Cervical cancer screening outcomes in Zambia, 2010–19: a cohort study

Jake M Pry, Albert Manasyan*, Sharon Kapambwe, Katayoun Taghavi, Miquel Duran-Frigola, Mulindi Mwanahamuntu, Izukanji Sikazwe, Jane Matambo, Jack Mubita, Kennedy Lishimpi, Kennedy Malama, Carolyn Bolton Moore*

Summary

Background Globally, cervical cancer is the fourth leading cause of cancer-related death among women. Poor uptake of screening services contributes to the high mortality. We aimed to examine screening frequency, predictors of screening results, and patterns of sensitisation strategies by age group in a large, programmatic cohort.

Methods We did a cohort study including 11 government health facilities in Lusaka, Zambia, in which we reviewed routine programmatic data collected through the Cervical Cancer Prevention Program in Zambia (CCPPZ). Participants who underwent cervical cancer screening in one of the participating study sites were considered for study inclusion if they had a screening result. Follow-up was accomplished per national guidelines. We did descriptive analyses and mixed-effects logistic regression for cervical cancer screening results allowing random effects at the individual and clinic level.

Findings Between Jan 1, 2010, and July 31, 2019, we included 183 165 women with 204 225 results for visual inspection with acetic acid and digital cervicography (VIAC) in the analysis. Of all those screened, 21 326 (10·4%) were VIAC-positive, of whom 16 244 (76·2%) received treatment. Of 204 225 screenings, 92 838 (45·5%) were in women who were HIV-negative, 76 607 (37·5%) were in women who were HIV-positive, and 34 780 (17·0%) had an unknown HIV status. Screening frequency increased 65·7% between 2010 and 2019 with most appointments being first-time screenings (n=158 940 [77·8%]). Women with HIV were more likely to test VIAC-positive than women who were HIV-negative (adjusted odds ratio 3·60, 95% CI 2·14–6·08). Younger women (≤29 years) with HIV had the highest predictive probability (18·6%, 95% CI 14·2–22·9) of screening positive.

Interpretation CCPPZ has effectively increased women's engagement in screening since its inception in 2006. Customised sensitisation strategies relevant to different age groups could increase uptake and adherence to screening. The high proportion of screen positivity in women younger than 20 years with HIV requires further consideration. Our data are not able to discern if women with HIV have earlier disease onset or whether this difference reflects misclassification of disease in an age group with a higher sexually transmitted infection prevalence. These data inform scale-up efforts required to achieve WHO elimination targets.

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*Co-first authors

Centre for Infectious Disease Research in Zambia, Lusaka, Zambia (J M Pry PhD, A Manasyan MD, M Duran-Frigola PhD, I Sikazwe MD, J Matambo MPH, J Mubita BSc, C Bolton Moore MD); **Department of Internal Medicine, School of Medicine, Washington University, St Louis, MO, USA** (J M Pry); **Department of Pediatrics** (A Manasyan) **and Department of Medicine** (C Bolton Moore), **School of Medicine, University of Alabama at Birmingham, Birmingham, AL, USA; Ministry of Health, Lusaka, Zambia** (S Kapambwe MD, M Mwanahamuntu MD, K Lishimpi MD, K Malama MD); **Institute of Social and Preventive Medicine** (K Taghavi MD) **and The Graduate School for Cellular and Biomedical Sciences** (K Taghavi), **University of Bern, Bern, Switzerland; Joint IRB-BSC-CRG Program in Computational Biology, Institute for Research in Biomedicine, The Barcelona Institute of Science and Technology, Barcelona, Spain** (M Duran-Frigola); **University Teaching Hospital, Women and Newborn Hospital, Lusaka, Zambia** (M Mwanahamuntu); **Ersilia Open Source, Cambridge, UK** (M Duran-Frigola)

Correspondence to: Dr Jake M Pry, Centre for Infectious Disease Research in Zambia, Lusaka, Zambia **jakepry@cidrz.org; jmpry@ucdavis.edu**

Introduction

Globally, approximately 527 000 new cases of cervical cancer and 265 000 deaths are recorded every year.[1] The burden of cervical cancer is projected to increase, and is compounded by the HIV epidemic.[1,2] Although primary and secondary screening strategies have greatly reduced cervical cancer in high-income countries, this approach has yet to reach low-income and middle-income countries.[3] Success in incidence reduction is reliant upon adequate coverage and adherence to screening services.[4,5] The WHO global strategy towards the elimination of cervical cancer as a public health problem requires that 90% of girls are vaccinated with the human papillomavirus (HPV) vaccine by the age of 15 years, 70% of women are screened with a high performance test by 35 years with a repeat screening by 45 years, and 90% of women identified with both pre-cancerous and invasive cervical cancer receive treatment.[6] However, targets pertaining to women with HIV have yet to be distinguished from the general population. Previous research has established women with HIV to be at an earlier and more persistent risk of cervical cancer than their counterparts who do not have HIV. However, sufficient data to define a minimum set of age-specific screening targets in this high-risk group have yet to be presented.[7–10]

