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COMPARISON OF TWO ANAL CYTOLOGY PROTOCOLS TO PREDICT HIGH-GRADE ANAL INTRAEPITHELIAL NEOPLASIA

Dorothy J. Wiley, PhD[a], **Hilary Hsu, BS**[a], **Robert Bolan, MD**[b], **Alen Voskanian, MD**[c], **David Elashoff, PhD**[d,e], **Stephen Young, PhD**[f], **Ruvy Dayrit, BS(c)**[a], **Provaboti Barman, PhD**[a], **Katherine DeAzambuja, BS**[a], **Emmanuel V. Masongsong, BS**[a], **Otoniel Martínez-Maza, PhD**[g,h], and **Roger Detels, MD, MS**[i]

[a]Translational Science Section, School of Nursing, University of California at Los Angeles (UCLA), 700 Tiverton Avenue, Rm 5-151, Los Angeles, CA 90095-6919

[b]Los Angeles Gay & Lesbian Center, Jeffrey Goodman Clinic, 1625 Schrader Blvd., Hollywood, CA 90028

[c]Center for Clinical AIDS Research and Education (UCLA-CARE Center), 1399 Roxbury Dr., Suite 100, Los Angeles, CA 90035

[d]Department of Medicine, David Geffen School of Medicine, UCLA, 911 Broxton Avenue, Los Angeles, CA 90095-1736

[e]Jonsson Comprehensive Cancer Center (JCCC), 8-684 Factor Building, Tiverton Avenue, Los Angeles, CA 90095-1781

[f]Tricore Diagnostic Laboratories, University of New Mexico, Albuquerque, NM 87102

[g]UCLA AIDS Institute, BSRB 173, 615 Young Drive, Los Angeles, CA 90095-7363

[h]Department of Obstetrics and Gynecology, David Geffen School of Medicine, UCLA, 153 BSRB, Los Angeles, CA 90095-1740

[i]UCLA Jonathan & Karin Fielding School of Public Health, Box 951772, 16-035 CHS, Los Angeles, CA 90095-1772.

INTRODUCTION

Invasive anal squamous cell cancer (IAC) is a health crisis for gay, bisexual, and other men who have sex with men (MSM), and for male-to-female transgendered women who have had sex with men (TWSM), especially within the context of HIV-coinfection where risk for

Corresponding Author: D.J. Wiley, Ph.D. School of Nursing University of California at Los Angeles (UCLA) 700 Tiverton Avenue, Factor Building Rm 5-151 Los Angeles, CA 90095-6919 dwiley@ucla.edu TEL: 1-310-825-0540 FAX: 1-310-206-0606.

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invasive malignancy is greatest (1-6). Currently, experts recommend using the Dacron swab for anal cytology (Pap test) specimen collection at annual and semi-annual intervals for HIV-infected and -uninfected MSM, respectively (7, 8). Dacron-swab anal cytology poorly correlates with histological evaluation of disease (9) and while cervical-cytology sampling has informed anal-cytology specimen collection, cervical screening tools may not be appropriate for analcancer screening. For example, cytobrushes with and without spatulas, cytopicks; and cotton, Dacron, rayon, and nylon-flocked (NF)-swab have been evaluated in genital sampling for pathogens, including HPV, and for cervical cytology (10-14). Cytobrushes improved cervical sampling over cotton swabs by 58-76% for detecting endocervical cells in a sample of >800 adult females >29 years of age (14) and are shown superior to Ayers spatulas (10). One report suggests the cytobrush may be effective in anal cytology,(15) but may be uncomfortable in blind sampling (16). The NF-swab is evaluated extensively for respiratory-pathogen and -cytology sampling, yielding more cells and pathogens than other collection protocols (17-20). For example, Daley et al. report >2-fold cell yield of respiratory epithelial cells using NF-over Dacron swabs, and Krech et al. report a 5-fold greater yield of *Chlamydia trachomatis*, as well as greater HPV yield using NF-over rayon-wrapped swabs in cervicovaginal tissues (17, 21). Further, unsatisfactory cervical cytology findings range from 0.3-10.9% and 0.17-2.7% for specimens preserved using PreservCyt® (Hologic, Inc., Marlborough, Massachusetts) and SurePath™ (TriPath Imaging, Inc., Burlington, N.C.) preservatives, respectively (22-25), whereas the prevalence of unsatisfactory anal cytology specimens may range from 1% to upwards of 14% (26-33).

The cervix and the anal canal are distinct anatomical targets that might easily require different sampling tools. The cervix is firm and sampling is more akin to hitting the *bulls-eye* on a target while the anal canal is soft and folds much like the surface of a deflated balloon. Cervical cytology uses a speculum to visually guide sample collection and the *transformation zone* (TZ) of the cervix closely approximates the cervical os. The *dentate line* lies approximately ~5 centimeters proximal to the anal verge, and the *anal TZ* immediately adjoins it about ~0.5-1 cm, just cephalad (34). Current anal cytology recommendations are to blindly insert a Dacron swab through the anal verge ~5 cm, approximate it to the anal wall, and rotate the swab using lateral pressure to sample the canal circumferentially as it is withdrawn over 10-20 seconds and stored in liquid preservative for laboratory examination (35).

Although experts suggest screening in high-risk populations is important and data show it is cost-effective, there is no current national consensus for screening methods or frequency for anal cancer screening using Papanicolaou staining (Pap test) (8, 36-38). To date, no large studies evaluate the risks or benefits of early detection and treatment for preventing anal cancer and general reluctance among clinicians for anal cytology screening may be due to the imprecision of the test, the rarity of malignancy, and the limited success of available treatments, especially within the context of HIV infection where there is poor control over HPV infections (39-41). Developing a screening strategy with modest-to-high sensitivity and specificity for anal precancers, high-grade anal intraepithelial neoplasia (HG-AIN), is an important public health goal. Thus, to evaluate the sensitivity and specificity for two cytology collection procedures and compare their efficacy for predicting HG-AIN, we evaluated a protocol using an NF-swab (Copan Diagnostics Inc., Murrieta, CA) and the Dacron swab (Thermo Fisher Scientific, Miami, OK), each with preservative, for anal cytology.

MATERIALS AND METHODS

Subjects and Sampling

Fifty-eight adult MSM provided written informed consent for an IRB-approved study (University of California, Los Angeles, Medical IRB2 #11-000668) and all were enrolled in 1 of 4 Multicenter AIDS Cohort Study groups. Prior to examination, examiners collected a self-reported history for HIV infection, AIDS-defining conditions, anal treatments, and presence of recent anal bleeding, discharge, or pain. Men lay in the left lateral position for the exam, with legs flexed, and the anogenital region exposed. External genitalia were examined.

