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Authors

Massad, L Stewart
D'Souza, Gypsyamber
Darragh, Teresa M
et al.

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Accuracy of colposcopy in HIV seropositive and seronegative women with abnormal Pap tests

L. Stewart Massad [a,*], Gypsyamber D'Souza [b], Teresa M. Darragh [c,d], Howard Minkoff [e], Rodney Wright [f], Seble Kassaye [g], Lorraine Sanchez-Keeland [h], Charlesnika T. Evans [i,j]

[a] Department of Obstetrics and Gynecology, Washington University School of Medicine, St. Louis, MO, USA
[b] Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA
[c] Department of Pathology and Obstetrics, University of California, San Francisco, CA, USA
[d] Department of Gynecology and Reproductive Sciences, University of California, San Francisco, CA, USA
[e] Maimonides Medical Center, Brooklyn, NY, USA
[f] Montefiore Medical Center and Albert Einstein College of Medicine, Bronx, NY, USA
[g] Division of Infectious Diseases and Travel Medicine, Department of Medicine, Georgetown University, Washington, DC, USA
[h] University of Southern California, Los Angeles, CA, USA
[i] Department of Preventive Medicine and Center for Healthcare Studies, Northwestern University, Chicago, IL, USA
[j] Department of Veterans Affairs Center of Innovation for Complex Chronic Healthcare, Edward Hines J. VA Hospital, Hines, IL, USA

HIGHLIGHTS

- HIV seropositive women with abnormal cytology have more colposcopic abnormalities than HIV seronegative women.
- HIV seropositive and seronegative women have similar colposcopic findings after controlling for Pap grade and age.
- Agreement between colposcopists' impression and highest grade biopsy diagnosis was only fair and did not differ by HIV serostatus.

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ABSTRACT

Objective. The aim of this study is to compare colposcopic findings and the accuracy of colposcopic impression in HIV seropositive and seronegative women with abnormal Pap tests.

Methods. HIV seropositive and seronegative women in a national cohort study had Pap tests collected every six months, with colposcopy for any abnormal result. Prospectively collected colposcopy and histology findings were analyzed retrospectively using Pearson Chi-square, *t*-test and Wilcoxon two-sample tests, logistic regression models, and Kappa coefficients.

Results. After adjusting for age and Pap result, 1618 eligible HIV seropositive women were more likely than 406 seronegative women to have inadequate colposcopic examinations, abnormal colposcopic findings, and large cervical lesions. However, among those with abnormal colposcopy, colposcopic characteristics and lesion size and number did not differ by HIV serostatus. Agreement between colposcopists' impressions and highest grade biopsy diagnoses was fair (kappa coefficient 0.35, 95% C.I. 0.31, 0.38). Agreement did not differ by HIV serostatus and did not improve with multiple biopsies (weighted kappa coefficient 0.35, 95% C.I. 0.32, 0.39) or after including all histology results over two years following colposcopy.

Conclusion. Although HIV seropositive women with abnormal cytology are more likely to have colposcopic abnormality, the performance of colposcopy appears to be similar to that in HIV seronegative women. Biopsy is required to confirm colposcopic impression.

Introduction

Effective cervical cancer prevention relies on triage of women with abnormal Pap results to treatment or observation using colposcopy. Older studies suggested that colposcopy was highly accurate [1], but recently the accuracy of colposcopy has been challenged [2–8]. Colposcopic accuracy may be age dependent, with older women having

* Corresponding author at: Box 8064, Dept. of ObGyn, Washington University School of Medicine, St. Louis, MO 63110, USA. Fax: +1 314 362 2893.
E-mail address: massadl@wudosis.wustl.edu (L. Stewart Massad).

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thinner and less apparent colposcopic lesions [9,10] Lesions associated with HPV 16 are the most serious but also most apparent colposcopically [11], as are larger lesions and those associated with higher Pap grades [12]. The correlation between colposcopic impression and biopsy grade has been shown to vary by training, being highest in nurse colposcopists and lowest in junior residents [13]. Taken together these studies suggest that colposcopic accuracy is variable and that confirmatory biopsy is usually required to guide management.