Screening coverage needs to reach 70% of eligible women to result in a decrease in the incidence of cervical cancer.[11] Zambia's cervical cancer prevention programme has been very effective in terms of increasing women's engagement in screening since its inception in 2006. It has used various strategies for increasing screening coverage, including educational interventions, physician reminders, or incentive programmes, as well as strategies

Research in context

Evidence before this study

We searched MEDLINE and PubMed without language restrictions and last updated the search on Jan 19, 2021, using the search terms "cervical cancer screening" and "Zambia", which yielded 55 results. We found that the last publication evaluating cervical cancer screening in Zambia (published in 2015) reports on the Cervical Cancer Prevention Program in Zambia (CCPPZ) from 2006 to 2013. We also searched "cervical cancer screening", "sensitization", and "HIV", which yielded 118 results. We reviewed these publications, national and international guidelines for cervical cancer screening, and other relevant studies known to our research group. Few longitudinal studies have been done in sub-Saharan Africa to assess cervical cancer screening outcomes, especially in the context of the current guidelines. Furthermore, to date there are no studies to our knowledge that have evaluated cervical cancer screening sensitisation strategies. We believe that the findings of our study are novel and could help drive tailored approaches for improved cervical cancer screening programmes.

Added value of this study

The present study is a novel assessment of cervical cancer screening uptake, sensitisation, and outcomes by age and HIV status in Zambia from 2010 to 2019. We evaluated a large, programmatic cervical cancer screening cohort of 183 165 women at 11 health facilities in Lusaka, Zambia. This evaluation has not been done previously using national cervical cancer screening data from Zambia. We highlight some key findings. Firstly, the results of this study show that the predictive probability of screening positive was highest among women who were HIV-positive aged 20–29 years, followed very closely by those younger than 20 years. Secondly, we found that the possibility of receiving same-day treatment for pre-cancerous lesions was significantly higher for women who were HIV-negative than for women who were HIV-positive. This finding is particularly important in the Zambian context, where providing same-day treatment is favoured to enable a strong link between screening and treatment. Thirdly, we found that follow-up intervals are currently similar for both women who are HIV positive or negative. Lastly, we found that customised sensitisation strategies relevant to different age groups might increase the uptake to cervical cancer screening in Zambia.

Implications of all the available evidence

Cervical cancer is largely preventable but remains one of the leading causes of cancer-related death for women living in sub-Saharan Africa. Scale-up of screening services is required to achieve the WHO targets (ie, 90% of girls vaccinated by the age of 15 years, 70% of women screened at 35 years and 45 years, and 90% of women identified with both pre-cancerous and invasive cervical cancer receive treatment) in Zambia and regionally. These findings could assist policy makers and stakeholders with strategies to enable evidence-based expansion of cervical cancer screening services. These data support consideration of customised sensitisation strategies by demographic and clinical characteristics to increase uptake of screening for cervical cancer. Furthermore, regular programme evaluations might provide useful information for the prioritisation of investments and support health system strengthening. As we transition to human papillomavirus testing strategies, ongoing monitoring including indicators for long-term outcomes for women, could help to further strengthen the programme.

targeting the community, such as mass media campaigns, outreach to community members, and leveraging community health workers.[12–16] Evaluation of effective referral mechanisms for cervical cancer screening by age and HIV status and cervical cancer screening retention or follow-up have not been fully described in sub-Saharan Africa, to our knowledge.

The Cervical Cancer Prevention Program in Zambia (CCPPZ) is the largest nurse-led public sector programme of its kind in sub-Saharan Africa, training nurses to provide eligible women with free, personalised cervical cancer screening through visual inspection with acetic acid and digital cervicography (VIAC) as an adjunct for quality assurance.[17–19] In Zambia, women aged 30–59 years are screened every 5 years while women with HIV aged 25–59 years are screened at an interval of 3 years if they have had a previously negative screening result.[20] Women outside of these target groups are also considered for screening on the basis of individual risk assessment. Women who have a positive result are offered cryotherapy or thermal ablation on the same day as screening if the lesion covers less than 75% of the cervix, can be completely covered by the cryotherapy probe, is fully visible on the ectocervix, and is not suspicious for cancer according to clinical judgment. This approach reflects the so-called see and treat model endorsed by WHO and adapted by the Ministry of Health Zambia.[18,19,21] If the lesion does not meet the criteria for immediate treatment, patients are referred for histological evaluation with either large loop electrical excision of the transformation zone or punch biopsy, punch biopsy if the lesion is clinically suspicious for invasion. If treatment for pre-cancer was indicated, follow-up after 1 year is recommended in both the general population and women with HIV.