Cytology specimens

were collected in order so that the swab procedures could be compared without biasing cytology findings for specimens collected using Dacron swab (42). Briefly, a Dacron swab was lightly moistened with water, inserted blindly beyond the anal verge ~5 cm, firmly approximated to the anal wall and circularly rotated while being withdrawn over ~30 seconds; thereafter, the swab was deposited into PreservCyt® (Dacron-protocol). Early experience showed the NF swab had a larger diameter that was difficult to pass through the verge unaided. Accordingly, the protocol was amended to use a disposable anoscope (CooperSurgical, Inc., Trumbull, CT) with water-soluble lubricant lightly applied to the leading edge, allowing for comfortable passage of the instrument. Once inserted just beyond the verge, the obturator was removed, and the internal aspect of the anoscope was cleared of residual lubricant using a dry Scopette swab (Owens & Minor, Mechanicsville, VA). Thereafter, an NF-swab passed through the anoscope was approximated to the anal wall ~5 cm beyond the verge close to the anal *dentate line*, circularly rotated, using lateral pressure during withdrawal, over 20-30 seconds using a standard procedure (35). The NF-swab specimen was placed into SurePath™ preservative and the anoscope was removed (NF-protocol). For both swab protocols, swabs were agitated several minutes in the specimen containers to dislodge the collected material.

Following cytology specimen collection

high-resolution anoscopy (HRA) was performed. First, a 4X4-gauze-padded swab soaked with 3-5% acetic acid was passed through an anoscope, the anoscope was withdrawn, and the gauze was left in place one minute before being withdrawn. The anoscope was reintroduced using water-soluble lubricant, and the anal canal was examined using a colposcope for magnification and bright light. Biopsy was performed where acetowhite lesions showed punctation, friability, or highly vascularized appearances. Where hemorrhoids were significant and obstructed the ability of the examiner to evaluate the tissue, a 2% lidocaine/1:100,000 epinephrine solution was distributed evenly, with <0.5cc in each of four quadrants, using a 25-30 gauge needle. Biopsies were performed using Tischler (Sklar, West Chester, PA) or endoscopic (Pentax Corporation, Montvale, NJ) forceps and hemostasis was achieved using Monsel's solution (ferric subsulfate; CooperSurgical, Inc., Trumbull, CT) as needed.

Board-certified cyto- and histo-pathologists

in one CLIA-certified laboratory used standard procedures to evaluate cytology and biopsy specimens, blinded to clinical examination findings. The Bethesda Classification System (43, 44) and the International Classification of Diseases for Oncology (45) were used to evaluate cytology and histology specimens, respectively. Cytology specimens were classified as negative for intra-epithelial lesion (NIL); atypical squamous cells, either of unknown significance (ASC-US) or favoring high-grade dysplasia (ASC-H); or low- or

high-grade squamous intraepithelial lesions (LSIL and HSIL, respectively). PreservCyt®/Dacron-swab specimens showing fewer than 1-2 nucleated squames/high-power field (hpf) and SurePath™/NF-swab specimens showing fewer than 3-6 nucleated squames/hpf were evaluated as insufficient and reported as *unsatisfactory* (46). Histology was classified as negative for specimens showing keratosis, and benign hyperplasia, acute inflammation or reactive changes in the absence of dysplasia; low-grade anal intraepithelial neoplasia or mild dysplasia (LG-AIN); and HG-AIN for AIN 2/moderate dysplasia, AIN 2- 3/moderate-to-severe dysplasia, or AIN 3/severe dysplasia. For these analyses, the histology outcome is the most severe of findings where multiple biopsy specimens were evaluated. The sensitivity and specificity for cytology to predict HG-AIN was evaluated first excluding unsatisfactory cytology and then classified.

Sexual, behavioral, and other laboratory data

are part of the Multicenter AIDS Cohort Study repository, and in the case of one subject, by self-report. Demographic, health and illness events, and laboratory data, including HIV infection characteristics, are collected semi-annually using standardized instruments. However, to control for the effects of immune and disease characteristics, adjusted analyses were limited to HIV-infection (versus not) and chronological age at the time of the examination, evaluated as a continuous variable.

Statistical Analysis

Descriptive and tabular analyses evaluated associations between the two protocols and cytology findings to predict risk for HG-AIN. Kappa statistics, sensitivity and specificity were estimated using SAS PROC FREQ (47). To evaluate sensitivity and specificity, cytology specimens showing ASC-US, ASC-H, LSIL or HSIL (≥ASC-US) were compared to findings of NIL, excluding unsatisfactory cytology from the analyses. A series of logistic regression models, using SAS PROC LOGISTIC, (48) examined the crude and adjusted odds of HG-AIN for NF- and Dacron-protocols individually, controlling for the effects of HIV-infection and age. Last, receiver operating characteristic (ROC) curves and the corresponding area under each curve (AUC_{ROC}) were estimated for logistic regression analyses to evaluate the accuracy of Dacron- and NF-protocol cytology methods to predict HG-AIN, adjusting for the effect of age and HIV-infection (49). The AUC_{ROC} globally evaluates test accuracy, estimating the mean specificity across the range of possible sensitivity estimates for the models (49). Model fits were evaluated using the deviance statistic and were rejected or not using a 0.05 level of significance.

RESULTS

The study sample is best described as white, HIV-infected, and older MSM (Table 1). Most participants were Caucasian (85%, 49/58), 5% (3/58) were Black, and 10% (6/58) reported “other” race groupings; 5% (3/58) reported Hispanic ethnicity. The mean age was 57.9 (+6.6) years, ranging 39.5-72 years, not varying significantly for HIV-infected/-uninfected men. Overall, 36% (21/58) showed HG-AIN by HRA and biopsy, and although estimates did not reach statistical significance, the prevalence of HG-AIN was 62% higher among HIV-infected than uninfected men (Table 1). Older and younger men were equally likely to show HG-AIN (OR=0.9, p=0.2). For 40 of 42 HIV-infected men, infection duration could be estimated, and the average duration was 25.7 (+8.37) years, including estimated values for prevalent positive men (50). Among HIV-infected men, most reported no prior AIDS-defining conditions (79%, 33/40), and for the 36 whose data were complete, CD4+ count showed a downward trend before combined antiretroviral therapy (CART): μ=−340.9 (+/−208.8) cells/mm^3/year; however, following CART, CD4+ cell counts trended positively, increasing by 284.7 (+/−171.1) cells/mm^3/year.