The impact of HIV on colposcopic assessment has not been studied. HIV infection leads to impaired cell-mediated immunity, resulting in turn in a higher prevalence of HPV infections [14]. Women with HIV are at high risk for abnormal Pap test results, though most are minor in grade, either atypical squamous cells of undetermined significance (ASCUS) or low grade squamous intraepithelial lesions (LSIL) [15]. A better understanding of the nature of colposcopic findings and the correlation between colposcopic impression and biopsy in women with HIV may improve clinicians' ability to detect premalignant disease in these high risk women, while comparing results to HIV seronegative women may offer insight into whether women with abnormal colposcopy can be managed without confirmatory biopsies regardless of HIV status.

The goals of this study were to describe the colposcopic findings and the correlation between colposcopic impressions and biopsy diagnoses in HIV seropositive women with abnormal Pap tests and to compare those to results from HIV seronegative women, potentially drawing broader conclusions about the accuracy of colposcopy. Our objectives were to explore the colposcopic findings underlying our previous report that correlations between biopsy diagnoses and both cytology result and colposcopic impression are poor while restricting our focus to women with abnormal cytology [16].

Materials and methods

The Women's Interagency HIV Study (WIHS) is an ongoing U.S. multicenter cohort study of health outcomes among HIV seropositive women. The study also enrolled at-risk HIV seronegative comparison women who were frequency matched for demographic and key risk factors, including age, race/ethnicity, level of education, injection drug use since 1978, and total number of sexual partners since 1980. Enrollment began October 3, 1994 at 6 study consortia and over time enrolled 4068 women, including those who were enrolled during expansions from 2001 to 2002 and 2011–2012 in order to ensure that the cohort reflected the U.S. HIV epidemic in women [17,18]. At each site, human subject committees reviewed and approved the study. All participants gave written informed consent for study. Follow up continues, but this analysis includes information on colposcopies done between December 6, 1994 and November 28, 2012

According to study-wide protocol, single-slide conventional Pap smears were obtained every six months using spatula and brush. Smears were read at a central laboratory. Results were reported according to the 1991 Bethesda system for classification of cervicovaginal cytology [19]. HPV tests were performed for research purposes, but results were not available to clinicians for patient management.

To maximize cervical disease ascertainment, the study required colposcopy for any epithelial cytologic abnormality, including ASCUS, and colposcopists were aware of cytology results and HIV serostatus. Colposcopic findings were recorded prospectively, including adequacy of examination, percentage of cervix considered abnormal, and the number of lesions. For recording, a representative diagram of the cervix was divided into eight subquadrants (four quadrants divided into inner and outer portions) and the endocervix, and the number of abnormal subquadrants was recorded. Individual lesions were not graded, but the colposcopic impression of the worst lesion was graded as negative, low grade, high grade, and cancer. The presence or absence of leukoplakia, acetowhite epithelium, punctate and mosaic vascular patterns, and atypical vessels was noted. Colposcopists were selected by study principal investigators and were not credentialed or centrally trained in the use of any specific grading system; image recording for central review of colposcopy impression was not performed. For women with multiple colposcopies, the first colposcopy after abnormal WIHS cytology was analyzed. Colposcopists were identified by initials, and the minimum number of colposcopists involved in study was determined by combining potentially redundant initials (e.g., JS and JFS); information about individual colposcopist training and experience was not available.

Decisions on the number and location of biopsies and subsequent treatments were individualized. Endocervical curettage (ECC) was recommended for all nonpregnant patients. Random biopsies were not required, but acetowhite areas could be biopsied despite a negative colposcopic impression, and some colposcopists might have taken random biopsies on their own initiative. Biopsy results were interpreted at local sites and were not centrally reviewed. Abnormal results were categorized as cervical intraepithelial neoplasia (CIN) grade 1, 2, or 3, adenocarcinoma in situ (AIS), or cancer. Koilocytosis and other condylomatous changes were categorized with CIN1. Unspecified high grade dysplasia was classified with CIN3. For analysis, high grade disease included CIN2, CIN3, and AIS; no cancers were found.

