coagulation offers an effective alternative to cryotherapy and encouraged VIA screening of many more women.

Key words: cervical screening, ablative treatment, thermo-coagulation, VIA, 'screen and treat'

Ethical Approval: The proposal was submitted to the Malawian National Health Sciences Research Committee for ethical review. The Committee recommended a waiver as the project was judged to be a service delivery quality improvement project rather than research.

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Cervical cancer is the commonest cancer and the leading cause of cancer deaths among women in low- and middle-income countries (LMIC).¹ In 2008, the World Health Organisation (WHO) reported >530,000 new cases and 275,000 deaths from cervical cancers worldwide, with more than 90% of cases from developing countries.² In the WHO African region, 75,000 new cases were recorded with more than 50,000 deaths.² Malawi was reported to have the highest rate of cervical cancer in the world in 2012 with a world age-standardised rate of 75.9 per 100,000,³ and high rates of cervical cancer are reported among human immunodeficiency virus (HIV)-infected women.⁴

The Malawian Ministry of Health Strategic Plan includes provision of cervical screening using Visual Inspection with Acetic Acid (VIA).⁵ Treatment of early lesions with cryotherapy is included in national policy, in line with the WHO's Comprehensive Cervical Cancer Control 'A Guide to Essential Practice'.⁶ WHO recommends cryotherapy or loop electrosurgical excision procedure for larger lesions for the majority of women who screen positive for cervical pre-cancer in 'screen-and-treat' programmes in LMIC.^{6,7}

While setting up a screen-and-treat programme of cervical screening in Central Region, Malawi, in 2013, it very quickly

What's new?

Malawi has the highest incidence rates for cervical cancer worldwide, and a "screen-and-treat" program is in place to identify and treat precancerous lesions. Conventional cryotherapy is challenging as gas supply is inconsistent, cylinders are difficult to transport and running costs are high. Here, the authors introduce thermo-coagulation as a treatment alternative, which proved feasible and acceptable in this resource-poor setting and could increase the number of women receiving timely treatment for precancerous lesions in low- and middle-income countries.

became evident that lack of availability of gas for cryotherapy and its prohibitive cost meant there was a need to urgently consider an alternative treatment modality. The evidence regarding the effectiveness of thermo-coagulation (also called cold coagulation), an ablative method for treatment of cervical intraepithelial neoplasia (CIN), led to our consideration of its use in Malawi. Thermo-coagulation has a number of attractive features making it suitable for use in LMICs: the equipment is small, portable and durable, destroys abnormal cells at 100–120°C in brief treatment applications using minimal electricity and allows punch biopsies to be taken in the screening clinic for investigation of potentially cancerous lesions. The PATH review of treatment modalities for precancerous cervical lesions considers there to be evidence to support either no or local anaesthesia for thermo-coagulation in LMIC settings.⁸ The absence of pain in the initial stages of cervical cancer, the cost of healthcare, the distance to health facilities covered usually by foot and the common experience of abnormal bleeding during reproductive years means that many Malawian women do not seek timely medical help. It is therefore important to provide treatment at the same time as screening, as the screening visit may be the only chance for intervention.

Cumulative evidence over the last three decades has demonstrated the effectiveness of thermo-coagulation treatment.^{9–11} A recent systematic review and meta-analysis of effectiveness of thermo-coagulation summarised data from 13 studies, reporting on the analyses of proportion of patients cured, with results stratified by lesion grade and study region.¹² Among 4,569 patients, summary proportions cured for CIN1 and CIN2–3 disease were 96 and 95%, respectively. However, few of the included studies were from low-income settings. Recent studies from India are beginning to provide such evidence.^{13,14} Preliminary findings indicated that use of thermo-coagulation for treatment of lesions suggestive of CIN among HIV-infected women in India was well tolerated without anaesthesia and was safe for delivery in out-patient settings, with 6-month cure rates of more than 80%.¹³ The overtreatment rate of 32% of women who had no histological evidence of CIN was similar to that of unnecessary treatment following ablative treatment using cryotherapy in 'see-and-treat' settings.¹⁵

Apart from the evidence from India there is as yet limited published data for effective delivery of thermo-coagulation in screening programmes in LMIC, with none from Sub-Saharan African countries. Crucially, the 2014 2nd Edition WHO CCCC Guidance⁷ does not mention thermo-coagulation, a major impediment to adoption of this technol-

ogy in LMIC. This article describes the use of thermo-coagulation within a screen-and-treat programme in Malawi.

