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HIV-RELATED DISCRIMINATION AND CERVICAL CANCER SCREENING IN ZAMBIA

CRYSTAL J. CAZIER

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CRYSTAL J. CAZIER, BA

APPROVED:

MARLYN A. ALLICOCK, MPH, PHD

KATELYN K. JETELINA, MPH, PHD

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by

CRYSTAL J. CAZIER
BA, University of Illinois at Urbana-Champaign, 2010

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PREFACE

Since 2011 I have had the privilege of working in the cancer space – first in a cancer center serving the rural United States and for the past five years on cervical cancer prevention and control in sub-Saharan Africa. In my experience, I have witnessed the determination of women diagnosed with cancer to fight the disease. I have also seen the devastation of cancer. While the loss is no easier for a family who has been able to explore a wide complement of treatment options than the family of a woman who succumbs to the disease because even basic options for care were not available to her, it is no secret that cervical cancer is a thief. It robs us of our mothers, sisters, and friends; and robs the world of innovative entrepreneurs, fierce leaders, and unrelenting change-makers, disproportionately affecting low- and middle-income countries. My decision to pursue an MPH came as a hope that by sharpening my capacity to meet the challenge of cancer, we will achieve better outcomes and survival for the women I have been privileged to serve.

ACKNOWLEDGMENTS

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Crystal J. Cazier, BA, MPH
The University of Texas
School of Public Health, 2019

Thesis Chair: Marlyn A. Allicock, MPH, PhD

Background: The Republic of Zambia has the third-highest incidence of cervical cancer in the world, where approximately 700,000 women over age 15 are living with HIV. Women living with HIV (WLHIV) are at increased risk for cervical cancer. While literature suggests that discrimination is a barrier to HIV care, no studies have explored if discrimination experienced in HIV clinics is related to cervical cancer screening using nationally representative datasets.

Objective: The primary objective of this study was to examine whether perceived discrimination by healthcare workers due to HIV status is related to having been screened for cervical cancer among WLHIV.

Methods: This study used the Zambia Population-based HIV Impact Assessment (ZAMPHIA) weighted data to examine the logistic bivariate and multivariate relationships between experienced discrimination and cervical cancer screening as well as key demographic and covariates among 1,182 WLHIV ages 15-59 in Zambia.

Results: Twenty-seven percent of WLHIV in Zambia had screened for cervical cancer and 5.5% experienced HIV-related discrimination. There was no significant relationship

between discrimination and cervical cancer screening (OR=1.26; 95% CI=0.69-2.29). In multivariate logistic regression, age (OR=1.03; 95% CI=1.02-1.05), having more than secondary education (OR=3.18; 95% CI=1.30-7.75), living in an urban area (OR=2.17; 95% CI=1.53-3.09), ethnicity (Tonga: OR=2.02; 95% CI=1.26-3.24; Lozi: OR=3.21; 95% CI=1.85-5.60; and Other: OR=1.61; 95% CI=1.11-2.34), being widowed (OR=0.60; 95% CI=0.38-0.95), and a history of sexual violence (OR=0.48; 95% CI=0.27-0.86) were significantly associated with cervical cancer screening.

Conclusions: With the support of international partners, the Government of Zambia is scaling up its national cervical cancer screening program within the HIV platform. This study provides validation for these efforts but also underscores the importance of the equitable distribution of services across rural and urban areas as well as ethnicities.

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BACKGROUND

Literature Review

Cervical Cancer Epidemiology

Globally, 569,847 women are diagnosed with cervical cancer each year, and over half of those women die of the disease, making it the fourth most common cancer for women in incidence and mortality (Ferlay et al., 2018). More than 85% of deaths from cervical cancer occur in low- and middle-income countries (LMIC; Ferlay et al., 2018). By 2040, mortality from cervical cancer is expected to increase by nearly 50% (Ferlay et al., 2018). In sub-Saharan Africa, there are an estimated 112,723 new cases of cervical cancer each year and 77,238 deaths from the disease (Ferlay et al., 2018). The Republic of Zambia has the third-highest age-standardized incidence (ASR) of cervical cancer in the world at 66.4 cases per 100,000 (Ferlay et al., 2018). In 2018, an estimated 1,839 women died of cervical cancer in the country (Ferlay et al., 2018).

Women diagnosed with cervical cancer report a decrease in quality of life (QoL). QoL can include decreased physical or sexual function, psychosocial and emotional consequences, and increased financial burden. Zayyan and colleagues assessed QoL among 378 patients with advanced cervical cancer presenting at Ahmadu Bello University, Zaria, Nigeria, between April 1 and December 31, 2014. The study reported that of the participants, 69.9% reported physical function complications, 57.7% reported issues with daily or leisure function, 60.8% reported decreased emotional function, 76.2% reported financial burden, and 85% reported decreased sexual function (Zayyan et al., 2018).

Because cervical cancer has a long latency period, early screening can detect precancerous lesions that can be removed before they become malignant. Due to the natural evolution of cervical cancer, screening has been proven to decrease the incidence of invasive cervical cancer (ICC) by detecting lesions before they become malignant (Canfell et al., 2006; Sasieni et al., 1996). The World Health Organization (WHO), Union for International Cancer Control (UICC), and the U.S. Centers for Disease Control and Prevention (CDC) have all established that screening is essential to cervical cancer control (World Health Organization, 2014; Union for International Cancer Control, 2019; U.S. CDC, 2019).

HIV Epidemiology

Concurrently, there are 18.8 million women living with HIV (WLHIV) globally (UNAIDS, 2019). In sub-Saharan Africa, women are disproportionately affected by HIV. In Zambia, women represented 59% of new HIV infections among adults age 15 and older in 2018 (UNAIDS, 2019). The same year, UNAIDS estimated that there were 25,000 new infections in women age 15 and older, contributing to approximately 700,000 women in that age group living with HIV in Zambia (UNAIDS, 2019).