Statistical analyses were performed using SAS software, version 9.3 (SAS Institute Inc, Cary NC). Demographic and clinical characteristics were compared by HIV status in unadjusted analyses using the Pearson Chi-square for categorical variables and *t*-test and Wilcoxon two-sample test for continuous parametric and nonparametric variables. Logistic regression models with odds ratios and 95% Confidence Intervals (CIs) adjusted for Pap result and age were fitted for each categorical colposcopy outcome to assess their association with HIV status. A similar Pap and age adjusted negative binomial model was fit to assess the association between the number of vaginal lesions and HIV status. Correlations between colposcopic impression and biopsy result were assessed using Kappa coefficients and 95% CIs for the overall study sample and also stratified by HIV status where women with negative colposcopy and no biopsy were considered free of disease. The strength of correlation was judged according to criteria of Landis and Koch, with Kappa statistic <0 considered poor, 0–0.20 slight, 0.21–0.40 fair, 0.41–0.60 moderate, 0.61–0.80 substantial, and 0.81–1.00 = almost perfect [20]. Sensitivity, specificity, and positive and negative predictive values were also calculated. Sub-analyses to assess agreement were conducted including assessing only women with adequate colposcopy and assessing only women with biopsies, eliminating the assumption that negative colposcopy because of no biopsy reflected absence of any CIN. In addition, we assessed the correlation of colposcopic impression and cervical histology, incorporating all histology results within two years of initial colposcopy using Kappa coefficients and 95% CIs. All statistical tests were significant at the <0.05 level.

Results

The derivation of the study group from the 2050 WIHS participants having a first colposcopy for abnormal Pap result is shown in Fig. 1. After exclusions, the study group was composed of 2024 women. Of these, 1618 were HIV seropositive and 406 seronegative, reflecting the higher frequency of Pap abnormality among HIV seropositive women [15] and the weighting of the WIHS cohort toward HIV seropositive women.

The demographic and clinical characteristics of these women are shown in Table 1. Cytologic abnormalities at the visit before colposcopy were more severely abnormal among seropositive than seronegative women, but most were atypical or low grade in both groups. HIV seropositive women also were older at the time of the abnormal Pap leading to colposcopy (median age 37.3 vs 34.7 years, $P < 0.001$) and were less likely to have five or more lifetime partners, with fewer partners since the last visit. Among HIV seropositive women, the median HIV RNA level was 6300 copies/ml and the median CD4 cell count 346/μl. HIV seropositive women had a shorter time to colposcopy after abnormal