Material and Methods**Settings**

CCAP Nkhoma Hospital serves the Lilongwe and Dedza Districts of Central Malawi, with a population of some 375,000.¹⁶ A service-level agreement with the Malawi Government enables provision of free care for mothers and children aged below 5 years. Together with the emphasis on strengthening reproductive health services,¹⁷ this has resulted in a dramatic reduction in maternal mortality in the area (from 1,518/100,000 live births in 2008 to 170/100,000 in 2014; Nkhoma Hospital audit, R. Ter Haar). The first two health centres to link into the programme were Kasina and Nthenje Health Centres.

Cervical screening in Nkhoma

A VIA service has been available in Nkhoma since 2005. In the 18 months prior to this project, a total of 618 women were screened, with just more than 6% VIA positivity, with a similar number of suspected cancers. There is, however, a lack of detail on treatment given and clinical outcomes. A service improvement was therefore planned which sought to redesign all aspects of the screen and treat programme. Initial steps included obtaining support and approvals from the Malawian Ministry of Health, Regional and Village Chiefs and sensitisation in hospital, health centre and village settings.

The Nkhoma Cervical Cancer Screening Programme (CCSP) has been integrated within an existing Reproductive Health Unit, allowing broadening of staff skills and ensuring consistency of messages to women. Attendance at the Malawian Ministry of Health VIA course is a prerequisite for all providers and is supplemented by additional training in VIA interpretation and treatment using thermo-coagulation at Nkhoma Hospital. Full details of the Nkhoma hub and spokes model of cervical cancer screening and supporting pathways of treatment will be published elsewhere (manuscript in preparation).

Daily screening and referral clinics were set up in Nkhoma Hospital, and within 3 months, weekly screening clinics were operating at Kasina and Nthenje Health Centres.

Women who come to screening clinics first attend a 30- to 40-minute verbal educational and interactive group session in the local Chichewa language.

Provision of VIA is in accordance with WHO Guidance,⁷ Malawian Ministry of Health policy,⁵ and draws on JHPIEGO materials.¹⁸ Women are seen in a private/curtained area and 5% acetic acid applied to the cervix for 1 minute.

Table 1. Characteristics of women attending cervical screening for the first time in Nkhoma Hospital and in Kasina and Nathenje Health Centres, Central Malawi

Location	Number of first attenders	% of total attendance	Age range (years)	Marital status	HIV status in first attenders						
				% never married	HIV+ (ART)	HIV+ (no ART)	% HIV+	HIV–	% HIV–	HIV unknown	% HIV status unknown
Nkhoma	4,730	87.2	16–86	1.8	257	38	6.2	1,963	41.5	2,472	52.3%
Kasina	1,393	94.6	16–82	3.2	35	14	3.5	614	44.1	730	52.4%
Nathenje	965	94.9	17–74	3.0	24	14	3.9	494	51.2	433	44.9%
Total	7,088	89.4	16–86	2.2	315	66	5.4	3,069	43.3	3,632	51.3%

VIA outcomes are documented as 'negative' (no aceto-white areas observed); 'positive' (well-defined areas of aceto-white covering <75% of transformation zone with the squamo-columnar junction fully visible and no evidence of entering the endo-cervical canal) and 'suspicious lesion, biopsy required' and 'advanced cancer'. Women who are VIA-negative are asked to return at 3 years (or 1 year if HIV-positive) for routine screening.

Women who are considered VIA-positive are offered immediate treatment with thermo-coagulation rather than cryotherapy. The heated probe is applied to the cervix for 30 seconds. Applications are repeated on all areas of the cervix which need treatment. No local anaesthetic is offered, consistent with the approach taken in other LMIC settings.^{13,14} Thermo-coagulation is not provided if there is any evidence of glandular neoplasia or cervical cancer or if the woman is pregnant. Women from all health centres for whom a suspicion of cancer is recorded are referred to Nkhoma for punch biopsy to confirm the diagnosis.

Women are directed to return for a follow-up review at 3–6 months and again at 1 year. The first visit was set at 3 months initially to meet Malawian guidelines for treatment with cryotherapy. Following discussion with senior Malawian service providers, this was changed after the first year of the programme to 6 months to be in line with guidance from users of thermo-coagulation, recognising that 3 months was too early for complete healing and could lead to false interpretation of faint aceto-white areas.

Pathways of care are in place for all women. Women from whom a punch biopsy has been taken return within 1 month for biopsy results and discussion of clinical management pathways, including surgical options or palliative care.

Interviews with providers

Six interviews were carried out with providers at Nkhoma Hospital, with consent from senior management and from the providers themselves for their anonymised views to be shared. All providers are involved in screening provision at Nkhoma Hospital and at rural health centres; three had experience of using both thermo-coagulation and cryotherapy as a treatment modality. Interviews were carried out in April

2015 using a brief questionnaire asking about provider experience and perspectives; responses were recorded verbatim.

