

# Frequency of Cervical Cancer and Breast Cancer Screening in HIV-Infected Women in a County-Based HIV Clinic in the Western United States

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## Abstract

**Background:** Women's primary-care services are frequently dispensed to HIV-infected women through HIV specialty clinics. Our objective was to evaluate cervical cancer and breast cancer screening practices in a county-based HIV clinic in San Mateo, California.

**Methods:** This was a retrospective cohort study of medical records of HIV-infected women obtaining HIV care at this site.

**Results:** Between January 1, 2002 and December 31, 2006, 69 women were documented to have at least 12 months of medical care at the clinic. Median followup time was 51 months. Over 253 person-years of followup, there were 656 pap smears performed per 1,000 person-years; 77.9% of women had at least one Pap smear during the study time period. A total of 59.5% (47/79) of normal pap smears had a followup pap smear within 18 months; 62.0% of abnormal pap smears had a followup pap smear within 12 months. A CD4 count of less than 200 cells/mm<sup>3</sup> was associated with not receiving a pap smear in multivariable analysis. Mammogram screening was performed on 64.7% of women aged 40 or older.

**Conclusions:** Based on the results of this study, the majority of HIV-infected women at this clinic received cervical and breast cancer screening at some point during their care. Only two-thirds of abnormal pap smear results had followup pap smear screening within a year. With the increased risk of cervical cancer in HIV-infected women, efforts should be made to promote cervical cancer screening, particularly in high-risk women.

## Introduction

HIV-INFECTED WOMEN are 5 times more likely to develop cervical dysplasia compared to HIV-negative women<sup>1-3</sup> and are at higher risk for invasive cervical cancer.<sup>4,5</sup> This association between HIV infection and cervical dysplasia is thought to be secondary to co-infection with human papilloma virus (HPV) in the face of immunosuppression.<sup>2,3,5-7</sup> Because of this increased risk, it is recommended that HIV-infected women should receive semiannual screening with Papanicolaou (Pap) smears in the first year of HIV-diagnosis. If these are normal, annual screening is recommended. Based on the 2006 American Society of Colposcopy and Cervical Pathology (ASCCP) guidelines, further diagnostic testing and

screening for HIV-infected women with abnormal pap smears is the same as HIV-negative women.<sup>8-10</sup> Previous studies of HIV-infected women report pap smear uptake of 59-88%.<sup>11-14</sup>

As women survive longer with HIV, other comorbid conditions will increase with age, including breast cancer.<sup>15</sup> In the United States, all women are recommended to undergo baseline mammogram screening at age 40.<sup>16,17</sup> Recommendations for screening are no different for HIV-positive women. Previous studies of HIV-infected women report mammogram uptake at 31-67%.<sup>13,14,18</sup>

Little information is available as to how well HIV primary-care clinics perform cervical cancer and breast cancer screening over an extended period of time. This study will review the frequency of pap smears and mammograms in

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HIV-infected women receiving care in an HIV primary-care clinic in order to assess the adequacy of provision of primary care to women in this setting.

## Materials and Methods

This was a retrospective cohort study of medical records of HIV-infected women obtaining primary care from the San Mateo County Medical Center, San Mateo, California. This is a public health care clinic, geographically proximal to San Francisco, California. Care providers include infectious disease specialists, general practitioners, and a physician's assistant. The referral gynecology practice is in a separate clinic within the same medical center. The following data were obtained from the HIV database and electronic medical record system: demographic information, antiretroviral therapy use, lowest CD4 count per year, pap smear results, and mammogram results in women age 40 years or more. Lack of followup was designated if there was no followup within 12 months of an abnormal pap smear, since recommended followup during the study time period was approximately 6 months; a followup interval of 18 months was chosen for normal pap smears, since the recommended followup was 12 months. These followup parameters were based on recommendations from the 2001 American Society of Colposcopy and Cervical Pathology<sup>19</sup>; since the study time period, new guidelines were published in 2006.<sup>8</sup> Data regarding diagnostic and therapeutic procedures such as colposcopy and cervical conization were not collected because of documentation issues. HPV screening was not routinely performed at the facility during the study time period.

Chi-square analysis, with receipt of pap smears and mammograms as the outcome, was performed. In addition, two multivariable logistic regression models, with receipt of pap smears as one outcome and receipt of mammograms as a second outcome, were created. Because of small cell sizes, exact logistic regression was used for mammograms as an outcome. For both models, the predictors were age, race, primary language, AIDS-related virus (ARV) use during the study time period, and having had a CD4 count below 200 cell/mm<sup>3</sup>. The *p* value for significance was set at *p* < 0.05. All analyses were performed in SAS 9.1 (SAS Institute, Cary, North Carolina). This study was conducted after Ethical Review Committee approval of the Mills-Peninsula Health Services and Research Compliance Office of Stanford University Medical Center.

