

Comparison of Patient- and Clinician-Collected Anal Cytology Samples to Screen for Human Papillomavirus–Associated Anal Intraepithelial Neoplasia in Men Who Have Sex with Men

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Background: Human papillomavirus (HPV)–associated anal cancer is increasing in prevalence and is more common among men who have sex with men and HIV-positive individuals than cervical cancer is among women in the United States. Cytology screening can detect the anal cancer precursor, anal intraepithelial neoplasia (AIN). Little is known about self-collected samples for AIN screening, and few community-based AIN estimates exist.

Objective: To compare the sensitivity of self-collected versus clinician-collected anal cytology specimens to detect biopsy-confirmed AIN and the prevalence estimate of AIN in a community sample.

Design: Cross-sectional study. Participants were mailed anal cytology self-collection kits with instructions. Clinicians repeated anal cytology and performed high-resolution anoscopy with biopsies as the diagnostic reference standard.

Setting: San Francisco, California.

Patients: Community-based sample of men who have sex with men.

Measurements: Prevalence of anal HPV and AIN. Sensitivity and specificity of self-collected and clinician-collected anal cytology specimens to diagnose AIN were calculated.

Results: Biopsy-proven AIN was diagnosed in 57% of HIV-positive and 35% of HIV-negative participants ($P = 0.04$), and 80% provided adequate self-collected specimens for interpretation. The sensitivity of cytology to detect AIN in HIV-positive men was 75% (95% CI, 51% to 93%) when self-collected and 90% (CI, 68% to 99%) when clinician-collected; respective values in HIV-negative

men were 48% (CI, 26% to 70%) and 62% (CI, 38% to 82%). The specificity of cytology to detect AIN in HIV-positive men was 50% (CI, 22% to 78%) when self-collected and 64% (CI, 36% to 86%) when clinician-collected; respective values in HIV-negative men were 86% (CI, 71% to 94%) and 85% (CI, 72% to 93%).

Limitations: The study sample was from a narrowly defined geographical area. Participants self-reported HIV status.

Conclusion: In a community-based sample, a high proportion of HIV-positive and HIV-negative men who have sex with men have AIN. The sensitivity of cytology to detect AIN is higher for clinician-collected versus self-collected specimens and for HIV-positive versus HIV-negative men. The specificity of cytology to detect AIN is higher in HIV-negative versus HIV-positive men. However, the probability of AIN in a patient with a negative cytology result may not be low enough (23% for HIV-negative men and 45% for HIV-positive men with a patient-collected specimen) for clinicians to be comfortable recommending no anoscopy for those with a negative cytology result if done as a one-time test. These data raise the question of whether the optimal population screening strategy is cytology screening with anoscopy only for those who test positive or whether anoscopy should be recommended for everyone in these risk groups. Given limited resources and the limited number of clinicians trained in anoscopy, cytology screening may be the best current approach to identifying disease in the at-risk population.

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Anal cancer incidence is increasing in men and women worldwide (1). Such subpopulations as men who have sex with men, HIV-positive men and women, transplant recipients, and women with cervical intraepithelial neoplasia have a higher risk for anal cancer than the general population. Men who have sex with men have a 44% greater risk for anal cancer than the general population (2). The risk for anal cancer is at least twice as great for HIV-

positive men who have sex with men than for HIV-negative men who have sex with men (3).

Anal cancer, similar to cervical cancer, is potentially preventable. Anal cytology has been systematically studied among men who have sex with men as a screening test to detect anal intraepithelial neoplasia (AIN). Soost and colleagues (4) and Palefsky and colleagues (5) demonstrated that anal cytology was similar to cervical cytology for detection of biopsy-proven AIN using high-resolution anoscopy. However, several barriers to instituting anal cytology screening in targeted populations remain: An infrastructure for training clinicians to identify and treat AIN is needed (6), health care providers may feel uncomfortable and unprepared to discuss anal cytology screening, and patients may feel embarrassed to discuss this topic and fear an uncomfortable and awkward screening examination.