Data collection and analysis

To date, 18 months data from Nkhoma Hospital (from October 2013 to end of March 2015) and 11 months data from Kasina HC and Nathenje HC (from May 2014 to end of March 2015) have been analysed. Data were recorded in standard Malawian Ministry of Health VIA screening registers, and then entered into an Excel database, using numerically coded menus to allow for easy analysis and data checking. Descriptive statistics were used to summarise outputs of interest.

Results

Screening attenders

Between October 2013 and March 2015, a total of 7,910 women were screened by VIA. This included 5,424 women seen at daily clinics in Nkhoma Hospital, and 1,472 and 1,014 women seen at Kasina and Nathenje, respectively. The vast majority of women (7088; 89.6%) had never attended for cervical screening before. Programme descriptors for those attending screening for the first time are presented in Table 1. Amongst first attenders, 381 were known to be HIV-positive (5.4%).

Age distribution

The age distribution was similar at each site, with peak attendance between ages 20 and 39 years in all three centres. Percentage age distribution for those aged 20–29 years ranged from 24% Nathenje to 31.7% Kasina; conversely, the % aged 30–39 years in Nathenje was 37% compared to 28% in Kasina. A sizeable proportion of women who attended were aged more than 60 years (6.7%), whereas only 1.5% were aged below 20 years; however, 24 women did not know their age.

Attendance by site

Quarterly numbers by site are presented in Figure 1 and show a steep rise in activity in the first quarter after sensitisation, followed by a reduction. As the Health Centre clinics became more experienced and extended their capacity, the number of women attending locally increased, whereas the number attending Nkhoma Hospital reduced.

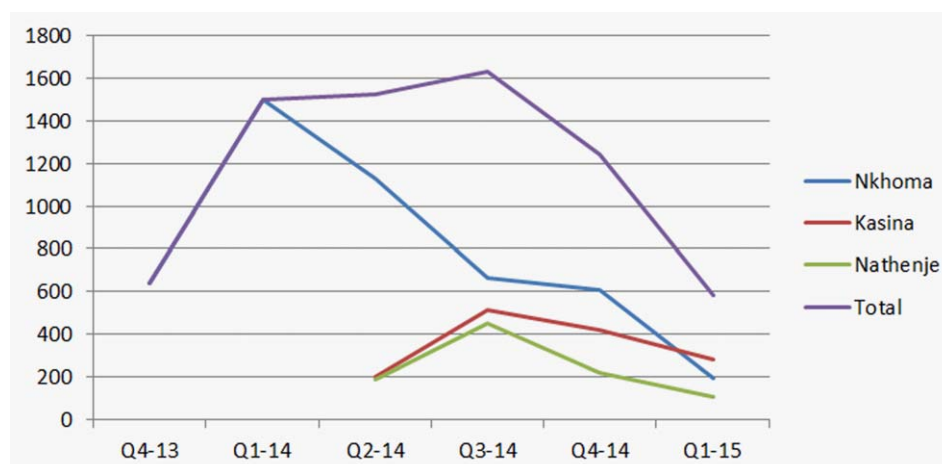


Figure 1. Quarterly first attendance by clinic site in Central Malawi.

Table 2. Outcomes of 'screen-and-treat' programme in Central Malawi by site and age

Clinic location	First attenders	Number of patients with VIA-positive	%	Number of patients treated same day	%	Number of patients returned in <1 month for treatment	Total treated (%)
Nkhoma	4,730	299	6.3	267	89	9	276 (92.3%)
Kasina	1,393	85	6.2	65	68	8	73 (86%)
Nathenje	965	45	4.7	29	64.4	3	32 (71.1%)
Total	7,088	429	6.1	361	84.1	20	381 (88.8%)

Table 3. Outcomes of 'screen-and-treat' programme in Central Malawi by clinical assessment and age

VIA result in first attenders	Nkhoma	Kasina	Nathenje	Total
VIA+	299	85	45	429
VIA-	4,264	1,287	907	6,458
Suspicious cancer	58	14	6	78 (1.1%)
Advanced cancer	20	2	0	22 (0.3%)
Other gynaecological	39	5	7	51
Unknown	50	0	0	50
Total	4,730	1,393	965	7,088

VIA positivity

The number and percent of women who were considered VIA-positive reduced over time as experience to distinguish early/low-grade lesions from non-specific changes increased. This is summarised in Table 2 where the percent of VIA-positive women overall who were treated on the same day was 84%, was lower in the Health Centres (72.3%) and reached 89% in Nkhoma Hospital.