The Relationship between Cervical Cancer and HIV

WLHIV have weakened immune systems and are at a higher risk for high-risk human papillomavirus (hrHPV), which causes most cases of cervical cancer (Denny et al., 2013; Parham et al., 2006; World Health Organization, 2019). One study of WLHIV in Zambia found that over 85% had hrHPV (Parham et al., 2006), and another found 90% had hrHPV (Sahasrabuddhe et al., 2007). In a cross-sectional study of 150 WLHIV in Lusaka, Zambia, Parham and colleagues reported that HIV-positive women with hrHPV had a 12.4 times

greater chance of cervical abnormalities than women without hrHPV (95% CI=2.62-58.1; p=0.02; Parham et al., 2006).

Even with treatment for cervical cancer, WLHIV have poorer survival than women who are HIV-negative. A prospective cohort study of patients who had undergone radiotherapy and chemotherapy treatment for ICC at Tygerberg Hospital in Cape Town, South Africa followed 492 women between 2007 to 2011. Five-year survival of HIV-negative patients was 49.5% (95% CI=44.6-54.4), and the five-year survival of HIV-positive patients was significantly lower at 35.9% (95 % CI=23.9-48.0; Simonds et al., 2018).

Cervical Cancer Control in Zambia

Zambia has one of, if not, the most developed national cervical cancer control programs in sub-Saharan Africa. Established in 2006, cervical cancer screening and same-day treatment services were built into the HIV care delivery system. Initially intentioned to serve WLHIV, the program has expanded to screen and treat all women regardless of HIV status (Mwanahamuntu et al., 2013).

In 2016, Zambia launched a five-year national cancer control plan that outlines the national response to cervical cancer across the continuum of cancer care, from education and awareness-raising to treatment of advanced-stage cancers and palliative care. Over the five years outlined in the National Cancer Control Strategic Plan (NCCSP), the government established a target of reaching 80% of women of reproductive age in the country with screening services (Ministry of Health, Republic of Zambia, 2016). For WLHIV, the WHO recommends screening any sexually active HIV-positive female regardless of age (World Health Organization, 2014).

The U.S. government, through the President's Emergency Plan for AIDS Relief (PEPFAR), has been a consistent supporter of cervical cancer control activities in Zambia since 2006 (Mwanahamuntu et al., 2013). In 2018, PEPFAR, along with the George W. Bush Institute and UNAIDS announced a partnership that aims to scale up cervical cancer screening and treatment among WLHIV in eight countries in sub-Saharan Africa, including Zambia (The George W. Bush Institute, 2018). Since 2018, Zambia has received $9.7 million from PEPFAR under this partnership to expand screening and treatment for WLHIV (Partnership to End AIDS and Cervical Cancer Zambia Fact Sheet, 2019). UNAIDS reports that only 27.3% of women living with HIV have been screened for cervical cancer in Zambia as of 2016 (UNAIDS, 2019), highlighting the importance of expanding cervical cancer screening for HIV-positive women especially given their increased risk for cervical cancer.

Discrimination among Women Living with HIV

Experienced discrimination, perceived discrimination, or fear of discrimination are factors associated with HIV-related care services (Bibiana et al., 2018; Duff et al., 2010; Jürgensen et al., 2012), and may be even more poignant among high-risk populations including female sex workers (Chanda et al., 2017) or men who have sex with men (Li et al., 2011; Logie et al., 2017; Zhang et al., 2013). Despite evidence that discrimination can play a role in access to HIV-related services, integrating cervical cancer screening and same-day treatment for precancerous lesions within HIV care is an effective and acceptable avenue for reaching WLHIV (Huchko et al., 2011, Mwanahamuntu et al., 2009).

Several studies have examined the barriers and facilitators to cervical cancer screening among different populations, and have often found that discrimination is a barrier

to women screening for cervical cancer. Qualitative studies describe WLHIV's fear of discrimination as a barrier to accessing cervical cancer screening in diverse populations, including in Botswana (Upton et al., 2018), India (Kung et al., 2019), Nigeria (Modibbo et al., 2016), and South Africa (Oystacher et al., 2018). Further, WLHIV who identified past experiences of discrimination, have cited discrimination as a reason for their hesitancy toward cervical cancer screening. A factor identified for why low-income African American WLHIV had not screened for cervical cancer for at least five years was determined to be due in part to past experiences with uncaring healthcare workers or perceived discrimination (Andrasik et al., 2008). Semi-structured interviews with WLHIV in India also found that experiences of discrimination were a barrier to cervical cancer screening (Gordon et al., 2019).

Contrarily, positive experiences with healthcare workers have been identified as a facilitator to cervical cancer screening. In the United States, WLHIV who had received specialized cervical cancer care within a facility that regularly serviced WLHIV identified that receiving non-discriminatory care from healthcare providers who were accustomed to working with WLHIV was a facilitating factor to their decision to be screened for cervical cancer (Fletcher et al., 2014). In Zambia, having healthcare workers providing cervical cancer screening who were seen as caring were facilitators of cervical cancer screening (White et al., 2012).

Quantitative studies have also concluded that discrimination can be a factor associated with a lack of cancer screening. In a study of racial and ethnic minorities in California, women who had indicated they experienced discrimination by healthcare workers

were less likely to have adhered to colorectal (OR=0.66, 95% CI=0.64-0.69) or breast cancer screening (OR=0.52, 95% CI=0.51-0.54; Crawley et al., 2008). A cross-sectional study of 817 women in the San Francisco Bay area found that higher composite scores of perceived prejudice, including discrimination indicators, were less likely to adhere to cervical cancer screening guidelines (p=0.005; Facione, N. and Facione, P., 2007).

In a scoping literature review, Stockton and colleagues found that negative experiences in HIV care settings were negatively associated with accessing care for several non-communicable diseases (NCDs) across various sociocultural settings and countries (Stockton et al., 2018).

Gaps in the Literature

Understanding the factors influencing cervical cancer screening among women in various sub-Saharan African countries by using population-level demographic and health survey data has been previously reported (Tiruneh et al., 2017; Kangmennaang et al., 2015; Viens et al., 2016). Few studies, however, have focused on WLHIV despite the known increased risk of this population for cervical cancer. Further, aside from one conference abstract that aimed to explain the distribution of cervical cancer screening among WLHIV in Malawi using the Population-based HIV Impact Assessment (PHIA) data (Jonnalagadda et al., 2018), no studies have been published from the PHIA data that explore the motivating and inhibiting factors to cervical cancer screening among WLHIV. Because the PHIA project is focused on exploring the HIV epidemic in high-burden countries, as well as comorbidities of HIV, it is worth evaluating factors associated with cervical cancer screening and treatment using these publicly available datasets.