Since 2006, CCPPZ led by the Ministry of Health Zambia, and in close partnership with the Centre for Infectious Disease Research in Zambia (CIDRZ), has implemented cervical cancer screening using both a standalone and integrated model in government-led clinics.[2] The CCPPZ is the first large-scale, public sector cervical cancer prevention intervention effort in Zambia and remains one of the largest programmes of its type

	VIAC-negative (n=182 899)	VIAC-positive (n=21 326)	p value
Age, years			
Median	34 (28–42)	33 (27–40)	<0·0001
<20	2562 (1·4%)	247 (1·2%)	<0·0001
20–29	47 111 (25·8%)	5555 (26·0%)	..
30–39	53 738 (29·4%)	6877 (32·2%)	..
40–49	33 169 (18·1%)	3255 (15·3%)	..
≥50	17 962 (9·8%)	1327 (6·2%)	..
Unknown	28 357 (15·5%)	4065 (19·1%)	..
HIV status			
Negative	86 007 (47·0%)	6831 (32·0%)	<0·0001
Positive	65 244 (35·7%)	11 363 (53·3%)	..
Unknown	31 648 (17·3%)	3132 (14·7%)	..
Visit type			
Enrolment	142 404 (77·9%)	16 536 (77·5%)	0·29
Follow-up	40 495 (22·1%)	4790 (22·5%)	..
Referral			
Community	6213 (3·4%)	319 (1·5%)	<0·0001
Family and friends	3126 (1·7%)	290 (1·4%)	..
Health facility	28 144 (15·4%)	2320 (10·9%)	..
Media	3371 (1·8%)	237 (1·1%)	..
Peer educator	21 243 (11·6%)	1869 (8·8%)	..
Unknown	120 802 (66·0%)	16 291 (76·4%)	..
Year screened			
2010	12 660 (6·9%)	2692 (12·6%)	<0·0001
2011	13 008 (7·1%)	2569 (12·0%)	..
2012	17 494 (9·6%)	2950 (13·8%)	..
2013	17 263 (9·4%)	2354 (11·0%)	..
2014	16 047 (8·8%)	1789 (8·4%)	..
2015	14 198 (7·8%)	1123 (5·3%)	..
2016	13 266 (7·3%)	1071 (5·0%)	..
2017	22 313 (12·2%)	1928 (9·0%)	..
2018	22 955 (12·6%)	1843 (8·6%)	..
2019	23 493 (12·8%)	1946 (9·1%)	..
Unknown	10 202 (5·6%)	1061 (5·0%)	..
Health facility			
Bauleni	4048 (2·2%)	468 (2·2%)	<0·0001
Chawama	18 845 (10·3%)	1382 (6·5%)	..
Chelstone	16 537 (9·0%)	1968 (9·2%)	..
Chilenje	7411 (4·1%)	332 (1·6%)	..
George	23 069 (12·6%)	2263 (10·6%)	..
Kalingalinga	11 253 (6·2%)	1637 (7·7%)	..
Kanyama	28 002 (15·3%)	2970 (13·9%)	..
Matero Reference Hospital	18 439 (10·1%)	2264 (10·6%)	..
Mtendere	22 002 (12·0%)	2287 (10·7%)	..
Ngombe	6030 (3·3%)	873 (4·1%)	..
University Teaching Hospital	27 263 (14·9%)	4882 (22·9%)	..

(Table 1 continues in next column)

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Data are n (%) or median (IQR), unless specified. VIAC=visual inspection with acetic acid and digital cervicography.

Table 1: **Population characteristics among those screened**

in sub-Saharan Africa. Initially implemented as an intervention targeting women with HIV, it is now part of routine health service delivery for all Zambian women, irrespective of HIV status. We aimed to explore screening frequency successes, examine predictors of cervical cancer screening results and treatment outcomes, and describe sensitisation strategies—defined as reported screening referral methods (ie, peer educator, health facility)—among those accessing cervical cancer screening services according to age group and HIV status using 9 years of CCPPZ data.

Methods

Study design and participants

We did a cohort study in which we analysed data from the CCPPZ of women accessing cervical cancer screening through routinely offered screening services at all 11 government health facilities that provided screening services in Lusaka, Zambia. These facilities were Bauleni, Chawama, Chelstone, Chilenje, George, Kalingalinga, Kanyama, Matero Reference Hospital, Mtendere, Ngombe, and University Teaching Hospital. All study activity was done as part of monitoring and evaluation by the CIDRZ for the President's Emergency Plan for AIDS Relief funded Capacity Building and Strengthening Implementation of HIV Combination Prevention and Treatment Services (ACHIEVE) Project and the Ministry of Health. The ACHIEVE Project supports the HIV care cascade and cervical cancer screening services throughout Zambia.All women who underwent cervical cancer screening as part of routine care and had a valid result in the 11 government health facilities were included in the analysis cohort. Follow-up for women who underwent cervical cancer screening was determined based on their previous results per national guidelines. This study was approved by the University of Zambia Biomedical Research Ethics Committee (number 005-11-17) and the institutional review boards at Washington University (St Louis, MO, USA), without requiring patient consent given the use of de-identified, routinely collected programmatic data (number 201911143).