Additional via outcomes

Further clinical outcomes are presented in Table 3 and show 1.4% of women had suspicious or advanced cancers. When VIA outcomes are stratified by age (Fig. 2), it is clear that most early and

treatable lesions occur in age groups 20–39 years, whereas cancerous lesions are largely in the age groups 30–59 years. Of the 22 women who needed radical hysterectomy in the 18 months under discussion, eight (36%) were aged 60 years or above.

VIA results by HIV status

Overall, 5.3% ($n = 381$) of first attenders were known to be HIV-positive, most of them receiving anti-retroviral therapy (ART) on a regular basis. Forty HIV-infected women were also VIA-positive (10.4%; 33 on ART and 7 not on ART). This compares with a VIA positivity rate of 6.6% known to be HIV-negative or 5.1% in the overall population regardless of HIV status (Table 4).

Clinical follow-up

Between Nkhoma hospital and the two health centres, more than 63% of women have returned for a first follow-up visit, mostly at around 3 months after treatment. More than 90% of cervixes appeared well healed at this stage (Table 5). Seven women required further thermo-coagulation treatment, representing a 94.0% cure rate at first follow-up (220/234); assessment of outcome for a further seven women could not be made on the day of visit for a variety of reasons (e.g., thermo-coagulation scarring still evident, pregnancy and menstruation). When analysed by HIV status, no treatment failures were observed in HIV-positive women in our treated

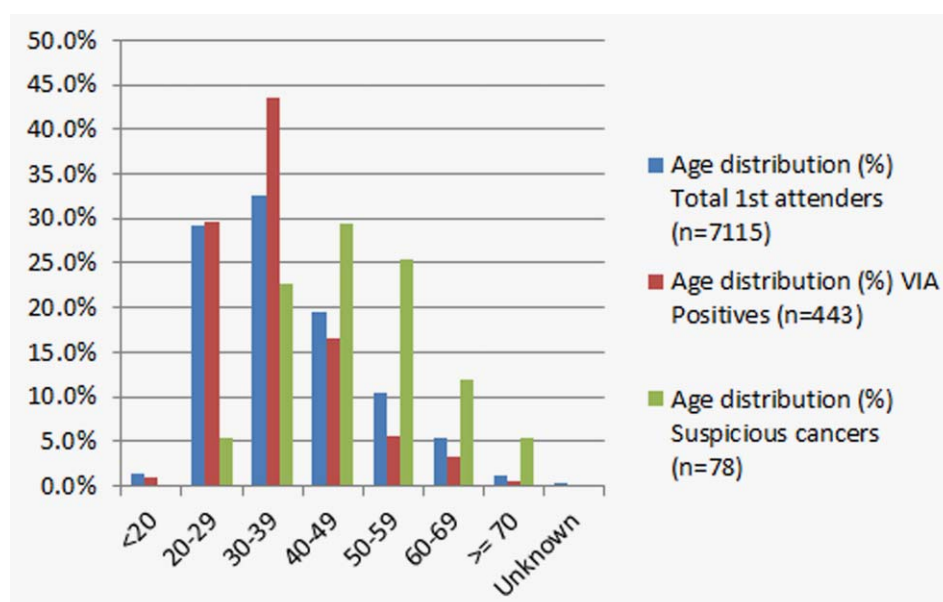


Figure 2. Screening outcomes (VIA-positive and suspicious cancers, by age) across three health centres in Central Malawi.

Table 4. VIA outcomes in a 'screen-and-treat' programme in Central Malawi according to HIV status

VIA result	HIV-positive on ART	HIV-positive not on ART	HIV-negative	HIV status unknown	Total
VIA+	33	7	203	186	429
VIA–	316	65	3,070	3,637	7,088
% VIA-positive	10.4	10.8	6.6	5.1	6.1

Table 5. Outcomes of first follow-up visit for 234 women attending VIA screening clinics in Central Malawi

	Number of patients with VIA-positive	Total number of patients treated (within 1 month)	Number of patients returned for first follow-up	Number of patients healed	Number of patients with continuing problem
Nkhoma	299	276	195 (73.8%)	182 (93.3%)	6
Kasina	85	73	23 (30.3%)	22 (95.7%)	1
Nathenje	45	32	16 (55.2%)	16 (100%)	0
Total	429	381	234 (63.4%)	220 (94.0%)	7 (3.0%)

cohort ($n = 12$), compared to 2/94 known HIV-negative, and 4/89 where HIV status was not known.