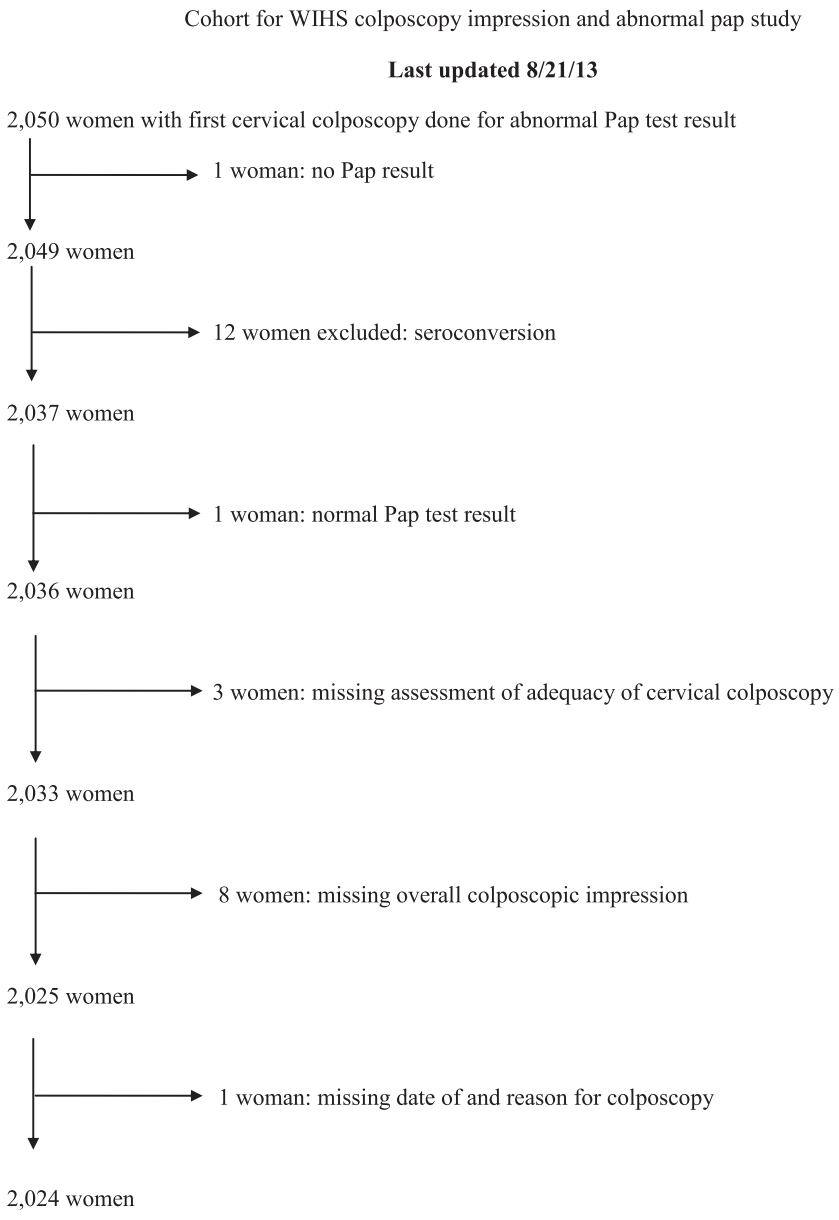

Fig. 1. Derivation of the study group from women having cervical colposcopy for first abnormal Pap result.

cytology (mean = 87 days, SD 207 days, median = 52 days) than HIV negative women (mean = 121 days, SD 298 days, median = 55 days, P = 0.04 by Wilcoxon two sample test).

Colposcopies were performed by at least 131 individual colposcopists, including physicians and advanced practice clinicians. We compared colposcopic findings among the HIV seropositive and seronegative women after adjustment for Pap result and age (Table S1). HIV seropositive women were more likely to have inadequate colposcopic examinations (635 (40%) vs 97 (24%), O.R. 1.95, 95% C.I. 1.51, 2.51, P < 0.0001) and a colposcopic impression other than normal (885 (55%) vs 175 (43%), O.R. 1.65, 95% C.I. 1.31, 2.08, P < 0.0001). HIV seropositive women also were more likely to have acetowhite changes (732 (45%) vs 154 (38%), O.R. 1.35, 95% C.I. 1.08, 1.69, P = 0.004), although vascular changes of punctation, mosaicism, and atypical vessels did not differ by serostatus. HIV seropositive women were more likely to have larger lesions, with 18% of seropositive women having colposcopic abnormalities covering more than 25% of the cervix compared to 12% of seronegative women (P = 0.003). Endocervical lesions were seen in 13.7% of HIV seropositive women and 10.8% of seronegative women (P = 0.22).

Different trends emerged when we assessed findings only among women with abnormal colposcopy (Table S2). When compared to HIV seronegative women and after adjusting for Pap grade and age, HIV seropositive women with abnormal colposcopy did not have more condylomas or lesions or more cervical subquadrants involved and were not more likely to have larger lesions. They also were not more likely to have acetowhite epithelium, vascular mosaic or punctation, or atypical vessels.

Biopsies were done in 855 (42%) women; colposcopic impression was negative with no biopsy collected in 1169 (58%) women. Among 1618 HIV seropositive women, 948 biopsies were done (mean 0.59/colposcopy), with a mean of 1.35 biopsies/colposcopy among women with at least one biopsy. Among 406 HIV seronegative women, 189 biopsies were done (mean 0.47/colposcopy), with a mean of 1.25 biopsies among women with at least one biopsy. The highest grade biopsy results across 855 individual colposcopic examinations included no

Table 1
Demographic characteristics of the 2024 women in the study group. n (%).