Procedures

All data were collected and entered on site by a trained nurse into an electronic database including socio-demographic data, method of cervical cancer screening referral, HIV status, cervical VIAC results, treatment referral, type, and post-screening clinical plan. Data queries were adjudicated from disparate electronic spreadsheets stored at the University Teaching Hospital,

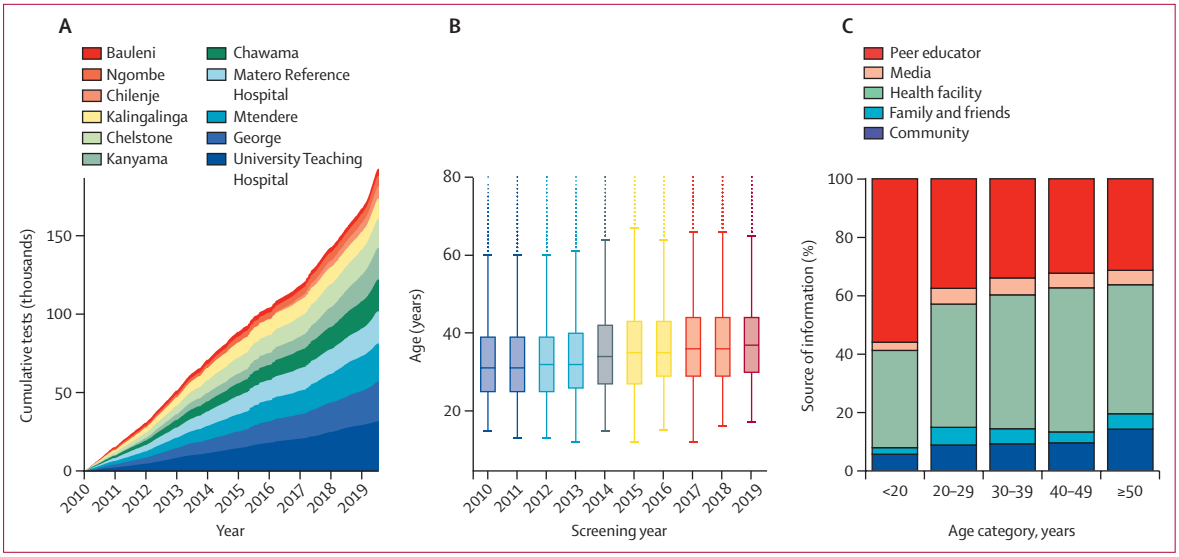


Figure 1: **Screening population characteristics**
(A) Cumulative number of screening tests done according to year and health facility. (B) Box plot of age by review year. (C) Referral source reported by age category.

maintained by CIDRZ-supported staff, and de-identified at CIDRZ headquarters in Lusaka, Zambia. To account for screening heterogeneity across facilities, we allowed for random effects at the facility level. We evaluated the predictors of VIAC positivity by HIV status and age.

Statistical analysis

We used mixed-effects logistic regression to evaluate screening results allowing for a random effect at the facility and individual level. All available covariates were included in the multivariate model per a priori identification of confounders via directed acyclic graph. We analysed the interaction between age and HIV status in the final regression model. Multiple imputation methods were considered for cases in which missing data were less than 15% and covariate values met assumptions to be considered missing at random. Longitudinal analysis was limited to within-facility observations (ie, across facility repeat testing and treatment was not possible). Predictive probability estimates were based on results of the mixed-effects regression model. All analyses were done using R, version 3.6.1, and Stata SE 15.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Between Jan 1, 2010, and July 31, 2019, data for 183 165 women with 204 225 VIAC screening results were collected. The median age of women was 34 years (IQR 28–42). Of the 204 225 screening results, 21 326 (10·4%) were VIAC-positive. Among those screening positive, 7165 (33·6%) completed cryotherapy at the screening visit. Of the 204 225 observations, 76 607 (37·5%) were in women who were HIV-positive, 92 838 (45·5%) were in women who were HIV-negative, and 34 780 (17·0%) had an unknown HIV status (table 1). At least one follow-up screening result was available for 14 677 (8·0%) women and referral information was recorded for 67 132 (32·9%) screenings.

Table 1 shows the demographic characteristics of the screened population. Most women attending screening were aged 30–39 years (n=60 615 [29·7%]) followed by 20–29 years (n=52 666 [25·8%]), and 40–49 years (n=36 424 [17·8%]). Overall, the number of women screened per year increased from 15 352 in 2010 to 25 439 in July, 2019 (partial year), corresponding to an increased annual uptake of 65·7% (figure 1A). A small proportion of women attending screening were aged 50 years and older (n=19 289; figure 1B). Women younger than 20 years comprised the smallest proportion of screening patients (n=2809 [1·4%]). Patient-reported method of uptake was answered by 67 132 (32·8%) women. Most women reported that they were referred by a health facility (n=30 464 [14·9%]), 23 112 (11·3%) reported that the method of referral was through a peer educator, 6532 (3·2%) via the community (ie, community health workers, community leaders, and churches), 3608 (1·8%) by the media, and 3416 (1·7%) by family and friends (table 1). There were significant differences in population characteristics across VIAC results in all covariates, except visit type (table 1).