Self-collection of anal cytology specimens may address some of these concerns. Self-administered screening has been studied in vaginal and vulvar sampling for HPV test-

See also:

Print

Editors' Notes 301
Summary for Patients 1-38

Web-Only

Conversion of graphics into slides

ing and found to be more acceptable than clinician sampling (7). The anal canal is easier to sample in a blinded manner than the cervix, and both patients and providers are capable of obtaining good specimens for cytology. One study of 102 men who have sex with men who were enrolled in the Anal Neoplasia Study in San Francisco (8) demonstrated that self-collected anal samples had similar sensitivity to clinician-obtained anal cytology samples. Another study (9), of men enrolled in an HIV epidemiology study in Vancouver, demonstrated moderate agreement between self- and clinician-collected anal cytology samples in a sample of young men who have sex with men.

These studies had several limitations. Cranston and colleagues' study (8) was conducted in men already enrolled in a well-established cohort of AIN who were accustomed to routine anal cytology tests and high-resolution anoscopy, which limited generalizability. In Lampinen and colleagues' study (9), the gold-standard test was not performed on all participants—only patients with abnormal anal cytology results were referred to high-resolution anoscopy for biopsy confirmation of disease.

We conducted this study to obtain community-based estimates of the prevalence of anal HPV and biopsy-confirmed anal precancer lesions, and to determine whether men in the community who have sex with men and have limited or no experience with cytology testing would be able to provide adequate specimens for anal cancer screening, according to a gold standard of biopsy-proven AIN.

METHODS

Study Population

We performed this study with the approval of the University of California, San Francisco, Committee on Human Research. We obtained informed consent from all participants. We drew our sample from participants in the 2002 Urban Men's Health Study (UMHS 2002), a household probability sample of adult men who have sex with men that was obtained by using random-digit dial sampling. The sampling methodology used in UMHS 2002 is published elsewhere (10). In brief, by using the same methodology as in UMHS 1997 (11), we performed sampling between May 2002 and January 2003 in telephone exchanges covering 13 ZIP codes in the San Francisco area where 87% of men who have sex with men are estimated to reside (12). Adult men (age ≥ 18 years) who reported same-sex behavior since age 14 years or who identified as homosexual or bisexual were eligible for the study, an approach that has been shown to identify more men who are not openly homosexual (11). If a household had more than 1 eligible man, 1 was randomly selected for an interview. The interview was offered in both English and Spanish. Between January and November 2004, we randomly selected 126 of 879 men in UMHS 2002 who have sex with men, contacted them by telephone or mail, and received their consent to participate in this study.

Context

Anal carcinoma is increasingly common among men who have sex with men, but data on the effectiveness of cytology screening are lacking.

Contribution

This study evaluated self-collected (that is, by the patient) and physician-collected cytology samples with high-resolution anoscopy in 126 men who have sex with men. Self-collected specimens were feasible. However, the probability of anal intraepithelial neoplasia in a patient with a negative cytology result was substantial: 45% and 23% of HIV-positive and HIV-negative men, respectively, with self-collected samples.

Implication

Self-collected samples could increase the appeal of screening, but the predictive value of negative cytology, even on physician-collected samples, may not be good enough to support using cytology instead of immediate anoscopy to screen high-risk patients.

—The Editors

Measurements

Participants provided demographic information, including age, race or ethnicity, income, and employment status, during the initial UMHS interview. Participants also reported same-sex sexual activity in the previous 12 months and type and frequency of recreational drug use in the past 6 months. Participants reported the month and year of their first and most recent HIV antibody test at UMHS enrollment; we asked about their HIV serostatus again during this study. Studies have demonstrated that self-reported HIV status by men who have sex with men is very accurate (13, 14).