Characteristics	No. (%)			P-value[a]
	Overall N = 2024	HIV seropositive N = 1618	HIV seronegative N = 406	
Antecedent Pap result				<0.0001
ASCUS[b]	1444 (71.3)	1092 (67.5)	352 (86.7)	
LGSIL[c]	513 (25.4)	472 (29.2)	41 (10.1)	
HGSIL[d] or cancer	50 (2.5)	45 (2.8)	5 (1.2)	
Glandular abnormality[e]	17 (0.8)	9 (0.5)	8 (2.0)	
Age at Pap visit (years) mean, median	37.2, 36.8	37.7, 37.3	35.0, 34.7	<0.0001[f], <0.0001[f]
Race, %(n)				0.14
White, non-Hispanic	263 (13.0)	221 (13.7)	42 (10.3)	
Hispanic	525 (25.9)	419 (25.9)	106 (26.1)	
Black, non-Hispanic	1168 (57.7)	929 (57.4)	239 (58.9)	
Other	68 (3.4)	49 (3.0)	19 (4.7)	
Smoking status				0.6608
Never smoked	630 (31.2)	496 (30.7)	134 (33.0)	
Current smoker	1029 (50.9)	827 (51.2)	202 (49.8)	
Future smoker	363 (18.0)	293 (18.1)	70 (17.2)	
Highest level of education				0.0741
No school	10 (0.5)	9 (0.6)	1 (0.3)	
Grades 1–6	82 (4.1)	77 (4.8)	5 (1.2)	
Grades 7–11	688 (34.0)	547 (33.9)	141 (34.8)	
Completed HS	626 (31.0)	498 (30.8)	128 (31.6)	
Some college	490 (24.3)	388 (24.0)	102 (25.2)	
Completed 4 years college	97 (4.8)	76 (4.7)	21 (5.2)	
Attended/completed grad school	28 (1.4)	21 (1.3)	7 (1.7)	
Number of lifetime sex partners at study entry				0.019
None	8 (0.4)	8 (0.5)	0 (0)	
1–4	741 (36.7)	611 (37.9)	130 (32.1)	
5 or more	1268 (62.9)	993 (61.6)	275 (67.9)	
Number of male sex partners since last visit (mean, median)	1.54, 1.0	1.45, 1.0	1.90, 1.0	
HIV viral load, copies/ml (mean, median)		11,7641, 6300		
CD4 count, cells/μl (mean, median)		385, 346		0.3440[g], <0.0001[f]

Missing data: age at baseline visit, n = 0; smoking status, n = 2; education, n = 3; lifetime sexual partners at baseline, n = 7; number of female sex partners, n = 5, number of male sex partners, n = 7; HIV viral load, n = 53; CD4n, n = 49.
[a] By Pearson chi-square test.
[b] Atypical squamous cells of undetermined significance. Includes 25 women (14 HIV positive, 11 HIV negative).women with ASC cannot exclude high grade intraepithelial lesion.
[c] Low grade squamous intraepithelial lesion.
[d] High grade squamous intraepithelial lesion.
[e] Includes atypical glandular cells and adenocarcinoma in situ with normal squamous cells. An additional eight women had glandular abnormalities with squamous abnormalities (5 ASC, 1 LSIL, 2 HSIL).
[f] By Wilcoxon two-sample test for medians.
[g] By TTest p-value for means.

lesions in 408 (47.7%), low grade lesions in 348 (40.7%), and high grade lesions in 99 (11.6%). Compared to seronegative women, HIV seropositive women were more likely to have biopsies (43.5% vs 37.2%, P = 0.02). Of the 704 HIV seropositive women who had biopsies, 341 had no lesions (48.4%), 275 (39.1%) had low grade lesions, and 88 (12.5%) had high grade lesions or cancer. Among 151 HIV seronegative women with biopsies 67 (44%) had no lesions, 73 (48%) had low grade lesions, and 11 (7%) had high grade lesions.