## Results

### Demographic characteristics of the women

Between January 1, 2002 and December 31, 2006, 125 women received medical care at the clinic. Of those, 69 (55.2%) women were documented to have at least 12 months of medical care at the site during the observational period. This was determined by having at least 12 months between the first documented visit and the last. Fifty-eight percent (40/69) of women had already initiated care at the clinic prior to 2002.

The median age of women at documented first visit was 42.0 years (mean 40.8, SD 9.4). By the end of the study, 73.9% (51) of these women were age 40 or older and, therefore, eligible for at least one mammogram. The largest racial/ethnic group represented in this sample was black women (29

women, 42.6%), followed by Hispanic women (19, 27.9%), and white women (17, 25.0%). The primary language of 48 (70.6%) of the women was English (Table 1).

### Clinical characteristics: HIV care

The median length of followup for women in this cohort was 51.0 months (mean = 43.9, SD = 15.3). Thirty-four of the women (49.3%) had at least one CD4 count below 200 during the time period. The majority of the women (63, 91.3%) were on ARVs at some point during the followup, and 46 (66.7%) were taking antiretroviral medications (ARVs) during all the years that they received care in the clinic.

### Clinical characteristics: pap smears

Fifty-three (77.9%) women had at least one pap smear during the study time period. Overall, there were 166 total pap procedures performed over 252.9 person-years of time, for a rate of 656 pap smears per 1,000 person-years. Of these 166 pap smears, 148 had a record of the type of provider that performed them. Specifically, 68 (45.9%) were performed by primary-care physicians, and 80 (54.1%) were performed by gynecologists. One hundred-eleven (66.9%) of the 166 pap smears were normal. Of these, 84 occurred between 2002 and 2005, allowing for analysis of followup during the study interval. After excluding 5 women whose followup could have been outside the study time period, 59.5% (47/79) of the women with normal pap smears had a followup pap smear within 18 months.

Twenty-three (33.3%) women had one or more abnormal pap smears, with a total of 55 abnormal pap smears among the 23 women. Twenty-eight out of 55 (50.9%) of these pap smears were composed of atypical squamous cells of undetermined significance (ASCUS), 20 (36.4%) were low-grade squamous intraepithelial lesions (LSIL), 6 (10.9%) were high-grade squamous intraepithelial lesions (HSIL), and 1 (1.8%) was composed of atypical glandular cells of undermined significance (AGUS). Of the 55 abnormal pap smears, 50 occurred between 2002 and 2005, allowing for analysis of followup during the study interval; only 62.0% of those with abnormal pap smears had followup pap smears within 12 months.

TABLE 1. DEMOGRAPHIC CHARACTERISTICS OF WOMEN RECEIVING CARE AT CLINIC SITE

Characteristic	Percentage
Age at first visit	
18–39	39.1 (27)
40–49	43.5 (30)
≥50	17.4 (12)
Race/Ethnicity	
Black	42.6 (29)
Hispanic	27.9 (19)
White	25.0 (17)
Other <sup>a</sup>	4.4 (3)
Primary Language <sup>b</sup>	
English	70.6 (48)
Spanish	26.5 (18)

<sup>a</sup>Other racial groups represented were native American (2.9%, *n* = 2), Asian (1.5%, *n* = 1).

<sup>b</sup>2.9% (2) of women's primary language was Portuguese.

Having had a CD4 count of less than 200 cell/mm<sup>3</sup> during the study period was associated with not having a pap smear in bivariate analysis. Twenty-two out of 33 (66.7%) women with a CD4 count of less than 200 cell/mm<sup>3</sup> had a pap smear during the years that they were enrolled in care at the clinic, whereas 31/35 (88.6%) of women who did not have low CD4 counts had a pap smear ( $p = 0.03$ ). This association persisted in multivariate analysis (OR = 4.3, 95% CI 1.1–16.9,  $p = 0.04$ ). None of the other predictor variables (age, race, primary language, ARV use) were significantly associated with receipt of pap smears or having had an abnormal pap smear, in bivariate or multivariable analysis; a CD4 count less than 200 cell/mm<sup>3</sup> was not associated with an abnormal pap smear.