To date, 61 women have also returned for 1-year follow-up: nine (14.7%) required further treatment and were considered treatment failures: the number attending 1-year review visits will increase over time. Treatment failure occurred in one of 11 HIV-positive women, compared to five of 26 HIV-negative women and three of 24 women whose HIV status was unknown.

Provider perspectives

Local providers reported satisfaction with comprehensive training in use of thermo-coagulation, perceived acceptability of treatment to women, satisfaction expressed by women regarding explanation of procedure and ease of practical

setup. Almost no pain was reported to the providers when women received treatment. Providers who had experience of use of both thermo-coagulation and cryotherapy reported shorter time taken for treatment with thermo-coagulation, perceived greater acceptability to women and anecdotally fewer treatment sequelae.

Discussion

Summary of findings

In our population, 6.1% of screened women were VIA-positive, of whom overall 84% received same-day treatment with thermo-coagulation. About 89% of women attending the daily screening clinics in Nkhoma Hospital received same-day treatment, compared to ~68 and 64% in the two health centres. These lower rates demonstrate the complexity of

service delivery in settings where thermo-coagulators for treatment are not always available when required (*i.e.*, may only be available one clinic in four), and where trained staff are few or deployed elsewhere. Nevertheless, the success of the Nkhoma model would suggest that there is an opportunity for expansion to impact significantly on population coverage and treatment of precancerous lesions. By March 2015, the numbers attending Kasina HC matched the number attending in Nkhoma Hospital, showing how outreach can reduce the burden on central resources while at the same time providing a service closer to home.

Comparisons with the literature

Widespread acceptance with varying rates of VIA positivity depending on setting are reported in sub-Saharan Africa.^{19–22} Our rates of VIA positivity and suspicious lesions are comparable to those found by others,^{13,21,23} and the higher rate in HIV-infected women (11.1% VIA positivity in HIV-positive women versus; 7.1% HIV-negative) reinforces the importance of offering cervical screening services to HIV-positive women, and where appropriate, encouraging women of unknown HIV status to consider HIV testing. In Malawi, the HIV status is unknown if testing has been carried out more than 1 year before, thus accounting for the large number of women of unknown HIV status ($n = 3,637$, 51.3%). The majority of the 'HIV status unknown' women were older (48.5% in women aged below 50 years compared to 64.5% in those aged above 50 years), which may account for the lower VIA positivity in this group.

We report on early outcomes of thermo-coagulation as the treatment modality within our VIA-positive population. There is now a growing body of evidence supporting the use of thermo-coagulation within screen-and-treat programmes, and our interim cure rate (3–6 months post-treatment) of 93.3% in 234 women compares well with preliminary cure rate with thermo-coagulation of >80% (at 6 months to 1 year) in HIV-positive women in India, 95.7% at 1 year in the United Kingdom and 96.5% for CIN1/95% for CIN2–3 from a meta-analysis.^{10,12,13} It also compares favourably with documented cure rates from cryotherapy.²⁴ Our preliminary results at 1-year follow-up from a small number of women (cure rate of 85%) are incomplete, but reinforce the need for regular follow-up and re-screening of treated women in accordance with national guidance. Importantly, cure rates at both time points did not differ by HIV status.

Others have reported on the experience of VIA-based "screen and treat" in Malawi. An early demonstration pilot found VIA positivity rates of 12.4%, but limited ability to provide same-day treatment.¹⁹ There are acknowledged health system and cultural challenges to delivery of cervical screening in Malawi,^{25,26} most pertinently that only one-third of facilities surveyed recently were able to provide treatment due to lack of cryotherapy equipment or gas.²⁷ There are also reports of patient satisfaction²⁸ and examples of successful integration with existing services.²³

The potential for overtreatment in screen-and-treat programmes with VIA is recognised.^{7,29} Discrimination of VIA positive lesions associated with pre-neoplasia from other cervical pathologies including chronic infection requires clinical skill and experience. The gold-standard confirmation would be biopsy which is not readily available in most low-resource settings. A screen-and-treat approach enables treatment on the same day to be offered to women, critical in many low-resource settings where patients are less likely to return for treatment in the absence of symptoms and where travel is costly and time consuming.^{12,13} WHO guidance considers the benefit to outweigh any harm from cryotherapy in VIA-based screen-and-treat programmes in low-resource settings.⁷ The same principle applies for treatment with thermo-coagulation.