While many studies have identified that perceived discrimination may be an inhibiting factor to women seeking cervical cancer screening, no known studies have explored the role of perceived or experienced discrimination in HIV care settings on other health-seeking behavior, including cervical cancer screening, particularly using population-based surveys. Furthermore, many of the studies that have explored the role of discrimination in cervical cancer screening are qualitative in design.

Public Health Significance

Because WLHIV are disproportionately at risk for cervical cancer, understanding the role that perceived discrimination due to HIV status has on their health-seeking behavior, particularly for cervical cancer, could have implications for care delivery in HIV clinical settings. Furthermore, because PEPFAR has recently increased funding for cervical cancer screening and treatment of WLHIV, this research may help explain any factors enabling or prohibiting this high-risk population from utilizing cervical cancer screening services. Evaluating the role of discrimination on cervical cancer screening and treatment could have implications for the ability of the PEPFAR-funded activities to reach scale. Recent estimates suggest less than one-third of WLHIV have been screened for cervical cancer in Zambia (UNAIDS, 2019). It is, therefore, important to understand individual-level factors related to screening and treatment behavior so that as infrastructure is being expanded to reach more women, other considerations are addressed so that the program can reach scale most efficiently. Finally, there could be important learnings related to using PHIA data to explore cervical cancer screening coverage and treatment rates as well as factors associated with each outcome, as PHIA projects in other countries have included similar questions in their data

collection instruments, and since select countries will be deploying second rounds of PHIA surveys starting in 2020.

Research Question, Hypothesis, and Specific Aims

Discrimination, or fear of discrimination, has been found to inhibit health-seeking behavior for NCDs, including in people living with HIV (Stockton et al., 2018). Zambia has a high prevalence of HIV, and because WLHIV are at an increased risk for cervical cancer, understanding if perceived discrimination in the HIV care setting due to HIV status affects their cervical cancer screening behavior is an important question. This study hypothesized that any perceived discrimination based on HIV status experienced in HIV care settings would be negatively associated with cervical cancer screening or treatment for positive screening results among WLHIV. To test this hypothesis, this study had several objectives:

1a. To evaluate the prevalence of cervical cancer screening among WLHIV in Zambia.

1b. To evaluate the prevalence of WLHIV who have had cervical cancer screening report positive results in Zambia.

1c. To evaluate the prevalence of WLHIV who have been treated for cervical (pre)cancerous lesions after a positive cervical cancer screen.

2a. To examine if perceived discrimination based on HIV status experienced in HIV care settings is related to having been screened for cervical cancer among WLHIV.

2b. To examine if perceived discrimination based on HIV status experienced in HIV care settings is related to completing treatment for cervical (pre)cancerous lesions among WLHIV who receive a positive screen on their cervical cancer test.

3. To identify covariates associated with cervical cancer screening among WLHIV in Zambia.

METHODS

Study Design

The PHIA project is a cross-sectional study of fourteen countries in sub-Saharan Africa plus Haiti funded by PEPFAR through the CDC and is managed by ICAP at Columbia University's Mailman School of Public Health (New York, NY). The PHIA project was undertaken to assess the national HIV epidemic in each country and explored the health sector's response by deploying household-level surveys across a nationally representative sample. The Zambia PHIA (ZAMPHIA) was led by the Ministry of Health of the Republic of Zambia and administered by ICAP. ZAMPHIA includes a series of three questionnaires (household, adult, and adolescent) and a biomarker tool (ZAMPHIA 2016). This project uses data from the household and adult questionnaires, plus indicators from the biomarker tool. These data were retrieved in a comprehensive dataset provided by ICAP.

Measures

Primary and Secondary Outcomes

The primary outcome for this study was self-reported *completion of a cervical cancer screening*. All women who participated in the study were given a short description of cervical cancer and possible screening modalities and then were asked "Have you ever been tested for cervical cancer?" to which they could respond 'yes', 'no', 'don't know' and 'refused.' Those who responded 'don't know' or 'refused' were considered missing for analyses. Screening within 12 months of the date an individual started the survey was also

reported. For women who could not remember the month of their screening, if they reported cervical cancer screening during 2016, they were included. Women who reported cervical cancer screening in 2015 must have also reported the month of the screening to be included in the analysis.

The secondary outcome for this study was self-reported *completion of treatment* for a positive screening result. Women who self-reported a completed screening were asked, "What was the result of your last test for cervical cancer?" to which they could respond 'negative/normal', 'abnormal/positive', 'suspect cancer', 'unclear/inconclusive', 'did not receive results', 'don't know', or 'refused'. For this study, the responses were categorized as 'negative/normal', 'abnormal/positive or suspect cancer', 'unclear/inconclusive' and all other responses were considered missing. Women who indicated 'abnormal/positive or suspect cancer' results were then asked, "Did you receive treatment after your last test for cervical cancer?" to which they responded, 'yes, I was treated on the same day', 'yes, I received treatment on a different day', 'no', 'don't know' or 'refused'. For this study, responses were coded as 'yes' or 'no' with 'don't know' or 'refused' considered missing.

Primary Exposure

Perceived discrimination was derived from two survey items that were asked only to those participants who self-identified as HIV-positive. If a participant responded 'yes' to either or both of the following questions, they were considered to have experienced perceived discrimination: "In the last 12 months, have health care providers talked badly about you because of your HIV status?" and "In the last 12 months, have you been denied health services including dental care, because of your HIV status?"

Covariates

Demographic covariates included *age* (years, continuous), *education* (none, primary, secondary, more than secondary), *residence location* (urban, rural), *ethnicity* (Bemba, Tonga, Lozi, other), *employment* in the past 12 months (yes, no), *religion* (Protestant, Catholic, other), and *relationship* status (married or living together, divorced/separated, widowed, never married). Other covariates included *number of pregnancies* (continuous), *age of first sex* (14 or under, 15 to 20, 21 or older), *history of violence* (no history, physical, sexual, physical and sexual), number of *lifetime sexual partners* (0 or 1, 2 or 3, 4 or more), lifetime *history of selling sex* (yes, no), and report of *current use of antiretroviral medication* (ARVs; yes, no).