We assessed the level of agreement between colposcopists' impressions and highest grade colposcopic biopsy diagnoses. Biopsies were done for 177 (13%) of 1305 women with negative colposcopic impression, including CIN1 in 65 (37%), CIN2 in 10 (6%), CIN3 in 4 (2.3%), and no AIS or cancer. Agreement between colposcopic impression and biopsy diagnosis was fair, based on a kappa coefficient of 0.35 (95% C.I. 0.31, 0.38). A weighted kappa coefficient yielded only a marginally better result (0.39 with 95% C.I. 0.35, 0.42). As shown in Table 2, only 14 (1%) of 1305 women with a negative colposcopic impression had high grade disease on biopsy. Only 45 (3%) of 1577 women with no biopsy-confirmed lesion had a high grade colposcopic impression. Taking multiple biopsies did not improve agreement (kappa 0.33, 95% C.I. 0.29, 0.37) and weighted kappa coefficient 0.38 (95% C.I. 0.33, 0.42). Similar results also were found when analysis was restricted to 1618 HIV seropositive women only, with a kappa correlation coefficient of 0.34 (95% C.I. 0.30, 0.38) and a weighted kappa coefficient of 0.38 (95% C.I. 0.33, 0.42). Similar results also were found when analysis was restricted to 1274 women with adequate colposcopy (kappa 0.37, 95% C.I. 0.32, 0.42, weighted kappa 0.41, 95% C.I. 0.36, 0.46), or when only HIV seropositive women with adequate colposcopy were considered (not shown). All of the above analyses were also evaluated separately for HIV seronegative women, and findings did not differ between HIV seropositive and HIV seronegative women (data not shown).

Correlation between colposcopic impression and biopsy result was slight when we limited assessment of the correlation between colposcopic impression and biopsy result to women with biopsies, eliminating the presumption that negative colposcopy but no biopsy

Table 2
Correlation between colposcopic impression and highest grade colposcopic biopsy for all women. Women with negative colposcopy and no biopsy were considered negative.

Colposcopic impression	Final result[a]			
	Negative	Low grade[b]	High grade[c]	Total
Negative[d]	1195 (91.6)	97 (7.4)	13 (1.0)	1305
Low grade	337 (55.4)	214 (35.2)	57 (9.4)	608
High grade	45 (40.5)	37 (33.3)	29 (26.1)	111
Total	1577	348	99	2024
Sensitivity			29/99 = 29%	
Specificity	1843/1925 = 96%			

Kappa correlation coefficient 0.35, 95% CI 0.31–0.38.
[a] Women with negative colposcopy and no biopsy were considered negative.
[b] Cervical intraepithelial neoplasia grade 1 (CIN1) or condyloma.
[c] CIN2, CIN3, or adenocarcinoma in situ. No invasive cancers were found.
[d] Includes non-neoplastic benign changes.

reflected absence of any CIN (kappa coefficient for all women 0.11, 95% C.I. 0.06, 0.17, with weighted kappa coefficient 0.16, 95% C.I. 0.11, 0.22). Correlation was slight regardless of HIV serostatus, though significantly worse for HIV seronegative women (kappa coefficient for HIV seropositive women 0.14, 95% C.I. 0.08, 0.20, with weighted kappa coefficient 0.18, 95% C.I. 0.12, 0.24; kappa coefficient for HIV seronegative women 0.02, 95% C.I. −0.12, 0.16, with weighted kappa coefficient 0.10, 95% C.I. −0.04, 0.24.)

Some cervical precancers may be colposcopically inapparent at initial Pap abnormality yet become visible over time. To further explore the accuracy of colposcopy, we assessed the correlation of colposcopic impression with cervical histology, incorporating all histology results within two years of initial colposcopy. This led to greater detection of abnormality, with low grade disease found in 560 (28%) and high grade disease in 267 (13%) of 2024 women. These included 296 (23%) with low grade disease and 94 (7%) with high grade disease among 1305 women with initial negative colposcopy. Although colposcopic impression was significantly associated with biopsy ($P < 0.0001$ by test of symmetry), the simple kappa correlation between colposcopic impression and these long-term results was 0.24, with the weighted kappa coefficient 0.28, indicating only fair agreement.