University Teaching Hospital reported the largest proportion of screening (n=32 145 [15·7%]) across all 11 health facilities, followed by Kanyama (n=30 972 [15·2%]), George (n=25 332 [12·4%], and Mtendere clinics (n=24 289 [11·9%]; figure 1A). We observed heterogeneity

across facilities by age, proportion VIAC-positive, and HIV status among those screened (appendix p 1).

The highest probability of screening positivity was identified among women with HIV aged 20–29 years followed closely by the youngest age group (<20 years; figure 2D). A significant difference was seen in probability of being screen positive across HIV status for all age groups except the oldest (≥50 years). Although there were fewer women screened in the younger than 20 years age group, this age group was associated with the highest probability of screening VIAC-positive. In all age groups, women with HIV had a greater risk of screen positivity than women who were HIV-negative (adjusted odds ratio [OR] 3·60, 95% CI 2·14–6·08; p<0·0001; table 2). Table 2 shows that referrals from family and friends were significantly more likely to screen positive (adjusted OR 1·73, 95% CI 1·13–1·67; p=0·012), compared with community referrals. No difference was observed in the risk of screening positivity at a follow-up visit compared with enrolment (adjusted OR 0·96, 95% CI 0·80–1·15; p=0·66; table 2).

Follow-up screening spacing differed depending on screening test result upon enrolment (figure 1B). The mean number of visits per participant was 1·11. Those who had a positive screening result at enrolment returned for follow-up screening more readily (mean follow-up interval 1·16 years, IQR 1·00–2·42) than those who had a negative VIAC result at enrolment (2·56 years, IQR 1·50–3·20; Mann-Whitney p<0·0001). Follow-up VIAC screening results were negative for 76·3% of those previously VIAC-positive with a specified treatment on record (14·3%). A known HIV status upon enrolment was not significantly associated with a median follow-up interval among women who were HIV-positive (2·25 years, IQR 1·08–3·09) or HIV-negative (2·18 years, 1·12–3·13).

Method of uptake for most women was by community health workers or other health facilities (eg, antiretroviral therapy clinics, sexual health clinics, and maternal child health clinics). Disaggregating by age group, we found that in the younger age groups, peer educator referrals resulted in the most number of enrolments resulting in a significant difference compared with the older age groups, for which health facility and community referrals resulted in the highest uptake (χ^2 p<0·0001; figure 1C).

Time to return to follow-up did not differ by HIV status; however, it was significantly different by previous VIAC result at 1, 2, and 3 years of follow-up time. The survival function for a previous VIAC-positive result compared with a previous VIAC-negative result was 0·70 (95% CI 0·69–0·71) and 0·51 (0·49–0·54) at 1 year of follow-up, 0·49 (0·48–0·50) and 0·17 (0·15–0·19) at 2 year follow-up, and 0·30 (0·28–0·31) and 0·09 (0·07–0·11) at 3 year follow-up.

Treatment with cryotherapy at screening visit was recorded for 33·6% of those who were VIAC-positive.