History of violence was a composition of multiple items including answering affirmative to a history of non-sexual violence including threats of violence (yes, no) for physical violence, or an affirmative answer to any of the following for sexual violence: "How many times has anyone ever touched you in a sexual way without your permission, but did not try and force you to have sex?", "How many times in your life has anyone tried to make you have sex against your will but did not succeed?", "How many times in your life have you been physically forced to have sex?", or "How many times in your life has someone pressured you to have sex through harassment, threats, and tricks and did succeed?".

Study Setting

The ZAMPHIA project was conducted in the Republic of Zambia by trained staff. ZAMPHIA includes a nationally representative population sample (Ministry of Health, Zambia, 2019).

Study Subjects

This study included a sample of 1,182 women ages 15 to 59 years who self-identified as HIV-positive and were confirmed with testing to be HIV-positive. Self-identification as HIV-positive was derived from four questions on the adult questionnaire asking about testing behavior and test results at different time points: before the most recent pregnancy, during the most recent pregnancy, during labor of the most recent pregnancy, or generally at the last test for HIV. A definitive diagnosis of HIV was determined with a biomarker tool and included in the retrieved comprehensive dataset.

Data Collection

Data for the ZAMPHIA project were collected between March to August of 2016 by trained field staff and recorded electronically. Detailed information about the sampling strategy can be found elsewhere (Ministry of Health, Zambia, 2019). Briefly, a two-stage stratified cluster sample design was used (i.e., enumeration areas (EA) were determined in the first stage, and households selected from each EA in the second stage).

Data Analysis

A weighted sample provided by PHIA was used for analyses. Characteristics of the sample were completed using count and weighted averages. Bivariate odds were used to determine the relationship between cervical cancer screening (main outcome) and potential confounders. Bivariate analyses for relationships between completing cervical cancer screening (main outcome) and covariates were conducted using chi-square for categorical covariates and t-test statistics for continuous covariates. Multivariate logistic regression was applied to analyze the factors that contributed to cervical cancer screening. A multivariate

logistic regression model was built using p-value selection. Backward and forward selection methods were employed on the unweighted sample. Covariates identified with forward and backward selection to be significant at $p<0.05$ were included in a multivariate logistic regression model with the primary exposure in the weighted sample and results reported for comparison. The f-value static was reported for overall statistical significance of the weighted models. The Akaike information criterion (AIC) of the unweighted models was determined and compared as a consideration for model fit.

The study included a sensitivity analysis of the bivariate relationship between HIV-related discrimination and cervical cancer screening, in which cervical cancer screening was restricted to those who reported screening within 12 months of the date the individual started the survey to align with the timebound questions measuring HIV-related discrimination (primary exposure).

While analyses were planned to examine if perceived discrimination by healthcare workers due to HIV status was related to treatment of cervical (pre)cancerous lesions among WLHIV who received a positive screen on their cervical cancer test, due to a small sample of women who reported a positive screening result (n=11), this analysis was abandoned.

To satisfy the assumptions of multicollinearity during model building, pairwise correlation of all unweighted demographic and confounding variables as well as the primary study exposure were reviewed. During model building, despite high correlation of covariates, covariates were retained given that their inclusion in the model did not impact the direction of the coefficient of the primary exposure.

All analyses were completed in STATA, version 15.1 (StataCorp., 2017). A p-value of 0.05 was set as the cut off level for significant results. For covariates with missingness less than 10%, missing values were dropped from the analyses. Missingness of 10% or greater were included in the bivariate analyses.

Human Subjects Considerations

Primary data collection was undertaken by ICAP at Columbia University. De-identified person-level data was obtained via the open-access website with permission granted by ICAP for purposes of this project. The project was submitted to the University of Texas Health Institutional Review Board Committee for Protection of Human Subjects and exemption granted (Appendix A).

RESULTS

A description of the study sample is provided in **Table 1**. The average age was 37 years old (SD=0.29), and most had primary (44.6%) or secondary (41.2%) education. Most WLHIV lived in urban areas (61.8%), and the largest individually-represented ethnic group was Bemba (27.0%). First sexual experience was reported to be between ages 15 to 20 for most women (74.2%). Fifty-five percent of WLHIV in Zambia are married. Violence was reported among 18% of respondents; information related to history of violence was missing for over one-third of the sample (35.4%). Eighty-four percent of women reported currently taking ARVs (84.7%).

Twenty-seven percent of WLHIV age 15 to 59 reported having a cervical cancer screening in their lifetime (26.8%), with 40.4% of those screenings taking place within the 12 months prior to the respondent's survey. Most with reported screenings found no cervical

abnormalities (95.4%), and among the 11 participants who reported an abnormal finding, nine reported receiving treatment. Most respondents reported no perceived HIV-related discrimination (94.5%).

Table 2 displays the bivariate odds of cervical cancer screening by key demographics and confounders for each variable component. **Table 3** displays the bivariate odds of cervical cancer screening and key demographics and confounders for overall significance of each variable. There was no significant bivariate relationship between discrimination and cervical cancer screening (OR=1.26; 95% CI=0.69-2.29). Age was associated with screening, with women who have had screening being older than women who reported no screening (χ^2=12.59, p<0.01). Women who had more than a secondary education were three and a half times more likely to have been screened for cervical cancer than women with no education (OR=3.57; 95% CI=1.52-8.37). Women who lived in urban areas were nearly twice as likely to have been screened for cervical cancer than women in rural areas (OR=1.98; 95% CI=1.40-2.78). All ethnicities were more likely to screen for cervical cancer than women who identified as Bemba (χ^2=19.8, p<0.01). Women whose first sexual experience was at age 21 or older were more than twice as likely to have screened for cervical cancer than women whose first sexual encounter was at age 14 or younger (OR=2.13; 95% CI=1.12-4.06).

History of violence was not significantly associated with cervical cancer screening (χ^2=5.92, p>0.05), but the odds of women who reported sexual violence having screened for cervical cancer was half as likely as that of women who reported no violence (OR=0.56; 95% CI=0.33-0.93). The bivariate relationship between cervical cancer screening and report of currently taking ARVs was significant (F-value=5.86, p<0.001), but there was no

significance of the bivariate odds for women who reported currently taking ARVs (OR=4.89; 95% CI=0.46-52.59), nor those with missing responses (OR=2.61; 95% CI=0.23-29.76).