The prevalence of unsatisfactory cytology specimens

was 15% (9/58), where one or both specimens were independently evaluated as insufficient. Of these, 33% (3/9) showed unsatisfactory results for both specimens. Half as many NF- as Dacron-protocol cytology specimens were evaluated as unsatisfactory by experts: 7% (4/58) versus 14% (8/58).

Agreement between NF- and Dacron protocol cytology

findings was poor to modestly poor (Table 2). Including those evaluated as unsatisfactory, 23 of 58 specimens agreed using either protocol procedure. The simple *Kappa* statistic, including 3 of 9 unsatisfactory specimens that were so classified by both procedures, was 16% (-1-33%). When values for unsatisfactory specimens were omitted from the analysis, agreement shifted somewhat; the simple and weighted *Kappa* statistics were 11% (-8-30%) and 24% (3-46%), respectively.

Sensitivity and specificity

NF-protocol cytology showed 56% greater sensitivity for detecting HG-AIN and 26% greater specificity than did Dacron-protocol cytology (Table 3). Specifically, sensitivity and specificity for NF-protocol cytology ≥ASC-US was 81% (58-95%) and 73% (50-89%), while Dacron protocol specimens showed 52% (30-74%) and 58% (34-80%) sensitivity and specificity, respectively.

Cytology using NF-protocol better predicted HG-AIN on histology than did the Dacron protocol cytology

Overall, 81% (17/21) of men with ≥ASC-US cytology on NF-protocol showed histological evidence of HG-AIN, while 52% (11/21) of Dacron-protocol cytology specimens tested similarly positive (Table 3). Put another way, findings from NF-protocol cytology would result in 50% (29/58) of men evaluated being referred for diagnostic follow-up as compared to 41% (24/58) of men showing ≥ASC-US using Dacron protocol. However, among those that would be referred for diagnostic follow-up, a higher proportion of HG-AIN-affected men would be detected using the NF-protocol procedure over Dacron: 59% (17/29) versus 46% (11/24), respectively. Conservatively, Dacron-protocol cytology misclassified men more often as *unaffected* when compared to NF-protocol findings, i.e., cytology showed NIL and histology showed LG- or HG-AIN: 58% (15/26) vs. 36% (9/25), respectively. HIV-infection and age alone did not predict HG-AIN well in this small sample using either Dacron or NF-protocol (Table 4, Unadjusted Analyses). For example, in unadjusted analyses, HIV-infected men showed 10% greater odds of HG-AIN than did uninfected men, and each additional year in age increased the odds of HG-AIN 10% (OR=1.1 and OR=1.1, respectively, p-values>0.05, Table 4).

The **multivariate analyses** suggests that after controlling for the effects of age and HIV infection, men who show ≥ASC-US cytology using the NF-protocol have 3-fold greater odds for HG-AIN over men showing NIL (adjusted OR=3.0 (1.5, 6.2), Table 4). However, men showing ≥ASC-US using the Dacron-procedure showed no statistically significantly greater odds of HG-AIN than men showing NIL on (Dacron) cytology (adjusted OR=2.0 (1.0, 4.0), Table 4). In both adjusted analyses, age and HIV-infection did not independently predict HG-AIN. Last, the AUC_{ROC} analysis suggested the accuracy of NF-cytology showing ≥ASC-US to predict HG-AIN was 21% greater than was Dacron cytology showing similar findings: C-statistics 0.776 vs. 0.643, respectively (Fig. 1).

DISCUSSION

Analyses showed HG-AIN was commonly detected among HIV-infected and –uninfected MSM screened using two anal cancer screening protocols. Currently, a blindly-passed Dacron swab is customary for anal cytology specimen collection (35, 51). However, sensitivity and specificity for detecting HG-AIN were higher for NF- than Dacron-protocol specimens: 81% vs. 52%, albeit confidence intervals overlapped. Sensitivity and specificity of Dacron cytology were within published ranges: 42-98% and 32-96%, respectively (9, 28, 44, 52-56). Comparatively, sensitivity and specificity of cervical cytology for detecting high-grade cervical intraepithelial neoplasia ranges 11-99% and 14-97%, respectively (57). Experts currently recommend HRA and biopsy for anal cytology > ASC-US (27, 58). Poor specificity, even in high-risk populations, makes the predictive value of positive cytology poor and escalates healthcare costs associated with unnecessary diagnostic follow-up. Nonetheless, even relatively costly strategies can improve screening-test specificity enough to provide significant overall cost-savings. For example, the addition of molecular HPV testing or repeat cytology improves the test performance of cervical cytology two-fold when compared to immediate colposcopy referral for ASC-US cytology (59). Future efforts are best directed toward developing adjunctive or alternative screening strategies that improve specificity for anal cytology, so as to assure that additional diagnostic follow-up and healthcare costs are offset by improved performance of screening tests.

This study compares two instruments and procedures for cytology collection. The NF-procedure described herein uses a small plastic anoscope to open the verge for comfortable passage of the NF-swab with larger surface area. We found no statistically significantly greater odds of HG-AIN for men showing ≥ASC-US on Dacron cytology, but found a 3-fold greater odds of HG-AIN for NF-cytology ≥ASC-US when compared to otherwise similar men showing NIL. Nonetheless, our sample population is small, the Dacron-procedure was systematically collected first, and some findings vary from published works. For example, Vajdic et al. report first-collected and blindly passed Dacron anal cytology was superior to anoscope-guided and second-collected Dacron specimens in a sample of 151 MSM, 63% of whom were HIV-infected (29). Conversely, Gage et al. reported no significant difference in the mean number of detectable anal epithelial cells using an endogenous retrovirus biomarker, when first-collected NF- and Dacron anal cytology specimens were compared (60). However, authors showed higher (log) cell counts for second-drawn NF- (over Dacron-swab) specimens and in the overall comparison: μ=8.1 vs. 7.1 (p=0.03) and 8.3 vs. 7.8 (p=0.03), respectively (60). Herein, the NF-protocol more precisely predicted HG-AIN and yielded half as many unsatisfactory cytology specimens despite that Dacron cytology sampling was performed first.