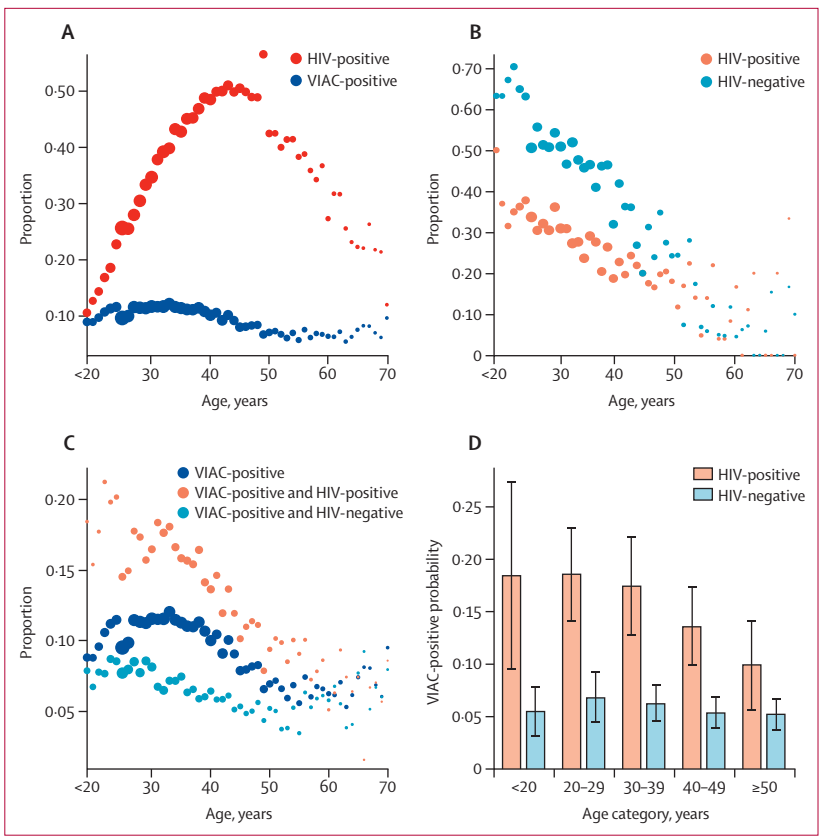


Figure 2: **Measures of VIAC screening result by HIV status and age**
(A) Distribution of HIV-positive and screen positive results by age. (B) Scatter plot of same-day cryotherapy appointment by age and HIV status (n=21 326). (C) Screening positivity given HIV status. (D) Probability of screening positivity according to age group and HIV status. VIAC=visual inspection with acetic acid and digital cervicography.

The rate of cryotherapy was higher among the younger age group (59·1%) than the 50 years and older age group (11·7%). Additionally, those who were HIV-negative (45·0%) were more likely to receive cryotherapy on the same day as screening than women who were HIV-positive (25·1; figure 2B).

Most recorded screenings were initial or enrolment visits (n=158 940 [77·8%]), with the remaining 45 285 being follow-up visits, of which 24 225 individuals enrolled before our review period. A large proportion of the enrolment screenings were among women with HIV (n=76 607 [37·5%]), which is likely to be related to the initial CCPPZ directive to target women with HIV first and then expand to include the HIV-negative population. We did not observe a significant difference in VIAC screening result by visit type (ie, enrolment visit or follow-up visit; OR 0·97, 95% CI 0·84–1·12).

Over the 9-year period reviewed, screening enrolment increased from 18 671 to 25 562 women and more than 200 000 screenings were done in Lusaka, Zambia.

Discussion

Our study of a large, programmatic cohort found that women with HIV aged younger than 30 years had the

See **Online** for appendix

	Crude		Adjusted	
	Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value
Age, years				
<20	1·45 (1·08–1·78)	0·011	1·31 (0·95–1·82)	0·098
20–29	1·84 (1·33–2·18)	<0·0001	1·81 (1·32–2·47)	<0·0001
30–39	2·00 (1·57–2·14)	<0·0001	1·69 (1·33–1·97)	<0·0001
40–49	1·43 (1·18–1·61)	<0·0001	1·22 (0·98–1·51)	0·077
≥50	1 (ref)	..	1 (ref)	..
HIV status				
Negative	1 (ref)	..	1 (ref)	..
Positive	2·19 (2·12–2·26)	<0·0001	3·60 (2·14–6·08)	<0·0001
Unknown	1·25 (1·19–1·30)	<00001	1·37 (1·15–1·64)	<0·0001
Referral				
Community	1 (ref)	..	1 (ref)	..
Media	1·38 (0·82–2·34)	0·23	1·11 (0·70–1·77)	0·65
Family and friends	1·98 (1·27–3·08)	0·0030	1·73 (1·13–1·67)	0·012
Health facility	1·77 (1·23–2·54)	0·0020	1·07 (0·69–1·67)	0·76
Peer educator	1·73 (0·90–3·32)	0·10	1·16 (0·72–1·88)	0·54
Unknown	2·67 (1·78–4·00)	<0·0001	1·20 (0·79–1·84)	0·39
Visit type				
Enrolment	1 (ref)	..	1 (ref)	..
Follow-up	0·83 (0·71–0·97)	0·020	0·96 (0·80–1·15)	0·66
Year screened				
2010	2·42 (1·90–3·10)	<0·0001	4·34 (2·92–6·46)	<0·0001
2011	2·22 (1·75–2·82)	<0·0001	4·16 (2·77–6·25)	<0·0001
2012	1·87 (1·49–2·34)	<0·0001	3·31 (2·20–4·98)	<0·0001
2013	1·52 (1·11–2·08)	0·0090	2·74 (1·56–4·81)	<0·0001
2014	1·22 (1·12–1·33)	<0·0001	1·84 (1·65–2·05)	<0·0001
2015	0·88 (0·70–1·10)	0·25	1·39 (1·12–1·73)	0·0030
2016	0·95 (0·81–1·10)	0·48	1·37 (1·14–1·65)	<0·0001
2017	1·00 (0·83–1·21)	0·10	1·36 (1·12–1·64)	0·0020
2018	0·93 (0·76–1·14)	0·49	1·28 (0·99–1·20)	0·062
2019	1 (ref)	..	1 (ref)	..

Data are odds ratio (95% CI). VIAC=visual inspection with acetic acid and digital cervicography.