Table 4 includes the results of the final multivariate logistic regression model between cervical cancer screening and discrimination determined with p-value selection. The model identified by forward and backward selection methods was presented for comparison. Discrimination was not significantly associated with having a cervical cancer screening in either model (p-value selection: OR=1.20; 95% CI=0.62-2.31; forward and backward selection: OR=1.15; 95% CI=0.60-2.22). In the final model, the chance of having screened for cervical cancer increased with age (OR=1.03; 95% CI=1.02-1.05). Women with more than secondary education were three times more likely to have screened for cervical cancer than women withno education (OR=3.18; 95% CI=1.30-7.75). WLHIV who resided in urban areas were more than twice as likely to have screened for cervical cancer compared with WLHIV who lived in rural areas (OR=2.17; 95% CI=1.53-3.09). All ethnicities were significantly more likely to have screened for cervical cancer than women who identified as Bemba (Tonga: OR=2.02; 95% CI=1.26-3.24; Lozi: OR=3.21; 95% CI=1.85-5.60; Other: OR=1.61; 95% CI=1.11-2.34). Widowed WLHIV were 40% less likely to have screened for cervical cancer than married women (OR=0.60; 95% CI=0.38-0.95). Women who reported sexual violence were half as likely to screen for cervical cancer than women who reported no history of violence (OR=0.48; 95% CI=0.27-0.86), but reporting both physical and sexual violence was not significant (OR=0.72; 95% CI=0.31-1.66).

The model that included variables identified with forward and backward selection included the same variables with the addition of currently taking ARVs. Currently taking

ARVs was identified as a significant covariate using forward and backward selection, but when included in the model with discrimination, it was no longer significant.

A sensitivity analysis of the bivariate association between HIV-related discrimination and screening for cervical cancer within 12 months of the survey date found no significant association between the outcome and exposure (results not displayed).

DISCUSSION

This study adds to a white space in the discrimination literature, assessing whether perceived discrimination experienced in an HIV healthcare facility is predictive of cervical cancer screening among WLHIV. Contrary to our hypothesis, this study found that perceived discrimination is not significantly related to cervical cancer screening among WLHIV in Zambia. While perceived stigma is documented as a barrier to cervical cancer screening in sub-Saharan Africa, including in Zambia (Chidyaonga-Maseko et al., 2015; Lim and Ojo, 2016; Nyambe et al., 2018; White et al., 2012), discrimination originating within the HIV-care setting was not significant per this study. Our results aligned to those of two U.S.-based studies that found no significant relationship between perceived discrimination and cervical cancer screening among WLHIV (Bynum et al., 2016; Fletcher et al., 2013). Despite the hypothesis being unfounded, these results are encouraging for the approach PEPFAR is taking in partnership with the national government to scale up the integration of cervical cancer screening and treatment in existing HIV-platforms and is evidence that this approach should continue to be accelerated.

Although there was no significant association between perceived discrimination and cervical cancer screening in this study, and only 5.5% of Zambian WLHIV reported

experiencing HIV-related discrimination in the clinic, fear of, or experiences with, stigma and discrimination have recently been reported as a barrier to accessing health services, including HIV-related services, in Zambia (Qiao, 2018), particularly for key populations including sex workers (Chanda et al., 2017). Discrimination indicators in our study were within the parameters of HIV care providers in a clinic setting, whereas discrimination and stigma referenced in the literature originated from diverse sources, including communities, family members, and clinic settings. While fear of discrimination is documented as a barrier to initial care, once individuals enter regular care they may find that their fear is unrealized, which could be a reason for the lower rate of perceived discrimination in our study compared to existing literature. If HIV clinics are to be the healthcare system entry point for cervical cancer screening, continuing to prioritize nonjudgmental and differentiated services for HIV care should continue to be a priority, so WLHIV are also reached for cervical cancer screening.

In Zambia, 26.8% of WLHIV age 15 to 59 had screened for cervical cancer at the time of data collection. The data for this study was collected in 2016 when services were primarily only established at the provincial hospital level and would not have been reasonably available to every woman in the country (Chibwesha et al., 2017). Since the ZAMPHIA, the cervical cancer program in Zambia has expanded, and the opportunity for screening is available to more women, so this study's finding for the prevalence of cervical cancer screening among WLHIV in Zambia is likely outdated (Two New Cancer, 2019).

Although Zambia has had a national cervical cancer program since 2006, screening services have not been prioritized for WLHIV. After a retrospective review of the program

from 2007 to 2017, research suggested that WLHIV should be better prioritized in the national program moving forward (Matambo et al., 2018). PEPFAR support for cervical cancer screening and treatment of precancerous lesions also facilitates the prioritization of WLHIV (U.S. PEPFAR, 2019). Recognition of the need for prioritizing high-risk populations coupled with the directive of donors like PEPFAR is indicative of the direction in which Zambia's cervical cancer screening program is moving and suggests that the coverage of WLHIV who have screened for cervical cancer will rapidly increase in the coming years.

Among women who screened, 3.7% (n=11) said that their results were abnormal or suspect cancer. PEPFAR indicators suggest, however, that the positivity rate among WLHIV should be higher, between 5% to 28% (U.S. PEPFAR, 2018). The results of this study are not in-line with current literature showing higher screening positivity rates in WLHIV (Chibwesha et al., 2016; Dartell et al., 2014; Huchko et al., 2014). The reported lower positivity rates could be a limitation of the cross-sectional design of the study that relies on women's recollection of health services they have received and their results. Further, due to the existing stigma and myths around cervical cancer in Zambia, another explanation for this lower-than-expected positive screening rate could be reluctance on behalf of the women to disclose their results. Future studies could improve training of data collectors to ensure sensitivity around questions of cervical cancer. Future studies may also be able to build in document checks to confirm screening results and treatment outcomes. Women who screen for cervical cancer at a public facility in Zambia receive a client card that documents the date of their screening and the screening results as well as any follow-up care they received.

Of the 11 women who self-reported they screened positive, nine said that they had treatment. While this study had anticipated analyzing if perceived discrimination by healthcare workers due to HIV status was related to the treatment of cervical (pre)cancerous lesions among WLHIV who received a positive screen on their cervical cancer test, due to a small sample of women who screened positive, this aim was abandoned.