Strengths and weaknesses of this study

The Nkhoma CCSP represents a service improvement programme rather than a comparison study with other treatment modalities. This can be seen as both a strength (*i.e.*, real-time field testing) and a weakness (*i.e.*, no data to compare with Malawian Ministry of Health and WHO-recommended treatment modality of cryotherapy). We do not have colposcopic or biopsy confirmation for women who are VIA-positive, as this is truly a screen-and-treat service delivery approach. However, comparisons with published results from other papers suggest similar outcomes (described above). Nonetheless, we recognise the importance of ensuring adequate follow-up of all treated women, and the provision of messages about symptom recognition and access to relevant services.

Ensuring women do return for treatment, and/or for follow-up, is a recognised challenge. Although overall a high proportion of women (84%) did accept same-day treatment, some women felt obliged to seek permission from their husband before accepting treatment, in part due to the recommendation of sexual abstinence for 4 weeks post-treatment. We experienced more than 60% of women returning for first follow-up (at 3–6 months post-treatment) with only a date for return recorded in their Health Passport, and to date, 61 women have returned for their 1-year follow-up. This may be an under-reporting of the true figure due to women attending follow-up visit at their local health centre rather than Nkhoma Hospital, where they might be given a new clinic number. We now record mobile telephone numbers (where available) and village/territory addresses to increase the proportion of women returning for their 1-year review appointment (or within 2 months of the suggested date).

Anecdotal concerns have been raised about the level of pain associated with thermo-coagulation. However, treatment with thermo-coagulation was acceptable and well tolerated by women, as found by others^{13,30}: there is little evidence to suggest greater pain than with cryotherapy, with only one acknowledgement of pain beyond discomfort noted among over 200 treated women in our population. We recognise

that this low figure is based on provider report, and work is ongoing to directly capture detailed patient perspectives.

About 91.6% of our screened women were aged between 20 and 59 years, with 52% within the WHO-recommended screening ages of 30–49 years in LMIC settings.⁷ We found high levels of VIA positivity among younger women, but 43.6% of the suspicious cancers were among women older than 49 years. The Nkhoma cervical cancer prevention programme is not a formal screening programme, and the wide age range reflects the necessity of routine gynaecological health care among women in an unscreened population.

Implications for practice, policy and research

Practice. Introduction of a screen-and-treat programme requires initial familiarisation and training, but must also be accompanied by ongoing support, continuing professional education and quality assessment of providers. The Nkhoma programme developed bespoke standard operating procedures and assessment tools (competence assessment form, also called Objective Structured Clinical Assessment, OSCA); other clinical assessment tools are also available.¹⁸

Policy. Although WHO 2013 guidance does not include thermo-coagulation as a treatment modality, there is growing use of and support for thermo-coagulation in a number of LMIC settings.^{12,13,31–33} As evidence accumulates for non-inferior outcomes for thermo-coagulation pre-cancers compared to other treatment modalities,^{12,24,34} guidance should be reviewed and updated. Similarly, health care planners in LMICs should consider inclusion of thermo-coagulation in strategic planning for long-term cost-effectiveness and sustainable delivery of screening programmes.

Although we did not include formal cost-effectiveness analysis, capital outlay for thermo-coagulation indicated that cost savings can be made after ~80 to 90 women have been treated. Provided sufficient women are screened in the population and then the initial cost is recouped within a period of months, compared to the recurring costs for cryotherapy.

One drawback of thermo-coagulation is that currently there is only one supplier of suitable instruments³⁴ (WISAP, Germany): a more competitive market could drive down price. Battery-operated thermal coagulators are under development although it could take until mid-2016 to have a commercially available device.³⁵ Other ablative treatment

modalities are being developed and trialled, such as the Cryopen (PATH).⁸

Future research priorities. There is a need for further robust data collection regarding the use of thermo-coagulation in sub-Saharan Africa and other LMIC settings, as well as other programme indicators.³⁶ Comparative studies are not always possible in resource-constrained settings, but sufficient data points should be recorded of key indicators to allow outcomes and should include long-term efficacy through follow-up of treated women, safety profile (e.g., pregnancy outcomes), and data on client experience. Future models of screen-and-treat should explore the use of HPV testing for potential triage to VIA as recommended by WHO and others^{13,37–39}; refinement of optimal treatment strategies for HIV-positive compared to HIV-negative women,³⁷ as well as investment in effective, cost-effective and acceptable treatment such as thermo-coagulation. There is also a need for health systems research into how to implement evidence on screening delivery in practice,^{40,41} as well as integration with HIV/ART and reproductive health services.^{20,23} At Nkhoma Hospital, HIV testing and counselling is now offered in the VIA settings, and annual VIA screening is being introduced as the standard of care for women with HIV attending ART clinics.

