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# Changes in knowledge of cervical cancer following introduction of human papillomavirus vaccine among women at high risk for cervical cancer

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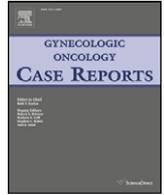
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## Survey Article

## Changes in knowledge of cervical cancer following introduction of human papillomavirus vaccine among women at high risk for cervical cancer



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## ABSTRACT

**Purpose:** To describe changes in knowledge of cervical cancer prevention, human papillomavirus (HPV), and HPV vaccination among women at high risk for cervical cancer in the first five years after introduction of HPV vaccination.

**Methods:** In 2007, 2008–9, and 2011, women in a multicenter U.S. cohort study completed 44-item self-report questionnaires assessing knowledge of cervical cancer prevention, HPV, and HPV vaccination. Results across time were assessed for individuals, and three study enrollment cohorts were compared. Knowledge scores were correlated with demographic variables, measures of education and attention, and medical factors. Associations were assessed in multivariable models.

**Results:** In all, 974 women completed three serial questionnaires; most were minority, low income, and current or former smokers. The group included 652 (67%) HIV infected and 322 (33%) uninfected. Summary knowledge scores (possible range 0–24) increased from 2007 (12.8, S.D. 5.8) to 2008–9 (13.9, S.D. 5.3,  $P < 0.001$ ) and to 2011 (14.3, S.D. 5.2,  $P < 0.0001$  vs 2007 and  $< 0.04$  vs 2008–9). Higher knowledge scores at first and follow-up administration of questionnaires, higher income, and higher education level were associated with improved knowledge score at third administration. Women not previously surveyed had scores similar to those of the longitudinal group at baseline.

**Conclusion:** Substantial gaps in understanding of HPV and cervical cancer prevention exist despite years of health education. While more effective educational interventions may help, optimal cancer prevention may require opt-out vaccination programs that do not require nuanced understanding.

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## Introduction

Indigent and minority women and those with multiple sexual partners are at particular risk for cervical cancer. These are also risk factors for infection with the human immunodeficiency virus (HIV), making HIV seropositivity a useful marker for cervical cancer risk. HIV increases HPV infections, abnormal Paps, and cervical cancer (Massad et al., 2008). Screening and precursor treatment reduce cancer risk even for

women with HIV (Massad et al., 2009). However, cervical cancer prevention is complex, involving HPV vaccination, screenings, triage with HPV tests and colposcopy, and therapy. High risk women including those with HIV are often noncompliant (Cejtin et al., 1999). Understanding what women with HIV know about cervical cancer prevention may offer insights into how educational efforts might target high risk women.

Previous research involving a national cohort of women with HIV and comparison HIV-uninfected women demonstrated knowledge gaps related to risk factors for and consequences of HPV infection. These women also have limited understanding of cervical cancer prevention methods (Massad et al., 2010a, 2010b). Knowledge correlated

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with HIV seropositivity, white ethnicity, higher income, more education, better reading skills, and prior abnormal Pap (Massad et al., 2010a). Knowledge had little impact on colposcopy compliance (Massad et al., 2012), perhaps because knowledge remained suboptimal despite improving after an educational intervention (Massad et al., 2010b).

Since vaccine introduction in 2006, marketing and media coverage have exposed many U.S. women to information about cervical cancer, HPV, and HPV vaccination (Kelly et al., 2009; Gottlieb, 2013), but the impact of these messages on high risk women is unclear. This analysis extends prior research by exploring trends over time in knowledge and attitudes. In addition, we assessed knowledge in a cohort of women without prior experience with our questionnaire enrolled after HPV vaccine release.

## Methods

This investigation was a part of the Women's Interagency HIV Study (WIHS), an ongoing U.S. multicenter prospective cohort investigation of HIV infection among HIV seropositive women and seronegative comparison women at risk for HIV. Protocols, recruitment processes, procedures, and baseline results have been described (Barkan et al., 1998; Bacon et al., 2005). Enrollment began with 2623 women in 1994–5 at 6 study consortia (Bronx, Brooklyn, Chicago, Los Angeles, San Francisco, and Washington, D.C.). To remain reflective of the demographics of the U.S. HIV epidemic, the cohort was expanded by 1143 additional women during 2001–2002 (Bacon et al., 2005) and by 371 more in 2011–2012. This analysis compares information from three cross-sectional questionnaires administered in English April–October, 2007 (baseline), October, 2008–April, 2009 (follow-up), and April–October, 2011 (third administration). Results of the first two iterations have been described (Massad et al., 2009, 2010b). Following baseline administration, women were provided with correct answers and explanations as an educational intervention to assess its impact on knowledge.