Our significant covariate results are largely comparable with existing research. Two studies in Kenya found that older women were more likely to screen for cervical cancer (Kangmennaang et al., 2018; Orong'o et al., 2016), and higher education was associated with screening in Kenya, Namibia, and Nigeria (Ezechi et al., 2013; Kangmennaang et al., 2015; Kangmennaang et al., 2018). Opposite of our findings, however, a study based in the U.S. found that lower levels of education were predictive of more frequent cervical cancer screening, compared to women who had completed university (Bynum et al., 2016).

Because most opportunities for screening in Zambia in 2016 were in urban areas, this may explain the significance of place of residence with cervical cancer screening, whereby women living in urban areas were twice as likely as women living in rural areas to have screened when controlling for other variables. This finding was also consistent with programs in other sub-Saharan African countries, including Kenya and Namibia (Kangmennaang et al., 2018; Tiruneh et al., 2017). Because the majority of Zambia's population resides in rural areas, the expansion of services in rural areas should be carefully considered and planned.

Ethnicity was also significantly associated with cervical cancer screening with all ethnicities included in the study being more likely to have completed cervical cancer

screening than Bemba, the largest ethnic group in Zambia. Additional exploration of the distribution of services among ethnicities, sociocultural influences specific to Bemba ethnicity related to cervical cancer screening, or other factors should be examined for deeper insight into this finding.

In bivariate analysis, relationship status was not significantly associated with cervical cancer screening but considered with other covariates, widowed women were less likely to have screened for cervical cancer. One potential reason could be that widowed women are less likely to seek sexual or reproductive health services, where cervical cancer services may be rendered. Kangmennaang and colleagues found that single Namibian women, although not necessarily widowed, were less likely to have been screened for cervical cancer (OR=0.63, p=0.01; Kangmennaang et al., 2015), but other studies conducted in sub-Saharan Africa found that marital status had no significant relationship with screening (Ezechi et al., 2013; Ndejjo et al., 2016; Orong'o et al., 2016).

Delgado and colleagues found no significant association between ARV use and cervical cancer screening among WLHIV in Peru (Delgado et al., 2016), but a study in Uganda found that being on ARVs was associated with women who received positive screens experiencing less time from diagnosis to treatment (Low et al., 2019). In our multivariate analysis, being on ARVs was not significantly associated with cervical cancer screening and better aligned with the outcomes of existing studies. Although in bivariate analysis, currently taking ARVs was associated with cervical cancer screening when analyzing the overall relationship between the two variables, there was no significant

relationship in the bivariate odds. This may be due to the small number of women who had screened for cervical cancer but reported not currently taking ARVs (n=2).

Women who delayed sex until at least age 21 were more likely to be screened for cervical cancer in this study when considering the bivariate relationship. While age of first sex was not found within existing literature as a predictor of cervical cancer screening, earlier age of first sex has been found to be associated with the development of cervical cancer (Louie et al., 2009). Furthermore, several studies have found that sexual autonomy is associated with cervical cancer screening or at least knowledge of screening (Kangmennaang et al., 2018; Tiruneh et al., 2017; Viens et al., 2016). When women have decision-making ability over their bodies and sexual relationships, including the ability to delay age of sexual debut, they are more likely also to have decision-making ability for the healthcare services they seek.

Related to sexual autonomy, women who experience sexual violence are less likely to seek healthcare services (Leddy et al., 2019; Oldenburg et al., 2018) and have poorer health outcomes (Mathur et al., 2018). In this study, women who reported a past experience with sexual violence were significantly less likely to complete cervical cancer screening. Women who reported both sexual and physical violence, however, were neither more or less likely to complete screening. This finding appears to be an anomaly in the data and is not in line with current research that would suggest any history of physical or sexual violence is negatively associated with cervical cancer screening (Viens et al., 2016; Leddy et al., 2019).

CONCLUSION

As a cross-sectional study, this analysis relied on client recall of cervical cancer services and may not provide accurate insight into cervical cancer screening coverage or screening results across the study population. Moreover, with a cross-sectional design, causality cannot be inferred. The misalignment of question timeframes was another limitation of this study. The survey items related to the exposure were within a time constraint, while the outcome was not. Because myths and stigma surrounding cervical cancer persist in Zambia, the items related to cervical cancer screening and treatment may have been perceived as sensitive, and respondents may have been hesitant to respond accurately. Further, the questions related to violence were only asked to a sub-set of the population, generating more than 30% missingness. Violence-related questions could have also been perceived as highly sensitive, and responses may not be accurate to women's experiences.

Despite the limitations of this study, there were notable strengths. This study used a nationally representative dataset, allowing for generalizability of results across the country of Zambia. With a large dataset, statistical analyses were robust. This study is confident of the HIV serostatus of women included in the sample as the PHIA included an on-site HIV test for survey respondents to confirm status rather than relying on participant disclosure. This study was further strengthened by the oversite provided by faculty at the University of Texas Health Science Center, Dallas campus.

As countries, including Zambia, prioritize the scale-up of national cervical cancer programs that are integrated into existing platforms such as HIV, this study is timely in understanding how the experience of WLHIV in the HIV clinic is related to cervical cancer

screening behavior. This study provides evidence for the rapid scale-up of cervical cancer screen and treatment programs within the HIV-platform in Zambia. Because this study suggests that experiences with HIV care are not a barrier to cervical cancer screening among WLHIV, integration of services can ensure more women are reached for screening. In reaction to the findings of this study, the scale-up of integrated services should ensure equitable opportunity for screening for women from both urban and rural areas, as well as across ethnicities.

To validate the coverage of WLHIV who have been screened for cervical cancer, national databases should be consulted, and future population-based surveys could consider repeating questions related to history with cervical cancer screening and treatment. Conducting a qualitative study to better understand the experience of WLHIV in HIV clinic settings, as well as how best to meet women's expectations with HIV and cervical cancer care, would strengthen the results of the cross-sectional quantitative analysis and provide further insight for consideration in the implementation and scale-up of integrated national cervical cancer control programs.