Few head-to-head trials have been performed and a large number of published anal cytology studies employ Dacron protocol, with few using cytobrush or other specimen collection instruments (9, 53, 55, 61-63). Since ~1950, comparative studies informed cervical cytology specimen collection and improved care, showing cervical cytobrush to be superior to swab and spatula specimen collection methods (64-70). Our experience and that of experts suggests cervical cytobrushes cause discomfort, making them ill-advised for care (16, 46). NF-swabs are designed to collect more cells and pathogens over the conventional Dacron swabs; however, PreservCyt® and SurePath™ preservatives may have differentially affected the number of insufficient cytology specimens. One large cervical cytology study showed fewer unsatisfactory cytology results attributable to SurePath™ over PreservCyt®, and that by reprocessing using SurePath™ converted 60% of insufficient specimens to satisfactory for interpretation, suggesting some differences herein may be due to specimen processing alone (22). Additionally, data show water-based lubricants are associated with higher rates of unsatisfactory cytology specimens and, in one randomized dose-response

controlled trial, showed an inverse association for one water-soluble lubricant (0.1-0.5g/vial) and cell counts/field using PreservCyt® specimens and an overall lower number of cells per field using a second (42). However, one trial showed no association between cytology findings and (0.5 mL) water-based lubricant added randomly to 1 of 2 paired PreservCyt® specimens (n=200); for ~8% discordant specimens, 8/15 showed cytology less severe in the lubricant-contaminated specimens, 5/15 showed vice versa, and 2/15 showed unsatisfactory results in one (71).

Additional, albeit modest, costs of NF-protocol sampling increase individual cytology costs. The NF-swab and anoscope add ~$3.00 to the examination expense. However, some data show NF-swabs significantly improve the cell yield, while collecting comparable levels of nucleic acids, when compared to rayon swabs for respiratory sampling (17, 18). While an anoscope may be less comfortable than blind sampling with Dacron swab, men in this study voiced no complaints about the procedure. Thus, balancing cost, comfort, and yield of HG-AIN is an important public health goal. Herein, the NF-procedure netted a 31% greater yield of HG-AIN than Dacron-protocol but would result in 22% higher referral for diagnostic follow-up using current guidelines of ≥ASCUS (30).

Few studies have evaluated anal cytology in older men. Our analyses showed age had little effect on risk for HG-AIN. Nonetheless, population data show men over 60 are at higher risk than younger men for invasive anal cancer,(3, 72) and that invasive malignancy may show slightly earlier onset among HIV-infected MSM than -uninfected men. For example, among the 219 anal cancer cases reported to the HIV/AIDS Cancer Match Study (N=263,254), the median age at diagnosis was ~3 years younger than expected: 42 versus 45 years (73).

A small sample size may limit these analyses and self-report data may contribute to misclassification of some characteristics. Systematic sampling may have introduced some bias; however, the ordered collection and choice of preservatives was based on randomized control trial findings that show water-soluble lubricants produce unpredictable artifacts and lower cell counts per field in PreservCyt®-preserved cytology specimens that are not seen with SurePath™(42, 71, 74). However, Dacron swab collection into PreservCyt® is the current standard for anal Pap test against which the NF-swab collection and SurePath™ were compared (35). Also, Scopette swabs removed lubricant from the internal wall of the anoscope, were not used to swab anal tissues, and facilitated unimpeded passage of the NF-swab. Albeit infrequent, some studies show wiping increases drying and crush artifact and more frequently noted limited cellularity by pathologist in cervical sampling (75, 76). Also, there may be residual confounding that is not controlled for solely by adjusting for age and HIV-infection in the multivariate analyses (77). Differences in unsatisfactory cytology specimens we measured cannot be attributed solely to the swab collection device. One meta-analysis of >2-million cervical cytology specimens analyzed in 42 studies shows the prevalence of unsatisfactory cytology was 0.3% and 1.3% for SurePath™ and PreservCyt® specimens, respectively, and three head-to-head comparisons show SurePath™ yields fewer unsatisfactory test results than does PreservCyt® (25). Last, samples were collected systematically, not randomly, as even small amounts of water-soluble lubricant might have irreparably disadvantaged the Dacron-collection procedure. Reports show first-collected Dacron cytology specimens more often detect HG-AIN over second-collected swabs, where specimens are discordant ($p<0.001$) (29). Thus, if biased, our findings may conservatively estimate of the sensitivity and specificity of the NF-swab procedure.

Future research should focus on improving anal cancer screening specificity to lower overall costs and improve the predictive value of positive screening tests. For example, molecular HPV testing to triage ASC-US cervical cytology for diagnostic colposcopy has significantly reduced the overall cost of mass cervical cancer screening and improved detection of HG-

disease (78). Finding similar effective adjunctive tests for anal cytology holds promise of improving care for individuals and minimizing healthcare expenditures.

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References

1. Frisch M, Smith E, Grulich A, Johansen C. Cancer in a population-based cohort of men and women in registered homosexual partnerships. Am J Epidemiol. Jun 1; 2003 157(11):966–72. [PubMed: 12777359]
2. Frisch M, Glimelius B, van den Brule AJ, Wohlfahrt J, Meijer CJ, Walboomers JM, et al. Sexually transmitted infection as a cause of anal cancer. N Engl J Med. 1997; 337(19):1350–8. [PubMed: 9358129]
3. Frisch M, Melbye M, Moller H. Trends in incidence of anal cancer in Denmark. BMJ. 1993; 306(6875):419–22. [PubMed: 8461721]
4. Clifford GM, Polesel J, Rickenbach M, Dal Maso L, Keiser O, Kofler A, et al. Cancer risk in the Swiss HIV Cohort Study: associations with immunodeficiency, smoking, and highly active antiretroviral therapy. J Natl Cancer Inst. Mar 16; 2005 97(6):425–32. [PubMed: 15770006]
5. Seaberg EC, Wiley D, Martinez-Maza O, Chmiel JS, Kingsley L, Tang Y, et al. Cancer incidence in the Multicenter AIDS Cohort Study before and during the HAART era: 1984 to 2007. Cancer. Dec 1; 2010 116(23):5507–16. [PubMed: 20672354]
6. Simard EP, Pfeiffer RM, Engels EA. Spectrum of cancer risk late after AIDS onset in the United States. Arch Intern Med. Aug 9; 2010 170(15):1337–45. [PubMed: 20696958]
7. Darragh TM, Winkler B. Anal cancer and cervical cancer screening: key differences. Cancer Cytopathol. Feb 25; 2011 119(1):5–19. [PubMed: 21319310]
8. Goldie SJ, Kuntz KM, Weinstein MC, Freedberg KA, Welton ML, Palefsky JM. The clinical effectiveness and cost-effectiveness of screening for anal squamous intraepithelial lesions in homosexual and bisexual HIV-positive men. JAMA. 1999; 281(19):1822–9. [PubMed: 10340370]
9. Panther LA, Wagner K, Proper J, Fugelso DK, Chatis PA, Weeden W, et al. High resolution anoscopy findings for men who have sex with men: inaccuracy of anal cytology as a predictor of histologic high-grade anal intraepithelial neoplasia and the impact of HIV serostatus. Clin Infect Dis. May 15; 2004 38(10):1490–2. [PubMed: 15156490]
10. Boon ME, de Graaff Guilloud JC, Rietveld WJ. Analysis of five sampling methods for the preparation of cervical smears. Acta Cytol. Nov-Dec;1989 33(6):843–8. [PubMed: 2588917]
11. Gao L, Zhou F, Li X, Yang Y, Ruan Y, Jin Q. Anal HPV infection in HIV-positive men who have sex with men from China. PLoS One. 2010; 5(12):e15256. [PubMed: 21151900]