Anal Cytology Sample Collection and Evaluation

According to a protocol already developed and used for self-collection of anal cytology (8), we mailed each participant a self-collection anal cytology kit with a 1-page instruction sheet and made an appointment for each participant to be seen by a study clinician. We asked participants to obtain self-collected specimens no earlier than 1 or 2 days before their scheduled clinic appointment. Participants collected anal specimens at home by rotating a water-moistened Dacron swab (Baxter Healthcare, McGraw Park, Illinois) in the anal canal without direct visualization. The swab was then agitated vigorously in a methanol-based fixative (PreservCyt; CYTYC, Boxborough, Massachusetts) for the preparation and interpretation of slides for cytology and for HPV DNA testing by using polymerase chain reaction. Participants personally returned their self-collected specimens to the University of California, San Francisco, General Clinical Research Center outpatient clinic at the time of their scheduled appointment. Clinicians experienced in high-resolution anoscopy evaluated all partici-

Table 1. Patient Characteristics

Characteristic	Value
Median age (IQR), y	44 (24–73)
College degree, n (%)	84 (67)
Annual income >\$40 000, n (%)	79 (63)
Race, n (%)	
Asian	6 (5)
African American	4 (3)
Native American	3 (2)
White	110 (87)
Mixed	4 (3)
Ethnicity, n (%)	
Latino	10 (8)
Non-Latino	116 (92)
Median male sexual partners (IQR), n*	5 (2–20)
Anal sex, n (%)*	91 (72)
Always used condoms, n (%)*	50 (40)
Sildenafil use, n (%)†	39 (31)
Methamphetamine use, n (%)†	18 (14)
Previously screened for anal intraepithelial neoplasia, n (%)	9 (7)
Previous anal cytologic abnormality, n (%)	5 (4)
HIV-positive, n (%)	38 (30)

IQR = interquartile range.

* Previous 12 months.

† Previous 6 months.

pants. Trained providers repeated anal cytology sampling in each man by using the methods described and then performed high-resolution anoscopy.

Anal cytology was evaluated by a pathologist who had no knowledge of the clinical status of the participants, including HIV status, questionnaire responses, or other test results. The study pathologist also did not know whether a particular specimen was self-collected or clinician-collected. Anal cytology specimens were classified as adequate (sufficient nucleated squamous epithelial cells present) or inadequate for evaluation. If adequate, specimens were classified as normal, atypical squamous cells (comprising both atypical squamous cells of undetermined significance and atypical squamous cells—cannot exclude high-grade squamous intraepithelial lesions), low-grade squamous intraepithelial lesions, or high-grade squamous intraepithelial lesions by using the Bethesda criteria for evaluating cervical cytology. We defined abnormal anal cytology as any cytologic finding other than normal.

Anal HPV Testing

To prepare DNA from the anal specimen, we swirled the PreservCyt solution to suspend the cells and then removed 1.5 mL of the solution to a labeled microfuge tube with a transfer pipette and spun the tube at 16 g for 15 minutes.

We decanted the tubes and dried them overnight or in a 65 °C hot block for 1 hour. We suspended the pellets in 100 μ L of Sample Transport Medium (Digene, Silver Spring, MD), and 200 μ g/mL of proteinase K. We vortexed the samples, digested them in a waterbath at 56 °C for 1 hour, heated them at 95 °C for 10 minutes to inactivate proteinase K, and froze them until use. We per-

formed polymerase chain reaction amplification on 5 μ L of each sample according to a standard 40-cycle protocol to detect the presence of 1 or more HPV types by using a generic probe set. We also typed polymerase chain reaction products from samples that had a positive result with the generic probe set by dot-blot hybridization using 29 individual type-specific probes and 10 individual HPV types combined into 1 probe set. We classified HPV infection as high-risk (types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, or 73) or low-risk (types 6, 11, 53, 54, 55, 66, Pap 155, or Pap 291) on the basis of the strength of association of specific HPV types with invasive anogenital cancer (15).

High-Resolution Anoscopy and Histopathologic Evaluation

Clinicians conducted a thorough anal examination of each participant. Men had high-resolution anoscopy as described elsewhere (16) with application of a 3% acetic acid solution to aid in the visualization of lesions. Study clinicians performed biopsy in participants if a lesion was present. We fixed biopsy specimens in 10% formalin for routine histopathologic examination. One pathologist examined all biopsy specimens and classified them as normal or abnormal; those designated abnormal were further classified as AIN 1, AIN 2, or AIN 3, depending on the observed degree of histologic abnormality.