Using data in Table 2, we further assessed the accuracy of a high grade colposcopic impression for predicting high grade disease identified at colposcopy, assuming negative colposcopy without biopsy reflected no disease. Sensitivity was 29/99, or 29%. Specificity was 1843/1925, or 96%. Positive predictive value was 29/111, or 26%. Negative predictive value was 1843/1913, or 96%. Using a low grade colposcopic impression improved sensitivity to 86/99 (87%).

Discussion

For both HIV seropositive and seronegative women, the correlation between colposcopic impression and biopsy result was only fair to slight. The correlation between colposcopy and biopsy did not improve when adjusted for biopsy number or after results were restricted to women with adequate colposcopic exams. The sensitivity of a colposcopic impression of high grade disease for a high grade biopsy result was only 29%, despite our assumption that negative colposcopy reflected absence of disease; true sensitivity may be substantially lower. Specificity and negative predictive value were high, however.

Data on the accuracy of colposcopy in HIV seropositive women with abnormal cytology are limited. Kitchener and colleagues found that a low grade colposcopic impression had 98% sensitivity and 63% specificity with a positive predictive value of 22% among HIV seropositive women [21]. Differences may reflect variations in colposcopic skills or differences in lesion size arising from differences in the threshold for colposcopy.

In this study, HIV seropositive women with abnormal cytology were more likely to have abnormal colposcopy than similar seronegative women. However, when colposcopy was abnormal, findings did not appear to differ by HIV serostatus. Colposcopy is recommended for all U.S. HIV seropositive women with abnormal cytology. Because they have a higher risk of abnormal Pap results than seronegative women [15], the burden of colposcopy will be greater for them, and more will require biopsy.

Strengths of this study include the large number of colposcopists and of HIV seropositive and seronegative women, and the multi-institutional nature of the study, which lend generalizability to results. Our study was limited by several factors. Colposcopists' skills and experience were not assessed, and we did not impose formal common colposcopic grading criteria or require colposcopy training or certification. However, our study combines results from more than 130 individual colposcopists, including a range of training from nurse colposcopists to gynecologic oncologists, so our results should reflect common U.S. standards. We assumed that negative colposcopy reflected absence of significant lesions. Verification bias might have caused us to overestimate the accuracy of colposcopic impression, but this would reinforce our conclusion about the importance of biopsy confirmation. The number of biopsies per patient was relatively low, as most were performed prior to studies showing the value of multiple biopsies. Random biopsies were not done but might have identified disease in colposcopically normal cervices. Including cervical histology results from within two years of colposcopy increased the number of high grade lesions found but did not meaningfully change correlations between colposcopic impression and biopsy.

Compliance with recommended colposcopy was sometimes delayed. Different results might have been found had colposcopy occurred consistently within weeks of an abnormal Pap result. Although time between cytology and colposcopy was about a month longer for HIV seronegative women, relatively brief delays are unlikely to have influenced findings. Colposcopists were not blinded to HIV serostatus and might have sought lesions more assiduously in HIV seropositive women.

Although we controlled for Pap results in our comparisons, we did not have data on cytology or colposcopy results or cervical treatments prior to WIHS initiation, and HIV seropositive women in particular may have had persisting abnormalities that led to a greater likelihood of abnormal colposcopy than seronegative women with transient HPV infections. Our data are focused on initial WIHS colposcopy, and it is unclear whether colposcopy is sufficiently sensitive to detect the development of CIN3 in previously biopsied CIN1 lesions being observed without treatment. We have shown that progression of CIN1 is unusual, even in HIV seropositive women [22], but prospective studies are needed to assess the performance of colposcopy in detecting progression.