Table 2: **Crude and adjusted predictors for screening VIAC-positive**

highest predictive probability of being VIAC-positive compared with their older counterparts. Although previous research reported that those on antiretroviral therapy have a chronic, deficient immunity, which predisposes them to cervical cancer between the ages of 30–40 years, we found that younger women with HIV aged 20–29 years had the highest predictive probability of being screen positive (18·6%, 95% CI 14·2–22·9) followed very closely by those younger than 20 years (18·4%, 9·6–27·3).[22–24] These findings build on previous work identifying those younger than 37·5 years to be at higher odds (adjusted OR 1·6, 95% CI 0·9–2·9) for cervical lesions compared with those aged 37·5 years and older.[9] With our large sample size, we were able to show that the highest odds for screening positive are among women aged 20–29 years (adjusted OR 1·81, 95% CI 1·32–2·47).

In general, women in the 30–39 years age group had the highest proportion of positive screening results (11·3%) among those with age recorded; however, there was a significant difference by HIV status with women who were HIV-positive aged 30–39 years with more than twice the predictive probability of having a positive result. Women who were HIV-positive and younger than 20 years had more than three times the predictive probability (18·4, 95% CI 9·56–27·32) for being positive compared with women who were HIV-negative in the same age group (predictive probability 5·5%, 95% CI 3·2–7·8). The increased prevalence of cervical lesions in sub-Saharan Africa, especially among young women, might be associated with early age of marriage or first sexual intercourse, multiple sexual partners, and low HPV vaccination awareness, accessibility, or availability.[8]

Overall, we observed a significantly increased odds (OR 3·60, 95% CI 2·14–6·08) for being screen positive among women with HIV compared with women who were HIV-negative, which supports previous findings in the region including South Africa, Uganda, and Zimbabwe.[9,25–30] Mechanisms for increased odds for being VIAC-positive among women with HIV might be explained, in part, by the effect of HIV on the immune system, which could lead to chronic HPV infection and increased susceptibility to new lesions.[31,32]

We identified a significant difference in the self-reported source of referral for cervical cancer screening by age group, most notably in the youngest (<20 years) age group compared with those aged 20 years and older. Young women reported referral predominantly from peer educators, whereas older women more often reported referral by their health facility or community. This finding suggests that different strategies should be considered to target and increase uptake among different groups of the population. The data also indicate that the programme successfully engaged women to attend a single-visit service. However, because women with HIV are at greatest risk of a persistent pre-cancerous lesion, recurrent disease, and ultimately invasive cervical cancer, adherence to follow-up recommendations should be reinforced.[33] More resources to increase re-screening could be considered in the next stage of scale-up. In the general population, seeking twice per lifetime screening (at 35 years and 45 years) could also be considered as an interim step.[6] Additionally, high prevalence of screening positivity among adolescent girls coupled with the preferred mode of sensitisation could be leveraged to improve targeted outreach and reduce cervical cancer risk among young women. These results highlight the importance of targeting women with HIV at first sexual intercourse and consolidate the case of implementation of a nationwide HPV vaccination programme.

Given that our data are dependent upon provider proficiency, there could be some misalignment between screening test positivity and neoplastic lesions, as visually, cervicitis and other benign cervical lesions could be mistaken for pre-cancerous disease (sharing

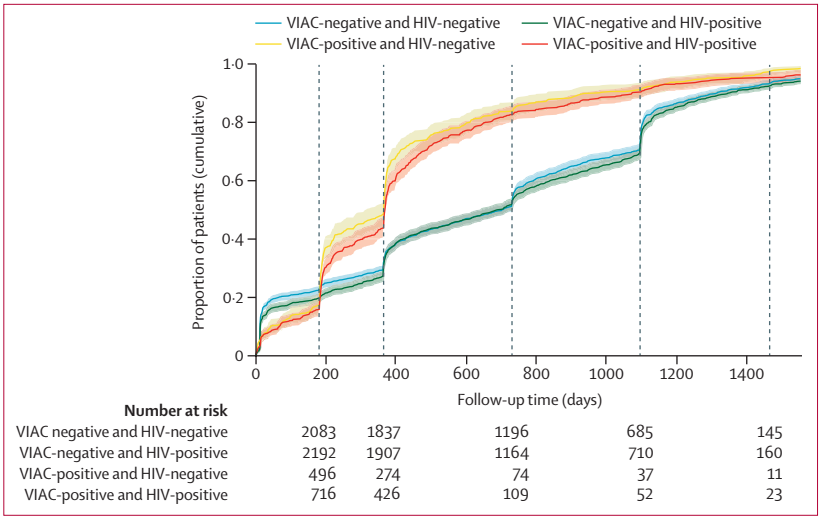
many of the same physical characteristics).[34] Thus, it is possible that women with HIV are more likely to be misclassified for increased cervical cancer risk as they might be less likely to clear infections because of their immune status.[35,36] These findings could also indicate that women with HIV have earlier disease progression, meaning that these women should be engaged in screening at a younger age. Efforts to change screening methods to HPV screening are underway and could help to prevent misclassification of disease in women with HIV. It is noted that in the absence of histopathology, we cannot comment on true disease and missed cases, which is a weakness of VIAC-based screening programmes. Without systematic histopathological evaluation, screening and treatment efficacy also remains difficult to evaluate. Current guidelines recommend that women with HIV should be referred for cervical cancer screening after their first sexual interaction, irrespective of age. However, this guideline is rarely implemented.