12. Benschop CC, Wiebosch DC, Kloosterman AD, Sijen T. Post-coital vaginal sampling with nylon flocked swabs improves DNA typing. Forensic Sci Int Genet. Feb; 2010 4(2):115–21. [PubMed: 20129470]

13. El Aila NA, Tency I, Claeys G, Saerens B, De Backer E, Temmerman M, et al. Genotyping of Streptococcus agalactiae (group B streptococci) isolated from vaginal and rectal swabs of women at 35-37 weeks of pregnancy. BMC Infect Dis. 2009; 9:153. [PubMed: 19747377]

14. Kristensen GB, Holund B, Grinsted P. Efficacy of the cytobrush versus the cotton swab in the collection of endocervical cells. Acta Cytol. Nov-Dec;1989 33(6):849–51. [PubMed: 2588918]

15. Calore EE, Nadal SR, Manzione CR, Horta SC, Santos RR, Nadal LM. Anal cytology in patients with AIDS. Diagn Cytopathol. Apr; 2010 38(4):260–3. [PubMed: 19813269]

16. Darragh, T.; Birdsong, G.; Luff, R.; Davey, D. Anal-Rectal Cytology. In: Solomon, D.; Nayar, R., editors. The Bethesda system for reporting cervical cytology: definitions, criteria, and explanatory notes. Springer Verlag; New York: 2004. p. 169-76.

17. Daley P, Castriciano S, Chernesky M, Smieja M. Comparison of flocked and rayon swabs for collection of respiratory epithelial cells from uninfected volunteers and symptomatic patients. J Clin Microbiol. Jun; 2006 44(6):2265–7. [PubMed: 16757636]

18. Esposito S, Molteni CG, Daleno C, Valzano A, Cesati L, Gualtieri L, et al. Comparison of nasopharyngeal nylon flocked swabs with universal transport medium and rayon-bud swabs with a sponge reservoir of viral transport medium in the diagnosis of paediatric influenza. J Med Microbiol. Jan; 2010 59(Pt 1):96–9. [PubMed: 19815662]

19. Scansen KA, Bonsu BK, Stoner E, Mack K, Salamon D, Leber A, et al. Comparison of polyurethane foam to nylon flocked swabs for collection of secretions from the anterior nares in performance of a rapid influenza virus antigen test in a pediatric emergency department. J Clin Microbiol. Mar; 2010 48(3):852–6. [PubMed: 20053857]

20. Walsh P, Overmyer CL, Pham K, Michaelson S, Gofman L, DeSalvia L, et al. Comparison of respiratory virus detection rates for infants and toddlers by use of flocked swabs, saline aspirates, and saline aspirates mixed in universal transport medium for room temperature storage and shipping. J Clin Microbiol. Jul; 2008 46(7):2374–6. [PubMed: 18463214]

21. Krech T, Castriciano S, Jang D, Smieja M, Enders G, Chernesky M. Detection of high risk HPV and Chlamydia trachomatis in vaginal and cervical samples collected with flocked nylon and wrapped rayon dual swabs transported in dry tubes. J Virol Methods. Dec; 2009 162(1-2):291–3. [PubMed: 19703493]

22. Nance KV. Evolution of Pap testing at a community hospital: a ten year experience. Diagn Cytopathol. Mar; 2007 35(3):148–53. [PubMed: 17304530]

23. Kirschner B, Simonsen K, Junge J. Comparison of conventional Papanicolaou smear and SurePath liquid-based cytology in the Copenhagen population screening programme for cervical cancer. Cytopathology. Aug; 2006 17(4):187–94. [PubMed: 16879266]

24. Ferris DG, Heidemann NL, Litaker MS, Crosby JH, Macfee MS. The efficacy of liquid-based cervical cytology using direct-to-vial sample collection. J Fam Pract. Nov; 2000 49(11):1005–11. [PubMed: 11093566]

25. Fontaine D, Narine N, Naugler C. Unsatisfactory rates vary between cervical cytology samples prepared using ThinPrep and SurePath platforms: a review and meta-analysis. BMJ Open. 2012; 2(2):e000847.

26. Zhao C, Domfeh AB, Austin RM. Histopathologic outcomes and clinical correlations for high-risk patients screened with anal cytology. Acta Cytol. 2012; 56(1):62–7. [PubMed: 22236747]

27. Berry JM, Palefsky JM, Jay N, Cheng SC, Darragh TM, Chin-Hong PV. Performance characteristics of anal cytology and human papillomavirus testing in patients with high-resolution anoscopy-guided biopsy of high-grade anal intraepithelial neoplasia. Dis Colon Rectum. Feb; 2009 52(2):239–47. [PubMed: 19279418]

28. Mathews WC, Sitapati A, Caperna JC, Barber RE, Tugend A, Go U. Measurement characteristics of anal cytology, histopathology, and high-resolution anoscopic visual impression in an anal dysplasia screening program. J Acquir Immune Defic Syndr. Dec 15; 2004 37(5):1610–5. [PubMed: 15577418]