Conclusions. Our study demonstrates that introduction of thermo-coagulation is feasible and acceptable within this LMIC setting. The same-day nature of a treatment acceptable to providers and to patients, the ease of transportation to rural health centres and the evidence of clinical effectiveness all argue for more widespread adoption of thermo-coagulation for sustainable and reliable screening provision in LMIC as an alternative to cryotherapy.

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References

1. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013. Available from: <http://globocan.iarc.fr>. Accessed on April 24, 2016.
2. Arbyn M, Castellsagué X, de Sanjosé S, et al. Worldwide burden of cervical cancer in 2008. *Ann Oncol* 2011;22:2675–86.
3. Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.1, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer, 2014. Available from: <http://globocan.iarc.fr>. Accessed on January 16, 2015.
4. Kohler RE, Tang J, Gopal S, et al. High rates of cervical cancer among HIV-infected women at a referral hospital in Malawi. *Int J STD AIDS*, 2015 Jun 30. pii: 0956462415592999. [Epub ahead of print]
5. The Malawi Health Sector Strategic Plan (HSSP), 2011–2016. Available from: [http://www.medcol.mw/commhealth/publications/3%20Malawi%20HSSP%20Final%20Document%20\(3\).pdf](http://www.medcol.mw/commhealth/publications/3%20Malawi%20HSSP%20Final%20Document%20(3).pdf). Accessed on October 7, 2015.
6. World Health Organisation. Comprehensive cervical cancer control: a guide to essential practice (C4-GEP). Geneva, Switzerland: Department of Reproductive Health and Research and Development of Chronic Diseases and