The 44-item questionnaire included items related to knowledge of HPV, cervical cancer risks, HPV vaccine, and abnormal Pap tests. A change score analysis, using the paired *t*-test, was conducted to assess whether and to what extent individual knowledge scores improved between baseline and follow-up. Analysis of covariance models examined change in knowledge between baseline and follow-up. Independent variables included baseline score, HIV status, and demographic and medical characteristics including age at questionnaire administration, ethnicity, education by study entry, and household income. Each variable was evaluated for fit using the type III SS value and *p*-value and was included in analyses if *p*-value < 0.05. Final models used the PROC Generalized Linear Models (GLM) procedure in SAS software 9.2 (SAS Institute Inc., Cary, NC). A separate analysis was conducted on only the third survey administration to evaluate for knowledge differences among recruitment waves. Chi-square tests compared recruitment cohorts by knowledge questions and final models were fit using similar techniques for the longitudinal analysis including recruitment wave as an independent variable.

## Results

Of 1451 women completing questionnaires in 2007, 974 (67%) completed three serial questionnaires. Of these, 652 (67%) were completed by HIV seropositive and 322 (33%) by seronegative women. Risk factors for cervical cancer including minority ethnicity, low annual income, and current or former smoking history were present in the majority of participants (Table 1). When compared to HIV seronegative women, HIV seropositive women were older, more likely to be non-Hispanic white, and less likely to currently use alcohol, tobacco, or drugs.

Individual component results of questionnaires across the three recruitment waves are presented in Tables 1–3, Supplemental digital content. Mean knowledge scores increased across administrations,

**Table 1**

Baseline demographic and medical characteristics of women who completed questionnaires at three consecutive surveys (n = 974). n (%).

	HIV + N = 652	HIV – N = 322	P-value <sup>a</sup>
Age at baseline interview (years)			
<30	5 (0.8)	30 (9.3)	<0.0001
30–39	116 (17.8)	85 (26.4)	
40–49	268 (41.1)	110 (34.2)	
50+	263 (40.3)	97 (30.1)	
Ethnicity			
Non-Hispanic African American	418 (64.1)	205 (63.6)	0.0054
Hispanic	115 (17.7)	78 (24.2)	
Non-Hispanic White	94 (14.4)	25 (7.8)	
Other	25 (3.8)	14 (4.4)	
Average annual household income (n = 941)			
≤\$6000	78 (12.3)	59 (19.3)	0.0011
\$6001–\$12,000	224 (35.3)	77 (25.2)	
\$12,001–\$18,000	69 (10.8)	45 (14.7)	
\$18,001+	264 (41.6)	125 (40.8)	
Education level (n = 973)			
Less than high school	213 (32.7)	109 (34.0)	0.3743
Completed high school	201 (30.8)	109 (34.0)	
Some college/college degree	238 (36.5)	103 (32.0)	
Site/location			
Bronx	101 (15.5)	60 (18.6)	0.0017
Brooklyn	201 (30.8)	69 (21.4)	
Washington DC	97 (14.9)	44 (13.7)	
Los Angeles	72 (11.0)	58 (18.0)	
San Francisco	87 (13.4)	54 (16.8)	
Chicago	94 (14.4)	37 (11.5)	
Alcohol use			
Abstainer	371 (56.9)	133 (41.3)	<0.0001
Light (<3 drinks/week)	200 (30.7)	111 (34.5)	
Moderate/heavy (3+ drinks/week)	81 (12.4)	78 (24.2)	
Current smoker			
Current user	235 (36.0)	143 (44.4)	0.0197
Former user	226 (34.7)	107 (33.2)	
Never	191 (29.3)	72 (22.4)	
Injection drug use status			
Current user	4 (0.6)	8 (2.5)	0.0361
Former user	42 (6.5)	24 (7.5)	
Never	606 (92.9)	290 (90.0)	
Non-injection drug use status			
Current user	119 (18.3)	94 (29.2)	<0.0001
Former user	242 (37.1)	132 (41.0)	
Never	291 (44.6)	96 (29.8)	
Lifetime nadir CD4 lymphocyte count (cells/mm <sup>3</sup> ) (n = 626)			
<200	200 (32.0)		
200–500	349 (55.7)		
>500	77 (12.3)		
CD4 lymphocyte count (cells/mm <sup>3</sup> ) at visit (n = 642)			
<200	75 (11.7)		
200–500	197 (30.7)		
>500	370 (57.6)		

<sup>a</sup> By chi-square test.