TABLES

Table 1: Characteristics of Women Living with HIV in Zambia (N=1182)

	n (weighted %)
Demographics	
Age (mean, SD)	37.0 (0.29)
Education	
No Education	68 (6.3%)
Primary	537 (44.6%)
Secondary	486 (41.2%)
More than secondary	91 (7.9%)
Residence	
Rural	450 (38.2%)
Urban	732 (61.8%)
Ethnicity	
Bemba	321 (27.0%)
Tonga	173 (15.0%)
Lozi	110 (9.9%)
Other	577 (48.1%)
Employed in Past 12 Months (yes)	355 (30.5%)
Religion	
Protestant	808 (67.9%)
Catholic	224 (19.2%)
Other	150 (13.0%)
Relationship Status	
Married or Living Together	646 (55.0%)
Divorced/Separated	200 (16.8%)
Widowed	205 (16.6%)
Never Married	127 (11.5%)
Confounders	
Number of Pregnancies (mean, SD)	4.2 (0.8)
Age at First Sex	
14 or under	126 (11.3%)
15 to 20	811 (74.2%)
21 or older	160 (14.5%)
History of Violence	
No History	561 (46.7%)
Physical	55 (4.7%)
Sexual	112 (9.5%)
Physical and Sexual	43 (3.8%)
Missing	411 (35.4%)
Lifetime Number of Sex Partners	
0 or 1	283 (25.8%)
2 or 3	542 (49.7%)
4 or more	269 (24.5%)

Table 1 (cont.): Characteristics of Women Living with HIV in Zambia (N=1182)

History of Selling Sex	
Yes	48 (4.3%)
No	1010 (84.8%)
Missing	124 (10.9%)
Currently taking ARVs	
Yes	1012 (84.7%)
No	23 (2.0%)
Missing	147 (13.3%)
Main variables	
Outcome Variables	
Cervical Cancer Screening	
Yes	311 (26.8%)
No	866 (73.2%)
Cervical Cancer Screening within 12 months of survey (n=311)	
Yes	128 (40.4%)
No	124 (40.1%)
Missing	59 (19.5%)
Result of Cervical Cancer Screening (n=311)	
Normal/Negative	290 (95.4%)
Abnormal or Suspect Cancer	11 (3.7%)
Unclear/Inconclusive	3 (0.9%)
Cervical (Pre) Cancer Treatment (n=11)	
Yes	9 (81.0%)
No	2 (19.0%)
Exposure Variables	
Experienced HIV-related Discrimination	
Yes	69 (5.5%)
No	1096 (94.5%)

Table 2: Bivariate odds of women living with HIV having been screened for cervical cancer by demographics and experience with healthcare workers

	Screened for Cervical Cancer Odds Ratio (95% CI)
Demographics	
Age	1.02 (1.01 – 1.04)**
Education	
No Education	Ref
Primary	1.26 (0.64 – 2.49)
Secondary	1.65 (0.83 – 3.30)
More than secondary	3.57 (1.52 – 8.37)**
Residence	
Rural	Ref
Urban	1.98 (1.40 – 2.78)***
Ethnicity	
Bemba	Ref
Tonga	1.60 (1.02 – 2.49)*
Lozi	2.79 (1.62 – 4.79)**
Other	1.43 (1.00 – 2.06)*
Employed in Past 12 Months (yes)	1.36 (0.99 – 1.87)
Religion	
Protestant	Ref
Catholic	1.01 (0.72 – 1.42)
Other	1.11 (0.74 – 1.67)
Relationship Status	
Married or Living Together	Ref
Divorced/Separated	1.10 (0.76 – 1.59)
Widowed	0.82 (0.55 – 1.22)
Never Married	0.70 (0.44 – 1.10)
Confounders	
Number of Pregnancies	1.00 (0.94 – 1.06)
Age at First Sex	
14 or under	Ref
15 to 20	1.51 (0.88 – 2.57)
21 or older	2.13 (1.12 – 4.06)*

Table 2 (cont.): Bivariate odds of women living with HIV having been screened for cervical cancer by demographics and experience with healthcare workers

History of Violence	
None	Ref
Physical	1.00 (0.51 – 1.98)
Sexual	0.56 (0.33 – 0.93)*
Physical and Sexual	0.94 (0.42 – 2.11)
Missing	1.06 (0.77 – 1.47)
Lifetime Number of Sex Partners	
0 or 1	Ref
2 or 3	0.91 (0.63 – 1.30)
4 or more	0.98 (0.63 – 1.52)
History of Selling Sex	0.96 (0.43 – 2.16)
No	Ref
Yes	0.96 (0.43 – 2.16)
Missing	1.01 (0.62 – 1.64)
Currently taking ARVs	
No	Ref
Yes	4.89 (0.46 – 52.29)
Missing	2.61 (0.23 – 29.76)
Exposure Variables	
Experienced HIV-related Discrimination (yes)	1.26 (0.69 – 2.29)

*p-value<0.5
**p-value<0.01
***p-value<0.001
CI = Confidence Interval

Table 3: Bivariate relationship between women receiving cervical cancer screening and covariates

	Has been screened for cervical cancer (n=866) n (weighted %)	Has not been screened for cervical cancer (n=311) n (weighted %)	χ^2 or F	Total Sample (n=1,177)
Demographics				
Age (mean, SD)	38.5 (0.47)	36.39 (0.35)	12.59**	1177
Education			23.78***	
No Education	13 (19.3%)	55 (80.8%)		68
Primary	121 (23.0%)	412 (77.0%)		533
Secondary	136 (28.2%)	350 (71.8%)		486
More than secondary	41 (46.0%)	49 (54.0%)		90
Residence			22.73***	
Rural	85 (19.0%)	364 (81.0%)		449
Urban	226 (31.6%)	502 (68.4%)		728
Ethnicity			19.8**	
Bemba	65 (20.3%)	255 (79.7%)		320
Tonga	49 (29.0%)	122 (71.0%)		171
Lozi	46 (41.6%)	62 (58.4%)		108
Other	151 (26.8%)	426 (73.2%)		250
Employed in Past 12 Months			4.88	
Yes	108 (31.1%)	246 (68.9%)		354
No	203 (24.9%)	619 (75.1%)		822
Religion			0.31	
Protestant	209 (26.5%)	595 (73.6%)		804
Catholic	58 (26.6%)	165 (73.4%)		223
Other	44 (28.6%)	106 (71.4%)		150
Relationship Status			4.27	
Married or Living Together	177 (27.8%)	464 (72.2%)		641
Divorced/Separated	59 (29.7%)	141 (70.3%)		200
Widowed	47 (23.9%)	158 (76.1%)		205
Never Married	26 (21.1%)	101 (78.9%)		127