29. Vajdic CM, Anderson JS, Hillman RJ, Medley G, Grulich AE. Blind sampling is superior to anoscope guided sampling for screening for anal intraepithelial neoplasia. Sex Transm Infect. Oct; 2005 81(5):415–8. [PubMed: 16199742]
30. Bean SM, Chhieng DC, Roberson J, Raper JL, Broker TR, Hoesley CJ, et al. Anal-rectal cytology: correlation with human papillomavirus status and biopsy diagnoses in a population of HIV-positive patients. J Low Genit Tract Dis. Apr; 2010 14(2):90–6. [PubMed: 20354415]
31. Cranston RD, Hart SD, Gornbein JA, Hirschowitz SL, Cortina G, Moe AA. The prevalence, and predictive value, of abnormal anal cytology to diagnose anal dysplasia in a population of HIV-positive men who have sex with men. Int J STD AIDS. Feb; 2007 18(2):77–80. [PubMed: 17331275]
32. Conley L, Bush T, Darragh TM, Palefsky JM, Unger ER, Patel P, et al. Factors associated with prevalent abnormal anal cytology in a large cohort of HIV-infected adults in the United States. J Infect Dis. Nov 15; 2010 202(10):1567–76. [PubMed: 20925532]
33. Kojic EM, Cu-Uvin S, Conley L, Bush T, Onyekwuluje J, Swan DC, et al. Human Papillomavirus Infection and Cytologic Abnormalities of the Anus and Cervix Among HIV-Infected Women in the Study to Understand the Natural History of HIV/AIDS in the Era of Effective Therapy (The SUN Study). Sex Transm Dis. Apr; 2011 38(4):253–9. [PubMed: 20966828]
34. Jorge, JMN.; Habr-Gama, A. Anatomy and Embryology. In: Beck, DE.; Roberts, PL.; Saclarides, TJ.; Senagore, AJ.; Stamos, MJ.; Wesner, SD., editors. The ASCRS Textbook of Colon and Rectal Surgery. 2nd ed. Springer Science & Businesss Media, LLC; New York: 2011.
35. Panther LA, Schlecht HP, Dezube BJ. Spectrum of human papillomavirus-related dysplasia and carcinoma of the anus in HIV-infected patients. AIDS Read. Feb; 2005 15(2):79–82. 85-6, 88, 91. [PubMed: 15712398]
36. Goldie S, Palefsky JM, Workowsi K. Anal cancer in HIV infection: to screen or not to screen? AIDS Clin Care. Jul; 2004 16(7):53–5. 57. [PubMed: 15300925]
37. Goldie SJ, Kuntz KM, Weinstein MC, Freedberg KA, Palefsky JM. Cost-effectiveness of screening for anal squamous intraepithelial lesions and anal cancer in human immunodeficiency virus-negative homosexual and bisexual men. Am J Med. 2000; 108(8):634–41. [PubMed: 10856411]
38. Division of STD Prevention. CDC Fact Sheet: HPV and Men. U.S. Center for Disease Control and Prevention; Atlanta, GA: 2007. Available from: http://www.cdc.gov/std/hpv/HPV&Men-Fact-Sheet-press.pdf [updated December 2007; cited 2009 April 25]
39. Goldstone SE, Hundert JS, Huyett JW. Infrared coagulator ablation of high-grade anal squamous intraepithelial lesions in HIV-negative males who have sex with males. Dis Colon Rectum. May; 2007 50(5):565–75. [PubMed: 17380365]
40. Wexler A, Berson AM, Goldstone SE, Waltzman R, Penzer J, Maisonet OG, et al. Invasive anal squamous-cell carcinoma in the HIV-positive patient: outcome in the era of highly active antiretroviral therapy. Dis Colon Rectum. Jan; 2008 51(1):73–81. [PubMed: 18066626]
41. Devaraj B, Cosman BC. Expectant management of anal squamous dysplasia in patients with HIV. Dis Colon Rectum. Jan; 2006 49(1):36–40. [PubMed: 16283561]
42. Holton T, Smith D, Terry M, Madgwick A, Levine T. The effect of lubricant contamination on ThinPrep (Cytyc) cervical cytology liquid-based preparations. Cytopathology. Aug; 2008 19(4): 236–43. [PubMed: 18093222]
43. Solomon D, Davey D, Kurman R, Moriarty A, O'Connor D, Prey M, et al. The 2001 Bethesda System: terminology for reporting results of cervical cytology. JAMA. Apr 24; 2002 287(16): 2114–9. [PubMed: 11966386]
44. Arain S, Walts AE, Thomas P, Bose S. The Anal Pap Smear: Cytomorphology of squamous intraepithelial lesions. Cytojournal. Feb 16.2005 2(1):4. [PubMed: 15715910]
45. Fritz, AG. International classification of diseases for oncology: ICD-O. 3rd ed. World Health Organization; Geneva: 2000.
46. Darragh TM, Winkler B. Anal cancer and cervical cancer screening: Key differences. Cancer Cytopathol. 2011; 119(1):5–19. [PubMed: 21319310]
47. SAS Institute Inc. BASE SAS 92 Procedures Guide, Statistical Procedures. 3rd ed. SAS Institute Inc.; Cary: 2010. The FREQ Procedure; p. 63-216.