from 12.8 (S.D. 5.8) at baseline to 13.9 (5.3) at follow-up (*P* < 0.0001) to 14.3 (S.D. 5.2) at third administration (*P* < 0.0001 vs baseline and <0.04 vs follow-up). As scores are out of a possible 24, even improved later scores reflect limited knowledge. Lower baseline scores of HIV seronegative women (11.7 with S.D. 6.0) versus HIV seropositive women (13.3 S.D. 5.7, *P* < 0.0001) were eliminated by the third questionnaire administration (13.9 with S.D. 5.3 among HIV uninfected vs 14.4 with S.D. 5.1 among HIV infected women, *P* = 0.12). No improvement in knowledge of HPV vaccine, its indications, or its target population was observed between the follow-up and third questionnaire administrations. Although small increases in knowledge were seen, at the third questionnaire administration only 56% of all women studied knew that Pap testing checked the cervix, 46% knew it should be repeated at 1–3 year intervals for women with HIV. In contrast, 83% of all women studied knew that annual Pap testing was indicated for women with

HIV and prior negative screening, 79% knew that Pap testing checks for precancer and cancer, 74% knew that HPV is a sexually transmitted virus that causes genital warts and cancers, and 78% knew that women with HPV are at higher risk for cancer. These results were minimally changed from the follow-up administration of the questionnaire.

Independent factors associated with an improvement in knowledge score at the third, previously unreported administration of the survey included higher knowledge scores at first and follow-up administration of questionnaires, higher income, and higher education level (Table 2). There was also a significant difference in knowledge score by site. R-squared for this model was 0.35, indicating that these factors explained approximately one third of the magnitude of change. HIV status was not significant after controlling for these factors, nor was drug use.

A cross-sectional analysis of the third administration of the survey evaluated knowledge among women in a recently enrolled cohort. The survey was completed by 1968 women (979 cohort 1, 734 cohort 2, 255 cohort 3). Overall there was a higher percentage of HIV seropositive women in the third compared to the first and second cohorts (82.5% vs 74.6% and 63.5%,  $P < 0.0001$ ). The average age in the first, second and third cohorts respectively were 51.4, 41.1, and 44.1 years. In addition, compared to the first and second cohorts, the third cohort was more likely to be non-Hispanic African-American, to have lower income, to report alcohol or drug use, and to be a current smoker. There also were differences in CD4 counts below 200 cells/mm<sup>3</sup>: cohort 1, 63.4%, cohort 2, 22.3%, cohort 3, 30.5%,  $P < 0.0001$ . Although mean scores did not differ between first and second enrollment cohorts (14.0 (S.D. 5.2) vs 13.8 (5.4),  $P = 0.27$ ), scores were lower for the third (12.5 (5.8),  $P = 0.0001$  vs the first cohort and  $P = 0.002$  vs the second cohort). Specific differences among cohorts are presented in Tables 1–3 of Supplemental digital content, but differences were present across all components of the questionnaire. Only 50–60% of women in all cohorts believed cervical cancer is preventable. Only about 60% of women in the first and second cohorts said that they had heard of the HPV vaccine (Table 3, Supplemental digital content), although all had been informed during previous iterations of the questionnaire; only 43% of women in the third cohort said that they had heard of the HPV vaccine ( $P < 0.0001$ ). Despite this, some three fourths of all cohorts knew that the HPV vaccine was targeted to adolescents

and teens. Furthermore, 71% of both the first and second enrollment cohorts knew that the vaccine prevented abnormal Pap tests and cervical precancer and cancer, though only 62% of women in the third cohort knew this ( $P = 0.01$ ). A multivariable model demonstrated that being in the first or second recruitment cohort wave was associated with a higher knowledge score compared to those recruited in the last wave. In addition, being HIV positive or a former or current drug user, younger age, having a higher income or education level, and being a white non-Hispanic respondent was associated with higher knowledge scores (Table 2).

## Discussion

Cervical cancer disproportionately afflicts poor and minority U.S. women, largely because they fail to receive screening. HPV vaccination lowers risk, but the U.S. vaccination program requires parents to elect vaccination for their children, which in turn requires understanding of risks and indications.

Among women at high cervical cancer risk, knowledge of cervical cancer prevention has improved, but gaps remain. Women newly enrolled into our cohort had knowledge scores lower than those of previously enrolled women but similar to baseline scores in prior cohorts, as previous administrations of the questions and an educational intervention involving provision of their answers improved knowledge (Massad et al., 2010b). Nevertheless, appreciation of cervical cancer prevention processes among similar women outside the study is likely to be less than optimal to support informed screening compliance and election of HPV vaccination for themselves and their children.

Our results are similar to others', though our study includes longitudinal results. Kelly and colleagues showed that despite a sharp increase in knowledge of the link between HPV and cervical cancer after vaccine introduction, knowledge leveled off below 60% (Kelly et al., 2009). Joseph and associates found that only half of low-income women surveyed in 2007–2012 knew that HPV causes cervical cancer and that knowledge deficits were greater among minority women (Joseph et al., 2014). Strohl et al. found low knowledge scores among Chicago African American women (Strohl et al., 2014).