HIV seropositive women may begin cervical cancer screening in their teens, but relatively few young women were included in WIHS. Our results suggest that HIV infection does not change colposcopic characteristics, though it increases the frequency of abnormal colposcopy for each grade of cytologic abnormality. The performance of colposcopy should be similar in young women, and we have shown that colposcopy effectively detected high grade cervical disease in HIV seropositive women ages 20 and younger at a rate three times greater than that among HIV seronegative women of similar age [23].

The paucity of abnormal cytology among HIV seronegative women limited our ability to make subgroup comparisons by serostatus. We did not have all biopsies centrally reviewed, but the range of sites participating should have resulted in diagnostic accuracy similar to that seen nationally.

Finally, only 2.5% of women in our study had high grade cytology. Our results may not be generalizable to women with high grade cytology results, and treatment based on colposcopic impression may be sufficient for those women. This may be particularly so when treatment is excisional, providing a specimen for histologic assessment.

These findings are similar to those reported in studies of U.S. women presumably not infected with HIV. In the ASCUS/LSIL Triage Study, more than 40% of women who developed CIN2+ over 2 years after an initial Pap abnormality did not have their disease detected at entry colposcopic exam [2,3] and interobserver variation in assessing colposcopic findings was high [4]. In a different study, expert colposcopists presented an overlapping set of colposcopic images disagreed about the presence and grade of lesions [5] and of colposcopic findings [6]. An Italian group found that colposcopists agreed on the presence or absence of cervical abnormality but not about specific colposcopic findings; the sensitivity of a high-grade colposcopic impression for high grade CIN was only 54% [7]. Areas of the cervix that colposcopists identified as having the worst lesion among women presenting for LEEP had no high grade disease 33% of the time, while 40% of biopsies taken from colposcopically normal areas in these women had CIN2+ [8]. A previous WIHS study had shown that agreement between colposcopic impression and biopsy was poor, but that study included women having colposcopy for reasons other than abnormal cytology, such as visible genital warts, and it did not explore differences in lesion number, size, or appearance by HIV

serostatus [16]. Again, contrary results have been published from Britain, including a finding that the three-year negative predictive value of an adequate, negative colposcopic impression for absence of CIN2 or worse among women with HPV-positive low-grade cytological abnormalities and in the NHS Cervical Screening Programme in England was only 4% [24]. Differences between U.S. and U.K. reports of colposcopic accuracy may reflect differences in training, with colposcopy centralized to expert centers in the U.K. and also may reflect differences in the referral threshold for colposcopy, with earlier referral more likely to result in smaller lesions being missed.

Colposcopy is changing as a result of new screening guidelines and HPV vaccination. The impact of these factors is unclear. Later initiation of screening and longer screening intervals should allow persistent lesions to become more prominent colposcopically. On the other hand, HPV vaccination should result in reduction in the proportion of cytologic abnormalities resulting from infection by HPV types 16 or 18, reducing the prominence of lesions [11]. For now, the performance of colposcopy in HIV seropositive women appears similar to that reported in other populations. Although we did not show an impact of biopsy number on colposcopic–histologic correlation, the sensitivity of colposcopy is high when all acetowhite lesions are biopsied [25], and maximal detection of CIN among both HIV seropositive and seronegative women with borderline cytologic abnormalities may require 3–4 biopsies including endocervical curettage for women with unsatisfactory colposcopy [26]. The role of random biopsy remains unclear. When combined with directed biopsies, colposcopy remains an important diagnostic tool for the management of cervical abnormalities among HIV seropositive women. However, biopsy confirmation of disease should precede treatment for both HIV seropositive and seronegative women with ASCUS or LSIL cytology. Better training and skills certification by national professional organizations using adjudicated images and cytohistologic correlation may be required to improve colposcopic accuracy.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ygyno.2014.08.007.

Disclosure of interests

Dr. Darragh is the only co-author who notes potential conflicts. These include:

Hologic: Research supplies for anal cytology, honorarium for webinar on anal cancer screening, October 2012

OncoHealth Advisory Board, Stock options, ongoing

Roche, October 2013: Honorarium paid to UCSF, October 2013.

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