Statistical Analysis

We used sample proportions with 95% CIs to estimate prevalence of anal HPV and AIN by HIV serostatus and compared the proportions by using the Fisher exact test. We defined the sensitivity of anal cytology to detect AIN as the number of specimens with abnormal cytology divided by the number of individuals with biopsy-proven AIN. We also used the Fisher exact test to determine whether the sensitivity of anal cytology to detect AIN differed by HIV serostatus.

Role of the Funding Source

The American Cancer Society, the National Institutes of Health, the California Universitywide AIDS Research Program, and CYTYC Corporation funded this study. The funding sources had no role in the study design; data collection, analysis, or interpretation; or writing of the report.

RESULTS

Participant Characteristics

We recruited a representative sample of 126 men from San Francisco who have sex with men. Of these, 30% were HIV-positive (Table 1). We excluded 1 participant from data analysis because he declined a clinical examination. The remaining 125 completed both the self-collection phase of anal cytology and the clinician-collection phase with high-resolution anoscopy. A median of 1 day (interquartile range, 0 to 6 days) elapsed between anal cytology self-collection and collection of the anal specimen by experienced clinicians.

Prevalence of Anal HPV Infection and Biopsy-Confirmed AIN, by HIV Status

Participants who were HIV-positive had a higher prevalence of anal HPV infection than HIV-negative participants (88% [95% CI, 80% to 100%] vs. 57% [CI, 46% to 68%]; odds ratio, 5.7 [CI, 1.9 to 18]; $P = 0.002$). Participants who were HIV-positive also had a higher prevalence of high-risk HPV types than HIV-negative men (72% [CI, 55% to 84%] vs. 34% [CI, 25% to 45%]; odds ratio, 4.9 [CI, 2.0 to 12]; $P = 0.001$) (Figure 1, top).

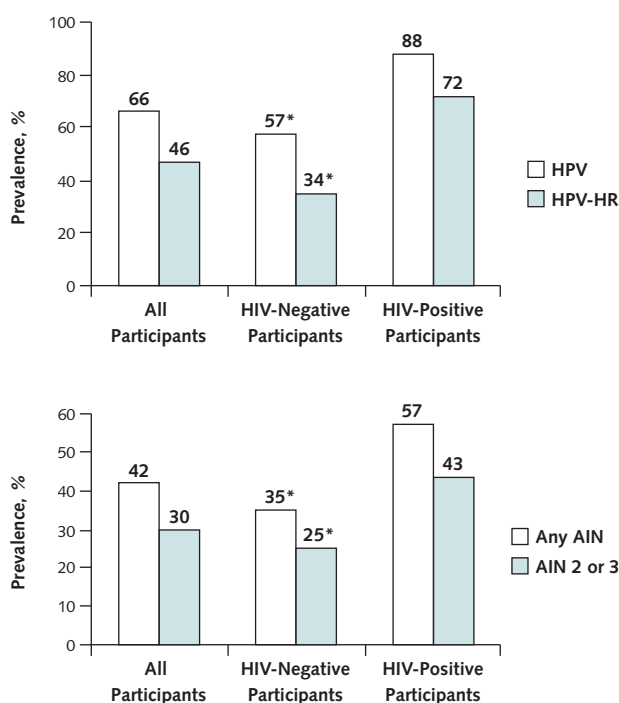
Participants who were HIV-positive had a significantly higher prevalence of AIN than HIV-negative participants (57% [CI, 41% to 72%] vs. 35% [CI, 26% to 46%]; odds ratio, 2.4 [CI, 1.01 to 5.9]; $P = 0.040$). Participants who were HIV-positive had a higher prevalence of high-grade AIN (AIN 2 or AIN 3) than HIV-negative participants; however, the difference was not statistically significant (43% [CI, 28% to 59%] vs. 25% [CI, 17% to 35%]; odds ratio, 2.3 [CI, 0.91 to 5.7]; $P = 0.080$) (Figure 1, bottom).