- Health Promotion, World Health Organisation, 2006.
7. World Health Organisation. Comprehensive cervical cancer control: a guide to essential practice, 2nd edn. 2014. Available from: http://apps.who.int/iris/bitstream/10665/144785/1/9789241548953_eng.pdf. Accessed on November 9, 2015.
 8. Treatment technologies for precancerous cervical lesions in low-resource settings: review and evaluation. PATH, 2013. Available from: www.rho.org/HPV-screening-treatment.htm. Accessed on April 21, 2016.
 9. Gordon HK, Duncan ID. Effective destruction of cervical intraepithelial neoplasia (CIN) 3 at 100°C using the Semm cold coagulator: 14 years' experience. *Br J Obstet Gynaecol* 1991;98:14–20.
 10. Parry-Smith W, Underwood MD, Bellis-Ayres S, et al. Success rate of thermo-coagulation for the treatment of cervical intraepithelial neoplasia: a retrospective analysis of a series of cases. *J Low Genit Tract Dis* 2015;19:17–21.
 11. Coupar E, McKenzie C. Results of Test of Cure (ToC) in patients undergoing treatment with cold coagulation and large loop excision of transformation zone (LLETZ). Paper presented at the British Gynaecological Cancer Society Annual Scientific Meeting, July 10–11, 2014, London, UK.
 12. Dolman L, Sauvaget C, Muwonge R, et al. Meta-analysis of the efficacy of thermo-coagulation as a treatment method for cervical intraepithelial neoplasia: a systematic review. *BJOG* 2014;121:929–42.
 13. Joshi S, Sankaranarayanan R, Muwonge R, et al. Screening of cervical neoplasia in HIV-infected women in India. *AIDS* 2013;27:607–15.
 14. Joshi S, Kulkarni V, Darak T, et al. Cervical cancer screening and treatment of cervical intraepithelial neoplasia in female sex workers using "screen and treat" approach. *Int J Womens Health* 2015;7:477–83.
 15. Nene BM, Hiremath PS, Kane S, et al. Effectiveness, safety, and acceptability of cryotherapy by midwives for cervical intraepithelial neoplasia in Maharashtra, India. *Int J Gynaecol Obstet* 2008;103:232–6.
 16. Nkhoma Hospital website. Available from: <http://nkhomahospital.org.mw>. Accessed on July 20, 2015.
 17. Vink NM, de Jonge HC, Ter Haar R, et al. Maternal death reviews at a rural hospital in Malawi. *Int J Gynaecol Obstet* 2013;120:74–7.
 18. Blumenthal PD, McIntosh N. Cervical Cancer Prevention Guidelines for Low-Resource Settings. Jhpigo 2005. <http://reprolineplus.org/system/files/resources/CeCaPfullmanual.pdf>. Accessed on April 21, 2016.
 19. World Health Organization. Prevention of cervical cancer through screening using visual inspection with acetic acid (VIA) and treatment with cryotherapy. A demonstration project in six African countries: Malawi, Madagascar, Nigeria, Uganda, the United Republic of Tanzania, and Zambia. Geneva, Switzerland: World Health Organization, 2012.
 20. Ramogola-Masire D, de Klerk R, Monare B, et al. Cervical cancer prevention in HIV-infected women using the "screen and treat" approach in Botswana. *J Acquir Immune Defic Syndr* 2012;59:308–13.
 21. Kapambwe S, Sahasrabudhe VV, Blevins M, et al. Implementation and operational research: age distribution and determinants of invasive cervical cancer in a "screen-and-treat" program integrated with HIV/AIDS care in Zambia. *J Acquir Immune Defic Syndr* 2015;70:e20–6.
 22. Khozaim K, Orang'o E, Christoffersen-Deb A, et al. Successes and challenges of establishing a cervical cancer screening and treatment program in western Kenya. *Int J Gynaecol Obstet* 2014;124:12–8.
 23. Phiri S, Feldacker C, Chaweza T, et al.; Light-house Group. Integrating reproductive health services into HIV care: strategies for successful implementation in a low-resource HIV clinic in Lilongwe, Malawi. *J Fam Plann Reprod Health Care* 2016;42:17–23.
 24. Sauvaget C, Muwonge R, Sankaranarayanan R. Meta-analysis of the effectiveness of cryotherapy in the treatment of cervical intraepithelial neoplasia. *Int J Gynaecol Obstet* 2013;120:218–23.
 25. Fort VK, Makin MS, Siegler AJ, et al. Barriers to cervical cancer screening in Mulanje, Malawi: a qualitative study. *Patient Prefer Adherence* 2011;5:125–31.
 26. Maseko FC, Chirwa ML, Muula AS. Health systems challenges in cervical cancer prevention program in Malawi. *Glob Health Action* 2015;8:26282.
 27. Munthali AC, Ngwira BM, Taulo F. Exploring barriers to the delivery of cervical cancer screening and early treatment services in Malawi: some views from service providers. *Patient Prefer Adherence* 2015;9:501–8.
 28. Maseko FC, Chirwa ML, Muula AS. Client satisfaction with cervical cancer screening in Malawi. *BMC Health Serv Res* 2014;14:420.
 29. Ferreccio C, Gage J. Visual Inspection of the Uterine Cervix with Acetic Acid (VIA): A Critical Review and Selected Articles. Washington, D.C.: PAHO, 2003. <http://www1.paho.org/hq/dmdocuments/2011/cc-via.pdf>. Accessed on April 21, 2016.
 30. Goodman JD, Sumner D. Patient acceptability of laser and thermo-coagulation therapy for pre-malignant disease of the uterine cervix. *Br J Obstet Gynaecol* 1991;98:1168–71.
 31. Sankaranarayanan R. Screening for cancer in low- and middle-income countries. *Ann Glob Health* 2014;80:412–7.
 32. Bateman AC, Katundu K, Mwanahamuntu MH, et al. The burden of cervical pre-cancer and cancer in HIV positive women in Zambia: a modelling study. *BMC Cancer* 2015;15:541.
 33. Soutter WP, de Barros Lopes A, Fletcher A, et al. Invasive cervical cancer after conservative therapy for cervical intraepithelial neoplasia. *Lancet* 1997;349:978–80.
 34. WISAP. Available from: <http://www.wisap.de>. Accessed on November 9, 2015.
 35. Tsu V, Jeronimo J. Are alternatives to traditional cryotherapy needed? What options exist? Paper presented at the HPV Conference, Lisbon, September 2015.
 36. Mwanahamuntu MH, Sahasrabudhe VV, Blevins M, et al. Monitoring the performance of "screen-and-treat" cervical cancer prevention programs. *Int J Gynaecol Obstet* 2014;126:88–9.
 37. World Health Organization. WHO guidelines for screening and treatment of precancerous lesions for cervical cancer prevention. 2014. Available from: http://apps.who.int/iris/bitstream/10665/94830/1/9789241548694_eng.pdf. Accessed on June 30, 2015.
 38. Basu P, Mittal S, Banerjee D, et al. Diagnostic accuracy of VIA and HPV detection as primary and sequential screening tests in a cervical cancer screening demonstration project in India. *Int J Cancer* 2015;137:859–67.
 39. Reddy D, Njala J, Stocker P, et al. High-risk human papillomavirus in HIV-infected women undergoing cervical cancer screening in Lilongwe, Malawi: a pilot study. *Int J STD AIDS* 2015;26:379–87.
 40. Peters DH, Adam T, Alonge O, et al. Implementation research: what it is and how to do it. *BMJ* 2013;347:f6753.
 41. Denny L. Control of cancer of the cervix in low- and middle-income countries. *Ann Surg Oncol* 2015;22:728–33.