Table 3 (cont.): Bivariate relationship between women receiving cervical cancer screening and covariates

	Has been screened for cervical cancer (n=866) n (weighted %)	Has not been screened for cervical cancer (n=311) n (weighted %)	χ^2 or F	Total Sample (n=1,177)
Confounders				
Number of Pregnancies (mean, SD)	4.19 (0.14)	4.19 (0.10)	0.00	1177
Age at First Sex			7.60*	
14 or under	25 (19.6%)	101 (80.4%)		126
15 to 20	214 (26.8%)	594 (73.2%)		808
21 or older	54 (34.2%)	105 (65.8%)		159
History of Violence			5.92	
No History	147 (27.3%)	413 (72.7%)		560
Physical	16 (27.4%)	39 (72.6%)		55
Sexual	21 (17.3%)	91 (82.7%)		112
Physical and Sexual	11 (26.1%)	32 (73.9%)		43
Missing	116 (28.5%)	291 (71.5%)		407
Lifetime Number of Sex Partners			0.43	
0 or 1	78 (28.0%)	205 (72.0%)		283
2 or 3	139 (26.0%)	401 (74.0%)		540
4 or more	73 (27.5%)	194 (72.5%)		267
History of Selling Sex (yes)			0.02	
Yes	11 (26.0%)	37 (74.0%)		48
No	268 (26.8%)	738 (73.2%)		1006
Missing	32 (26.9%)	91 (73.1%)		123
Currently taking ARVs (yes)			5.86**	
Yes	284 (28.6%)	724 (71.4%)		1008
No	2 (7.6%)	21 (92.4%)		23
Missing	25 (17.7%)	121 (82.3%)		146
Exposure Variables				
Experienced HIV-related Discrimination			0.67	
Yes	20 (31.1%)	48 (68.9%)		68
No	286 (26.5%)	806 (73.5%)		1092

*p-value<0.5
**p-value<0.01
***p-value<0.001

Table 4: Multivariate logistic regression models predicting cervical cancer screening

	Final Model (P-Value Selection) Odds Ratio (95% CI) (n=1,155)	**Comparison Model (Forward and Backward Selection)** Odds Ratio (95% CI) (n=1,155)
Study Variables		
Experienced HIV-related Discrimination	1.20 (0.63 – 2.31)	1.15 (0.60 – 2.22)
Control Variables		
Age	1.03 (1.02 – 1.05)**	1.03 (1.01 – 1.05)**
Education		
No Education	Ref	Ref
Primary	1.13 (0.54 – 2.37)	1.07 (0.52 – 2.23)
Secondary	1.44 (0.69 – 3.02)	1.37 (0.65 – 2.88)
More than secondary	3.18 (1.30 – 7.75)*	3.09 (1.26 – 7.60)*
Residence		
Rural	Ref	Ref
Urban	2.17 (1.53 – 3.09)***	2.19 (1.53 – 3.13)***
Ethnicity		
Bemba	Ref	Ref
Tonga	2.02 (1.26 – 3.24)**	1.97 (1.22 – 3.19)**
Lozi	3.21 (1.85 – 5.60)***	3.16 (1.79 – 5.58)***
Other	1.61 (1.11 – 2.34)*	1.62 (1.12 – 2.36)*
Relationship Status		
Married or Living Together	Ref	Ref
Divorced/Separated	1.00 (0.68 – 1.47)	1.01 (0.68 – 1.48)
Widowed	0.60 (0.38 – 0.95)*	0.62 (0.39 – 0.99)*
Never Married	0.65 (0.40 – 1.06)	0.65 (0.40 – 1.06)
Confounders		
History of Violence		
No History	Ref	Ref
Physical	0.84 (0.38 – 1.89)	0.89 (0.40 – 2.00)
Sexual	0.48 (0.27 – 0.86)*	0.48 (0.27 – 0.85)*
Physical and Sexual	0.72 (0.31 – 1.66)	0.80 (0.33 – 1.97)
Missing	0.95 (0.67 – 1.35)	0.95 (0.66 – 1.36)
Currently taking ARVs		
No	--	Ref
Yes	--	4.36 (0.47 – 40.04)
Missing	--	2.52 (0.26 – 25.10)
Intercept		
AIC	1277.49	1272.30
F-value	2.20	1.95

*p-value<0.5 **p-value<0.01 ***p-value<0.001 CI = Confidence Interval

APPENDICES

Appendix A: Letter of IRB Exemption

UTHealth
The University of Texas
Health Science Center at Houston

Committee for the Protection of Human Subjects
6410 Fannin Street, Suite 1100
Houston, Texas 77030

Crystal Cazier
School of Public Health

August 26, 2019

HSC-SPH-19-0700 - *HIV-related discrimination and cervical cancer screening in Zambia*

The above named project is determined to qualify for exempt status according to 45 CFR 46.101(b)

CATEGORY #4 *: Research, involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified directly or through identifiers linked to the subjects.*

CHANGES: Should you choose to make any changes to the protocol that would involve the inclusion of human subjects or identified data from humans, please submit the change via iRIS to the Committee for the Protection of Human Subjects for review.

INFORMED CONSENT DETERMINATION:

Waiver of Consent Granted

INFORMED CONSENT: When Informed consent is required, it must be obtained by the PI or designee(s), using the format and procedures approved by the CPHS. The PI is responsible to instruct the designee in the methods approved by the CPHS for the consent process. The individual obtaining informed consent must also sign the consent document. Please note that only copies of the stamped approved informed consent form can be used when obtaining consent.

HEALTH INSURANCE PORTABILITY and ACCOUNTABILITY ACT (HIPAA):

Exempt from HIPAA

STUDY CLOSURES: Upon completion of your project, submission of a study closure report is required. The study closure report should be submitted once all data has been collected and analyzed.

Should you have any questions, please contact the Office of Research Support Committees at 713-500-7943.

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