**Table 2**

Analysis of Covariance Models assessing factors associated with cervical cancer prevention knowledge score at third survey administration among high risk women. Both models controlled for study site.

	Model for women completing all 3 survey administrations N = 974	Model for women who completed the third survey administration N = 1968
Adjusted R <sup>2</sup>	0.35	0.10
F-value	46.98***	18.2***
Predictor variables		
Intercept	8.94 (7.47, 10.40)***	15.69 (14.60, 16.79)
Total baseline score (1st)	0.27 (0.22, 0.33)***	
Total follow-up score (2nd)	0.28 (0.22, 0.34)***	
Recruitment cohort (vs 3rd cohort)		
Cohort 1		1.12 (0.36, 1.88)**
Cohort 2		0.96 (0.20, 1.71)*
HIV seropositive (vs negative)	−0.18 (−0.75, 0.39)	0.52 (−0.003, 1.03)
Age less than 50 (vs 50+ years)		0.71 (0.17, 1.24)**
Ethnicity (vs White NH)		
Non-Hispanic African American		−1.76 (−2.52, −1.00)***
Hispanic		−1.50 (−2.36, −0.64)***
Other		−1.61 (−2.95, −0.27)**
Education (vs College)		
Less than high school	−0.88 (−1.57, −0.18)*	−2.61 (−3.20, −2.03)***
Completed high school	−0.10 (−0.76, 0.57)	−0.96 (−1.55, −0.37)***
Income < \$18,000 (vs > \$18,000)	−0.82 (−1.41, −0.24)**	−1.27 (−1.79, −0.75)***
Drug use (vs never)		
Former user		0.85 (0.30, 1.39)**
Current user		0.61 (−0.01, 1.22)

\*  $p < 0.05$ .

\*\*  $p < 0.01$ .

\*\*\*  $p < 0.0001$ .

U.S. HPV vaccination rates are suboptimal, and African-American adolescents and young uninsured women are less likely to be vaccinated (Pierce Campbell et al., 2012). Inadequate appreciation of vaccine benefits and risks pose a barrier to vaccination (Donadiki et al., 2014). Messages targeted to poor and minority women are needed to improve vaccination rates, and our results suggest that these messages may have to clarify very basic concepts.

Inclusion of women with HIV was a strength of the study. Such women are at particular risk, in part because of immunosuppression but also because they have multiple cancer risk factors such as smoking and multiple sexual partners. Other strengths include serial survey administration and the multisite cohort.

This study was limited by several factors. Women were participating in semiannual Pap screening as part of the WIHS, so we could not assess impact of knowledge on screening or vaccination. Screening guidelines changed after the 2011 administration of our questionnaire, and current understanding about screening intervals and tests might not reflect these new recommendations. Most study women were older than the target age for HPV vaccination, and we did not assess the impact of knowledge or attitudes on vaccination rates among young relatives who might be vaccination candidates. We could not determine whether differences between prior and most recent enrollees were due to longer experience with cervical cancer prevention in WIHS, familiarity with questionnaires, or other factors distinguishing enrollment cohorts. However, our finding that knowledge of cervical cancer prevention was lower among newest recruits indicates that passive learning from media, family and friends, and health care providers in recent years is insufficient. Finally, women enrolled in WIHS may be selected. However, women outside frequent care and women who have not dedicated themselves to a decade-long study are likely to be even less informed about cervical cancer prevention than participants in our study.

Not all items assessed in our question set may directly influence prevention and treatment behaviors. For instance, while women should be aware of guidelines on Pap frequency, knowing diet does not impact cervical cancer risk may be less important. Further research to better define determinants of HPV prevention and cervical cancer detection/treatment behaviors and to identify subgroups at greater risk based on these determinants may aid in designing and disseminating more effective strategies to improve these outcomes.

Misperceptions about cervical cancer prevention remain common among the largely poor and minority women in our study. While specific educational efforts may improve understanding and prevention behavior, school based or mandatory HPV vaccination may have greater long-term impact. Opt-out approaches may yield better vaccination rates than opt-in approaches that require weighing of vaccine benefits and risks. Long-term progress against cervical cancer may require additional messages on providing women at high risk for cervical cancer with the understanding they need to enroll their children in routine HPV vaccination programs.

### Compliance with ethical standards

The authors report no potential conflicts of interest. Funding is outlined in the Acknowledgement. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Specifically, informed consent was obtained from all individual participants included in the study, and the WIHS was approved by the local and national institutional review boards.

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### Conflict of interest statement

No authors report potential conflicts of interest.

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