48. SAS Institute Inc. SAS/STAT 922 User's Guide. SAS Institute Inc.; Cary, NC: 2010. The Logistic Procedure; p. 3861-4100.
49. Obuchowski NA, Lieber ML, Wians FH Jr. ROC curves in clinical chemistry: uses, misuses, and possible solutions. Clin Chem. Jul; 2004 50(7):1118–25. [PubMed: 15142978]
50. Munoz A, Carey V, Taylor JM, Chmiel JS, Kingsley L, Van Raden M, et al. Estimation of time since exposure for a prevalent cohort. Stat Med. May; 1992 11(7):939–52. [PubMed: 1351308]
51. Palefsky, J.; Handley, J. What your doctor may not tell you about HPV and abnormal pap smears. Warner Books; New York, NY: 2002.
52. Nathan M, Singh N, Garrett N, Hickey N, Prevost T, Sheaff M. Performance of anal cytology in a clinical setting when measured against histology and high-resolution anoscopy findings. AIDS. Jan 28; 2010 24(3):373–9. [PubMed: 20057313]
53. Fox PA, Seet JE, Stebbing J, Francis N, Barton SE, Strauss S, et al. The value of anal cytology and human papillomavirus typing in the detection of anal intraepithelial neoplasia: a review of cases from an anoscopy clinic. Sex Transm Infect. Apr; 2005 81(2):142–6. [PubMed: 15800092]
54. Papaconstantinou HT, Lee AJ, Simmang CL, Ashfaq R, Gokaslan ST, Sokol S, et al. Screening methods for high-grade dysplasia in patients with anal condyloma. J Surg Res. Jul 1; 2005 127(1): 8–13. [PubMed: 15964301]
55. Cranston RD, Darragh TM, Holly EA, Jay N, Berry JM, Da Costa M, et al. Self-collected versus clinician-collected anal cytology specimens to diagnose anal intraepithelial neoplasia in HIV-positive men. J Acquir Immune Defic Syndr. Aug 1; 2004 36(4):915–20. [PubMed: 15220697]
56. Chiao EY, Giordano TP, Palefsky JM, Tyring S, El Serag H. Screening HIV-infected individuals for anal cancer precursor lesions: a systematic review. Clin Infect Dis. Jul 15; 2006 43(2):223–33. [PubMed: 16779751]
57. Fahey MT, Irwig L, Macaskill P. Meta-analysis of Pap test accuracy. Am J Epidemiol. Apr 1; 1995 141(7):680–9. [PubMed: 7702044]
58. Darragh TM. Anal cytology for anal cancer screening: is it time yet? Diagn Cytopathol. Jun; 2004 30(6):371–4. [PubMed: 15176021]
59. Manos MM, Kinney WK, Hurley LB, Sherman ME, Shieh-Ngai J, Kurman RJ, et al. Identifying women with cervical neoplasia: using human papillomavirus DNA testing for equivocal Papanicolaou results. JAMA. 1999; 281(17):1605–10. [PubMed: 10235153]
60. Gage JC, Ghosh A, Borgonovo S, Follansbee S, Wentzensen N, Gravitt PE, et al. A comparison of dacron versus Flocked nylon swabs for anal cytology specimen collection. Acta Cytol. 2011; 55(4):364–7. [PubMed: 21791907]
61. Chin-Hong PV, Berry JM, Cheng SC, Catania JA, Da Costa M, Darragh TM, et al. 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. Ann Intern Med. Sep 2; 2008 149(5):300–6. [PubMed: 18765699]
62. Chin-Hong PV, Vittinghoff E, Cranston RD, Browne L, Buchbinder S, Colfax G, et al. Age-related prevalence of anal cancer precursors in homosexual men: the EXPLORE study. J Natl Cancer Inst. Jun 15; 2005 97(12):896–905. [PubMed: 15956651]
63. Palefsky JM. Anal squamous intraepithelial lesions in human immunodeficiency virus-positive men and women. Semin Oncol. 2000; 27(4):471–9. [PubMed: 10950374]
64. Brink AL, du Toit JP, Deale CJ. In search of more representative cervical cytology. A preliminary prospective study. S Afr Med J. Jul 15; 1989 76(2):55–7. [PubMed: 2749424]
65. Dotters DJ, Carney CN, Droegemueller W. Nylon brush improves collection of cervical cytologic specimens. Am J Obstet Gynecol. Oct; 1988 159(4):814–9. [PubMed: 3177528]
66. Rubio CA, Berglund K, Kock Y. Studies on the distribution of abnormal cells in cytologic preparations. IV. Importance of the topographical position of the cells in material collected by wooden spatulas. Gynecol Oncol. Oct; 1980 10(2):146–51. [PubMed: 7007176]
67. Rubio CA, Berglund K, Kock Y, Zetterberg A. Studies on the distribution of abnormal cells in cytologic preparations. III. Making the smear with a plastic spatula. Am J Obstet Gynecol. Aug 1; 1980 137(7):843–6. [PubMed: 6996484]

68. Rubio CA, Kock Y, Berglund K. Studies of the distribution of abnormal cells in cytologic preparations. I. Making the smear with a wooden spatula. Acta Cytol. Jan-Feb;1980 24(1):49–53. [PubMed: 6928335]
69. Rubio CA, Kock Y, Berglund K, Thomassen P. Studies on the distribution of abnormal cells in cytological preparations II. Making the smear with the cotton swab applicator. Gynecol Oncol. Apr; 1980 9(2):127–34. [PubMed: 7189498]
70. Trimbos JB, Arentz NP. The efficiency of the Cytobrush versus the cotton swab in the collection of endocervical cells in cervical smears. Acta Cytol. May-Jun;1986 30(3):261–3. [PubMed: 3521175]
71. Hathaway JK, Pathak PK, Maney R. Is liquid-based pap testing affected by water-based lubricant? Obstet Gynecol. Jan; 2006 107(1):66–70. [PubMed: 16394041]
72. Nielsen A, Munk C, Kjaer SK. Trends in incidence of anal cancer and high-grade anal intraepithelial neoplasia in Denmark, 1978-2008. Int J Cancer. Mar 1; 2012 130(5):1168–73. [PubMed: 21469144]
73. Shiels MS, Pfeiffer RM, Engels EA. Age at cancer diagnosis among persons with AIDS in the United States. Ann Intern Med. Oct 5; 2010 153(7):452–60. [PubMed: 20921544]
74. Alsharif M, McKeon DM, Gulbahce HE, Savik K, Pambuccian SE. Unsatisfactory SurePath liquid-based Papanicolaou tests: causes and significance. Cancer. Feb 25; 2009 117(1):15–26. [PubMed: 19347825]
75. AbdullGaffar B, Kamal MO, Khalid M, Samuel R, AlGhufli R. Lubricant, mucus, and other contaminant materials as a potential source of interpretation errors in ThinPrep cervical cytology. J Low Genit Tract Dis. Jan; 2010 14(1):22–8. [PubMed: 20040832]
76. Hild-Mosley KA, Lindblade JA, Julian TM. The Management of Cervical Mucus in Obtaining a Papanicolaou Smear. Journal of Lower Genital Tract Disease. Jan; 1997 1(1):1–4.
77. Kaslow RA, Ostrow DG, Detels R, Phair JP, Polk BF, Rinaldo CR Jr. The Multicenter AIDS Cohort Study: rationale, organization, and selected characteristics of the participants. American Journal of Epidemiology. 1987; 126(2):310–8. [PubMed: 3300281]

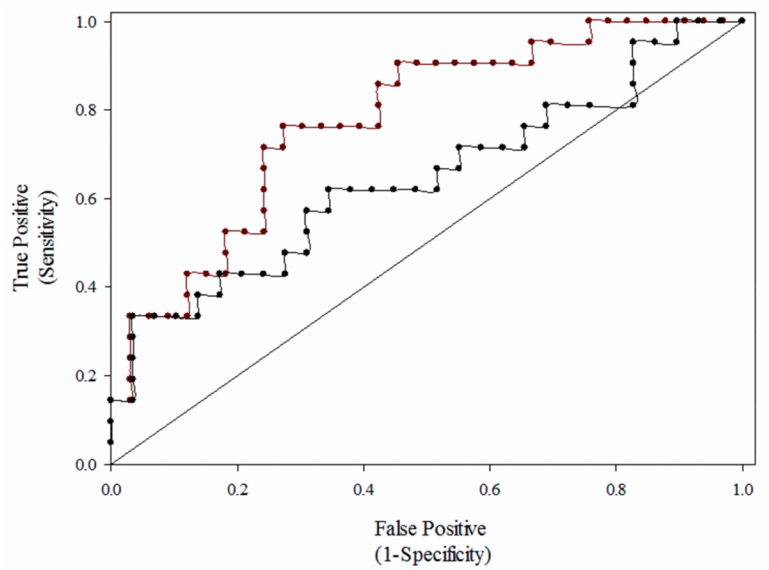

Figure 1.