Patient-Collected versus Clinician-Collected Anal Cytology Specimens

Participants' HIV status affected the sensitivity of anal cytology to detect AIN. Among 20 HIV-positive participants who had biopsy-proven AIN, anal cytology was abnormal in 15 self-collected specimens (sensitivity, 75% [CI, 51% to 93%]) and 18 clinician-collected specimens (sensitivity, 90% [CI, 68% to 99%]) (Table 2). In contrast, among 21 HIV-negative men who had AIN, anal cytology was abnormal in 10 self-collected specimens (sensitivity, 48% [CI, 26% to 70%]) and 13 clinician-collected specimens (sensitivity, 62% [CI, 38% to 82%]). We found moderate evidence that the sensitivity of anal cytology to detect AIN from self-collected specimens was higher in HIV-positive men than HIV-negative men (75% vs. 48%; relative risk, 1.6 [CI, 0.89 to 2.6]; $P = 0.110$). Clinician-obtained samples were also more sensitive in detecting AIN in HIV-positive men than HIV-negative men (90% vs. 62%; relative risk, 1.4 [CI, 0.96 to 1.8]; $P = 0.070$), although the difference was not statistically significant.

Among 15 HIV-positive participants with high-grade AIN (AIN 2 or AIN 3), anal cytology was abnormal in 73% of self-collected specimens (CI, 45% to 92%) and

Figure. Prevalence of anal human papillomavirus (HPV) and anal intraepithelial neoplasia (AIN).



* $P < 0.050$ for comparison between HIV-negative and HIV-positive participants. Top. Prevalence of anal HPV DNA, by HIV status and cancer-associated risk type. High-risk (HR) types are 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, and 73. Bottom. Prevalence of histologically confirmed AIN, by HIV status.

87% of clinician-collected specimens (CI, 60% to 98%) (Table 2). In contrast, among HIV-negative men with AIN, anal cytology was abnormal in 47% of self-collected specimens (CI, 21% to 73%) and 53% of clinician-collected specimens (CI, 27% to 79%). The sensitivities to detect high-grade AIN did not significantly differ between HIV-positive and HIV-negative participants for either self-collected or clinician-collected samples (both $P > 0.100$).

Table 3 shows the overall test characteristics of self-collected anal cytology specimens to diagnose biopsy-con-

Table 2. Sensitivity and Specificity of Patient-Collected versus Clinician-Collected Anal Cytology Specimens

Result and HIV Status	Sensitivity (95% CI), %		Specificity (95% CI), %	
	Patient-Collected Specimen	Clinician-Collected Specimen	Patient-Collected Specimen	Clinician-Collected Specimen
Any AIN				
HIV-positive	75 (51–93)	90 (67–98)	50 (22–78)	64 (36–86)
HIV-negative	48 (26–70)	62 (42–79)	86 (71–94)	85 (72–93)
High-grade AIN				
HIV-positive	73 (45–92)	87 (58–98)	41 (19–67)	47 (25–71)
HIV-negative	47 (21–73)	55 (32–76)	81 (67–91)	76 (64–86)

AIN = anal intraepithelial neoplasia.

Table 3. Test Characteristics of Patient-Collected Anal Cytology Specimens

Result and HIV Status	Sensitivity (95% CI), %	Specificity (95% CI), %	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	Positive Predictive Value (95% CI), %	Negative Predictive Value (95% CI), %
Biopsy-proven AIN						
HIV-positive	75 (51–90)	50 (22–78)	1.5 (0.81–2.8)	0.5 (0.2–1.3)	71 (48–88)	55 (25–82)
HIV-negative	48 (26–70)	86 (71–94)	3.3 (1.4–7.9)	0.61 (0.4–9.3)	63 (36–84)	77 (62–87)
High-grade AIN						
HIV-positive	73 (45–92)	41 (19–67)	1.7 (0.76–2.1)	0.65 (0.24–1.8)	52 (30–74)	64 (32–88)
HIV-negative	47 (21–73)	81 (67–91)	2.5 (1.1–5.5)	0.66 (0.41–1.1)	44 (21–69)	83 (69–92)