#### *Clinical characteristics: mammograms*

A percentage of 64.7% (33) of women age 40 or older had at least one mammogram during the study period. All mammogram results were normal. In bivariate analysis, race and the primary language spoken were associated with lack of mammograms, whereas age, a CD4 count less than 200, and marital status were not. Specifically, 100% (10) of Latinas over 40 had mammograms (this group is the reference group for the rest of the comparisons), while approximately 64% (16) of black women ( $p = 0.036$ ), 50% (6) of white women ( $p = 0.015$ ), and 0% (2) of Native Americans ( $p = 0.015$ ) had mammograms. In addition, primary the language was important, with 100% of women who spoke primarily Spanish receiving mammograms, but only 58% of primarily English-speakers receiving mammograms. The association between race and mammograms did not persist in an exact logistic regression model adjusting for ARV use, age, and CD4 count. The association between language and mammograms did, however, remain in a separate model (again, race and language could not be modeled together because of being tightly correlated), with English-speaking women less likely to have received a mammogram (exact OR = 0.09, 95% CIs: 0–0.69).

#### **Discussion**

This retrospective cohort study demonstrated that approximately 80% of women receiving care at an HIV primary-care clinic between 2000 and 2006 received pap smears, and 65% of women greater than age 40 years underwent mammogram screening. All of the women with one year or more of care in the clinic during the study's 5-year time interval are represented here, producing 253 person-years of data. This is the first study we know of to document followup frequencies for HIV-infected women with both normal and abnormal pap smears. Followup frequencies for both abnormal and normal pap smears were similar, despite the increased risk of cervical dysplasia in HIV-infected women with pap-smear abnormalities.

Findings from this study indicate that the pap smear and mammogram screening rates for HIV-infected women in this region of the United States are consistent with other regions of the U.S.<sup>11,12,18</sup> The notable finding in this study was the lack of followup of both normal and abnormal pap smears. Prior research indicates that women with a gynecologist and primary-care physician at the same clinical site were more likely to receive pap smears, and that outside referral led to diminished numbers of women screened.<sup>11,13</sup> In our study,

since management of an abnormal pap smear was referred outside the study clinic, the need for referral may also explain why only 62% of women with abnormal pap smear results in our study had followup pap smears in a timely fashion.

Other notable findings were the association of a low CD4 count with not receiving a pap smear, and the higher numbers of Hispanic and black women undergoing mammogram screening compared to white women. These findings contrast with previously reported literature.<sup>13,18</sup> These differences may be related to our small sample size, regional practice, or population differences. In addition, insurance data was not collected among the cohort. Though pap-smear uptake would not be affected by this issue, it could potentially affect radiologic procedures such as mammograms. Lack of insurance could account for access to mammograms rather than racial differences in referrals or uptake.

This study is limited because of its retrospective nature. Data was based on electronic medical documentation and, therefore, would not contain records of care from outside facilities. As a county-based clinic, however, all medical records from county-based clinics were included in the electronic medical record. Our study had a smaller number of women represented than previously published studies, which limits its generalizability. This study had an extended followup period, however, and was based on documented pap smear or mammogram results, as opposed to the much larger studies which were based on survey responses and could have been affected by recall bias, social desirability, or confusion as to whether a pelvic examination was a pap smear. Additionally, appropriate statistical analysis was used to account for small cell sizes.

Data were not collected regarding diagnostic and therapeutic procedures after abnormal pap smears in this study, which would have indicated appropriate management of the abnormal pap smear. Nonetheless, even if women underwent treatment procedures such as cryotherapy or conization after an abnormal pap smear, it would be expected that followup pap-smear screening would still occur. The Women's Interagency HIV Study (WIHS) cohort recently reported that treatment failure and recurrence was common in HIV-infected women after treatment procedures for documented cervical dysplasia.<sup>20</sup> However, it is important to acknowledge that screening recommendations have changed since the time of the study and that many of the ASCUS pap smears would not have required such close followup if the study was done today.

#### **Conclusions**

Based on the results of this study, HIV-infected women in this type of clinical setting in the western United States receive cervical and breast cancer screening comparable to other communities. Though pap-smear screening recommendations have changed since the study time period, this study ultimately tracks the delivery of reproductive health-related primary-care screening for women in an HIV primary-care clinic over a 5-year time period. The study shows that high numbers of minority women were getting appropriate preventative health screening. However, there was not consistent followup of pap-smear screening. Given the higher risks of cervical dysplasia associated with HIV infection, efforts should be made to promote consistent cervical cancer

screening, particularly in high-risk women with documented abnormal pap smears. Further research into “see and treat” approaches to management of high-risk pap smears, incorporation of gynecologic services into HIV primary clinics, triage of pap smears through high-risk HPV testing, or testing for E6/E7 oncogenes should be considered in future HIV clinical research and care.

#### Disclaimer

The authors have no conflicts of interest to report.

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