Comparison of Receiver Operating Characteristic (ROC) Curves for Anal Cytology Showing > Atypical Squamous Cells of Unknown Significance (ASC-US) Using Dacron- (black) and NF-swab (red) Protocols to Predict High Grade Anal Intraepithelial Neoplasia, Adjusted for the Effect of Age and HIV-infection Among 58 MSM (C=0.643 and C= 0.776, respectively).

Table 1

Sociodemographic (n=58) and HIV-infection Characteristics of Study Participants Evaluating NF- and Dacron-swab Anal Cytology Specimen Procedures

	Seropositives N (%)	**Seronegatives N (%)**
Total	42 (72)	16 (28)
Race [a]		
White	36 (86)	13 (81)
Black	3 (7)	0
Other	3 (7)	3 (19)
Hispanic ethnicity	3 (8)	0
Biopsy [a]		
NIL	18 (42.9)	7 (43.8)
LG-AIN	7 (16.7)	5 (31.3)
HG-AIN	17 (40.5)	4 (25.0)
	Mean (SD)	Mean (SD)
Age, years[a]	56.99 (5.7)	60.41 (8.2)
Range	41.2-66.1	39.5-72.0
HIV Infection Characteristics		
Years Duration: HIV infection	25.7 (8.4)	-
Range	0.5 – 34.0	-
Nadir CD4+ before HAART[b,c]	340.9 (208.8)	-
Range	1.0-819.0	-
Slope of CD4+ Counts before HAART	−30.84 (52.06)	-
Nadir CD4+ after HAART[b,c]	284.7 (171.1)	-
Range	10.0-835.0	-
Slope of CD4+ Counts after HAART	27.66 (64.77)	-
HIV-RNA peak after HAART[c]	4.9 (0.7)	-
HIV-RNA Set-Point before HAART[c]	3.8 (0.8)	-
AIDS-Diagnoses		
None	33 (79)	16 (100)
Kaposi's Sarcoma	1 (2)	-
Pneumocystis carinii Pneumonia	2 (4)	-
Cryptosporidiosis	1 (2)	-
Non-Hodgkin's Lymphoma	1 (2)	-
Candida Esophagitis	1 (2)	-
Wasting Syndrome	1 (2)	-
Pulmonary Tuberculosis	1 (2)	-
Multiple AIDS Diagnoses	1 (2)	-

[a] Non-significant (NS) between HIV groups

[b] T-lymphocytes/mm3

[c] $\log_{10}$ transformation

Table 2

Comparison of Dacron- and NF-Swab Cytology Specimen Cytology Results for 58 MSM

		Dacron-swab Unsatisfactory	NIL	ASC-US	ASC-H	LG-SIL	HG-SIL	Total
NF-swab	Unsatisfactory	3	0	1	0	0	0	4
	NIL	4	13	7	0	0	1	25
	ASC-US	0	8	5	0	1	0	14
	ASC-H	0	0	2	0	0	0	2
	LG-SIL	1	4	1	1	1	1	9
	HG-SIL	0	1	0	1	1	1	4
	Total	8	26	16	2	3	3	58

Simple Kappa = 0.11 (−0.08, 0.30), and Weighted Kappa = 0.24 (0.03, 0.46). Including unsatisfactory cytology: Kappa = 0.16 (−0.01, 0.33)

Table 3

Comparison of Dacron- and NF-Protocol Cytology to Histology for 58 MSM Evaluated Using High-Resolution Anoscopy and Biopsy for Histology

	Histology					Histology			
Dacron–Swab Cytology	**Normal (Col %)**	**LG-AIN (Col %)**	**HG-AIN (Col %)**	**Total (Col %)**	**NF-Swab Cytology**	**Normal (Col %)**	**LG-AIN (Col %)**	**HG-AIN (Col %)**	**Total (Col %)**
Unsatisfactory	6(24)	2(17)	0	8 (14)	Unsatisfactory	3 (12)	1 (8)	0	4 (7)
NIL	11(44)	5(42)	10(48)	26 (45)	NIL	16 (64)	5(42)	4 (19)	25 (43)
ASC-US	7(28)	5(42)	4(19)	16 (28)	ASC-US	4 (16)	1 (8)	9 (43)	14 (24)
ASC-H	0	0	2 (10)	2 (3)	ASC-H	0	2 (17)	0	2 (3)
LG-SIL	1(4)	0	2(10)	3 (5)	LG-SIL	2 (8)	3 (25)	4 (19)	9 (16)
HG-SIL	0	0	3(14)	3 (5)	HG-SIL	0	0	4 (19)	4 (7)
Total (Row %)	25(43)	12(21)	21(36)	58(100)	Total (Row %)	25 (43)	12 (21)	21 (36)	58(100)

Sensitivity: 52% (Exact 95% Confidence Interval (CI): 30-74%). Specificity: 58% (CI: 34-80%)

Sensitivity: 81% (CI: 58-95%). Specificity: 73% (CI: 50-89%)

Table 4

Two Multivariate Analyses Evaluating Dacron- and NF-swab Procedures for Predicting HG-AIN on Histology for 58 MSM

	Unadjusted Analyses (95% Confidence Interval)		Adjusted Analyses [a] (95% Confidence Interval)	
Cytology				
Dacron Swab[b]				
NIL	1		1	
≥ASCUS	2.0	(1.0, 4.0)	2.0	(0.9, 4.2)
Nylon-Flocked Swab[b]				
NIL	1		1	
≥ASCUS	2.7	(1.4, 5.3)[b]	3.0	(1.5, 6.2)[c]

[a] Adjusting for the effect of age and HIV infection (infected vs. not).

[b] 8 unsatisfactory Dacron-protocol cytology, n=50; and 4 unsatisfactory NF-protocol cytology, n=54.

[c] $p<0.05$