A greater proportion of women who are HIV-negative received same-day cryotherapy than their HIV-positive counterparts of the same age. This discrepancy could be related to the tendency for women who are HIV-positive to have more extensive lesions, which are ineligible for treatment with local ablative methods.[37,38]

This study has several limitations. First, we assessed screening outcomes only. The test accuracy of the VIAC method to identify pre-cancerous lesions (cervical intraepithelial neoplasia grade 2 or worse) is an inherent weakness.[8,22,38,39] The sensitivity of VIAC in Africa is reported to range greatly, with a sensitivity from 25% (95% CI 7–59) to 82% (66–95) and specificity from 74% (64–82) to 83% (77–87).[38,40] As a consequence, we cannot vouch for accuracy or effect of this service. Without histopathology, we are unable to comment on true disease, missed cases, overtreatment, or persistent disease. These efficacy measures are important outcomes of screening programmes, which also require consideration. Self-reported methods of uptake were also presented. One of the issues with self-reported questions is a response bias, and this factor should be considered in relation to women's responses to method of uptake. Lastly, complications associated with electronic records across several platforms could have resulted in some loss of data; however, we do not have reason to believe that these data were not missing at random across our measured covariates. These issues are also likely to be improved in the coming years with the initiation of a national electronic medical records system for cervical cancer called Smart-Cerv and the established population-based cancer registry for Lusaka District.

This study is a timely contribution that supports the WHO's guidance on eliminating cervical cancer.[6] We present health system data that show predominantly a single-visit approach to screening and treatment and highlights that where HIV prevalence is high, the target screening ages stated in the guidance (35 years and 45 years) might need to be earlier. We found the highest predictive probability and adjusted odds for VIAC-positive results among younger women aged 20–29 years who were HIV-positive. We note the limitations of VIAC in this assessment and argue the need for other methods of screening and diagnosis in Zambia and other low-income and middle-income country settings.

Zambia's cervical cancer prevention programme has been very effective in scaling up cervical cancer screenings in all ten provinces of Zambia and increasing women's engagement in services. More than 800 000 women have now been screened since the inception of the programme in 2006. This large cervical cancer screening programme review provides a strong real-world evidence base to inform the scale-up required to achieve cervical cancer elimination targets of 70% women screened by 2030 in Zambia and beyond.[6] These data suggest that customised sensitisation strategies relevant to different age groups might increase the uptake and adherence to cervical cancer screening in Zambia. We found that among women with HIV, the highest adjusted odds and predictive probability occurred in the 20–29 year age group, suggesting particular attention to be paid to this younger, high risk group. Overall, our data inform scale-up efforts required to achieve WHO elimination targets of 70% of women screened, and 90% treated by 2030 over and above the aim for 90% of girls to be vaccinated by the age of 15 years by 2030.



Number at risk					
VIAC negative and HIV-negative	2083	1837	1196	685	145
VIAC-negative and HIV-positive	2192	1907	1164	710	160
VIAC-positive and HIV-negative	496	274	74	37	11
VIAC-positive and HIV-positive	716	426	109	52	23

***Figure 3*: Kaplan-Meier estimates for time to follow-up screening**
Shading indicates 95% CI. VIAC=visual inspection with acetic acid and digital cervicography.

For more on the **national electronic medical records system for cervical cancer** see https://www.pciglobal.org/cervical-cancer-prevention/

Contributors
JMP and AM conceptualised the manuscript and was involved in data collection, data analysis, data interpretation, developing the tables and figures, and writing the manuscript. SK was responsible for data

collection and data interpretation. KT did the literature search and was responsible for data interpretation and writing of the manuscript. MD-F was responsible for data collection, data analysis, data interpretation, figures, and writing of the manuscript. MM and IS were responsible for data interpretation and writing the manuscript. JMa and JMu were responsible for data collection. KL and KM were responsible for writing the manuscript. CBM was responsible for data interpretation and reviewed and revised the manuscript for critically important content. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication. AM, KT, MD-F, JMP, IS, and CBM verified the data.

Declaration of interests

We declare no competing interests.

Data sharing

Individual, participant-level de-identified data, including the statistical analysis plan and the data codebook, will be made available upon request. Proposals should be directed to the corresponding author of this manuscript, who will share the data after a data sharing agreement has been signed between the Ministry of Health and the requestor.

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