AIN = anal intraepithelial neoplasia.

firmed AIN and high-grade AIN, stratified by HIV status. Among HIV-positive participants, abnormal anal cytology had good sensitivity to detect AIN (75%) but lower specificity (50% [CI, 22% to 78%]). The corresponding positive and negative likelihood ratios were 1.5 and 0.5, respectively. Among HIV-negative participants, abnormal anal cytology had low sensitivity to detect AIN (48%) but higher specificity (86%; CI, 71% to 94%), with corresponding positive and negative likelihood ratios of 3.3 and 0.61.

The specificity of abnormal anal cytology to diagnose AIN, when stratified by HIV status, was similar regardless of whether the sample was self-collected or clinician-collected (Table 2).

DISCUSSION

We found that a high proportion of men who have sex with men were infected with anal HPV (66%) and a correspondingly large proportion of participants (30%) had biopsy-proven high-grade AIN, which are potential anal cancer precursor lesions. Previously published estimates have reported similar numbers. One study of high-risk HIV-negative men who have sex with men that was conducted in 4 U.S. cities reported that 57% of the men were found to have anal HPV infection (17) and 20% were found to have anal cytologic abnormalities (18). Given that cytology is an insensitive marker of biopsy-proven AIN (19), the true prevalence of AIN in the previous study (18) is likely to be closer to the estimate demonstrated in our study. Our report confirms the high prevalence of anal HPV infection and AIN, including high-grade AIN, described in earlier studies performed in other clinical settings.

The prevalence of anal HPV infection and AIN in HIV-positive men was higher than that in HIV-negative men, which is also similar to the findings of other studies (20–23). One study that recruited men who have sex with men from 2 existing study cohorts in San Francisco (24) demonstrated that 36% of HIV-positive participants received a diagnosis of AIN. In a sample of HIV-positive men enrolled between 1998 and 2000 who had similar behavioral and demographic characteristics (25), 95% had anal HPV infection and 52% received a diagnosis of high-grade AIN.

Our data show that this community-based sample of men who have sex with men was able to self-collect high-quality anal cytologic specimens after reviewing simple printed instructions. Eighty percent of men with limited or no experience with anal cytology screening were able to collect a sample on the first attempt that was sufficient for interpretation by a pathologist. In addition, self-collected anal cytologic specimens had a sensitivity of 60% to detect AIN, similar to that reported by another study of self-collected anal cytology samples (8), in which 91% of samples were adequate for interpretation and the sensitivity to detect AIN by histology was 68%. All men in this previous study were already enrolled in an AIN natural history study and were accustomed to anal cytologic screening. In contrast, 93% of our participants had never been previously screened by using anal cytology.

When stratified by HIV status, the sensitivity of self-collected anal cytology to detect AIN was higher in HIV-positive men than in HIV-negative men. It is not clear why sensitivity would be higher in HIV-positive men, although it may reflect a higher burden of HPV-associated disease (more lesions and increased size of lesions) and the relative ease with which diseased cells from larger lesions can be sampled during screening. The spectrum of disease may also affect sensitivity. Individuals who are HIV-positive have a higher prevalence of AIN and are more likely to have a more serious case of AIN, which potentially increases the sensitivity of anal cytology to detect AIN in those individuals compared with HIV-negative men (26). Although self-collected anal cytology specimens had a lower sensitivity to detect AIN than did clinician-collected specimens, we believe that with repeated testing (for example, if cells are found to be insufficient), the relative disadvantage may be mitigated. Overall, if anal cytology self-screening were to be adopted on a large scale, the cumulative sensitivity of self-collected specimens would probably be even higher because performance characteristics improve over time.

We also explored additional test characteristics of self-collected anal specimens to diagnose AIN. Although anal Papanicolaou tests in HIV-negative men had a high specificity, similar to that of cervical Papanicolaou tests in women (27), the specificity in HIV-positive men was

lower. This could be because more nonspecific inflammation in the anal canal of HIV-positive individuals caused more false-positive cytologic test results than in HIV-negative men. Alternatively, the imperfection of the gold standard test could account for this finding: High-resolution anoscopy does not visualize all HPV-associated anal mucosal disease (5, 28). This could also reflect differences in the anal canal versus the cervix in HIV-infected individuals. Stool and mucosal folds in the anal canal may hide areas of dysplasia from high-resolution anoscopy, yielding a false-negative result (29). Given the relatively low positive likelihood ratios, anal cytology is probably not a good diagnostic test for AIN. As a screening test for AIN, however, further longitudinal studies incorporating both anal HPV testing and cytology will be needed to determine the best combination and periodicity of screening. Anal cytology is still useful as a screening test for AIN despite its low specificity in HIV-positive men, similar to how fecal occult blood tests can be used to screen for colorectal cancer even though diet or hemorrhoids may cause false-positive results (30). Unlike diagnostic colonoscopy, performance of high-resolution anoscopy after a positive result on a screening anal cytology test would be relatively straightforward and would not require sedation or special stool preparation regimens.

Our study has several limitations. Because we derived the study sample from a geographically restricted urban area, our results may not be generalizable to all men who have sex with men. The sample size was also relatively small, which affects the precision of our estimates of anal HPV infection and disease. Inaccurate reports of HIV status could have resulted in misclassification bias. However, studies done in similar populations of men who have sex with men have shown that participants' self-report of HIV status is accurate (13, 14). Even if misclassification had occurred, this would not affect the overall estimates of disease or the comparison of self-collected versus clinician-collected cytology to diagnose AIN.

Operational aspects of our study may also have limited our findings. Participants self-collected samples before the clinic visit, where experienced clinicians repeated anal cytology and performed gold-standard biopsy. If sufficient time elapsed between collections, HPV-associated lesions could have evolved, reducing the validity of both the sensitivity assessment for detecting AIN and the comparison between self-collected samples and clinician-collected samples. However, a median of only 1 day (interquartile range, 0 to 6 days) elapsed between the time when samples were self-collected and the time when participants were seen in clinic for repeated cytology and high-resolution anoscopy.

Finally, only 1 pathologist reviewed all of the cytology and biopsies for the study. Any potential underdiagnosis or overdiagnosis of AIN would probably affect only our prevalence estimates and not the comparison between participants and clinicians. In addition, the pathologist who interpreted the slides for this study participated in a study of

interobserver variability in anal cytology and biopsies. The data showed good interobserver agreement for anal cytology (κ , 0.55 to 0.88) and anal biopsies (κ , 0.76 to 0.94) between experienced pathologists to distinguish high-grade AIN from non-high-grade AIN (31).

Screening for anal precancer lesions and anal cancer requires not only increased awareness on the part of providers but also an extensive infrastructure, including a cadre of experienced high-resolution anoscopists who can evaluate and treat patients who have abnormal anal cytology on screening and experienced pathologists and anal surgeons for referral and treatment. Over the past several years, more clinicians have been trained to perform high-resolution anoscopy; the American Society for Colposcopy and Cervical Pathology has recently sponsored courses on this technique.

Our study demonstrates a high prevalence of anal HPV infection and anal precancer lesions in a community-based sample of men who have sex with men. Self-collected samples may facilitate the screening of large populations, including those with limited experience or who may not normally seek medical attention. Future effectiveness trials can confirm whether this is a viable method of conducting screening interventions on a population level. However, the probability of AIN in a patient with a negative cytology result may not be low enough (23% for HIV-negative men and 45% for HIV-positive men with a self-collected specimen) for clinicians to be comfortable recommending no anoscopy for those with a negative cytology result. These data raise the question of whether the optimal population screening strategy is cytology screening with anoscopy only for those who test positive or whether anoscopy should be recommended for everyone in these risk groups. However, given limited resources and the limited number of clinicians trained in anoscopy, cytology screening may be the best current approach to identifying disease in the at-risk population.

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