# Human Papillomavirus Vaccination History Among Women With Precancerous Cervical Lesions

## *Disparities and Barriers*

*Niti R. Mehta, MPH, Pamela J. Julian, MPH, James I. Meek, MPH, Lynn E. Sosa, MD, Alyssa Bilinski, Susan Hariri, PhD, Lauri E. Markowitz, MD, James L. Hadler, MD, MPH, and Linda M. Niccolai, PhD*

**OBJECTIVE:** To estimate racial, ethnic, and socioeconomic differences in human papillomavirus (HPV) vaccination history among women aged 18–27 years with precancerous cervical lesions diagnosed, barriers to vaccination, and timing of vaccination in relation to the abnormal cytology result that preceded the diagnosis of the cervical lesion.

**METHODS:** High-grade cervical lesions are reportable conditions in Connecticut for public health surveillance. Telephone interviews and medical record reviews were conducted during 2008–2010 for women (n=269) identified through the surveillance registry.

**RESULTS:** Overall, 43% of women reported history of one or more doses of HPV vaccine. The mean age at vaccination was 22 years. Publicly insured (77%) and uninsured (85%) women were more likely than privately insured women (48%) to report no history of vaccination ($P<.05$). Among unvaccinated women, being unaware of HPV vaccine was reported significantly more often among Hispanics than non-Hispanics (31% compared with 13%, $P=.02$) and among those with public or no insurance compared with those with private insurance (26% and 36% compared with 6%, $P<.05$ for both). The most commonly reported barrier was lack of provider recommendation (25%). Not having talked to a provider about vaccine was reported significantly more often among those with public compared with private insurance (41% compared with 18%, $P<.001$). Approximately 35% of women received vaccine after an abnormal cytology result; this occurred more frequently among African American women compared with white women (80% compared with 30%, $P<.01$).

**CONCLUSION:** Catch-up vaccination strategies should focus on provider efforts to increase timely coverage among low-income and minority women.

*(Obstet Gynecol 2012;119:575–81)*
*DOI: 10.1097/AOG.0b013e3182460d9f*

**LEVEL OF EVIDENCE: III**

Human papillomavirus (HPV) is the most common sexually transmitted infection in the United States and is an important cause of cervical cancer.[1,2] In 2006, a quadrivalent HPV vaccine (Gardasil) was approved for use in the United States by the U.S. Food and Drug Administration based on high efficacy in clinical studies.[3] A bivalent vaccine, Cervarix, was approved by the U.S. Food and Drug Administration in 2009.[4] Both vaccines offer protection against high-risk HPV types 16 and 18, which are known to cause 70% of cervical cancers. The Advisory Committee on Immunization Practices recommends a three-dose series of either vaccine for routine use among girls 11 or 12 years of age, with catch-up vaccination for girls and women 13–26 years of age.[5]

In the United States, cervical cancer disproportionately affects racial and ethnic minorities and women of low socioeconomic status.[6,7] Overall reductions in cervical cancer and a reduction of disparities

*From the Yale School of Public Health and Connecticut Emerging Infections Program, New Haven, Connecticut; the Connecticut Department of Public Health, Hartford, Connecticut; and the Centers for Disease Control and Prevention, Atlanta, Georgia.*

*Supported by Cooperative Agreement CIU01000307 from the Centers for Disease Control and Prevention (CDC). Its contents are solely the responsibility of the authors and do not necessarily represent the official views of CDC.*

*Corresponding author: Linda M. Niccolai, Yale School of Public Health, 60 College Street, New Haven, CT 06520; e-mail: linda.niccolai@yale.edu.*

***Financial Disclosure***
*The authors did not report any potential conflicts of interest.*


ISSN: 0029-7844/12

should occur if adequate vaccine coverage across all racial and ethnic and socioeconomic groups is achieved. Whereas variation in uptake by state has been reported,[8] data from the 2010 National Immunization Survey–Teen based on a representative sample of adolescents aged 13–17 years in the United States showed that receipt of at least one dose did not differ between African Americans (49%) and whites (46%) and was higher among Hispanics (56%); it did not differ between those living below the poverty level (52%) and those living at or above the poverty level (48%).[9] However, all of these rates remain suboptimal.

Disparities in cervical cancer incidence and mortality may be reduced if disparities in vaccine coverage are identified and addressed. In the present study, we sought to estimate history of vaccination among women with precancerous cervical lesions diagnosed. For unvaccinated women, we assessed barriers to vaccination by asking reasons for not receiving the vaccine. For vaccinated women, we examined timing of vaccine initiation in relation to abnormal cytology results that preceded the diagnosis of the cervical lesion.

## MATERIALS AND METHODS

In 2008, the Centers for Disease Control and Prevention began an effort through the Emerging Infections Program network to monitor effect of HPV vaccine through population-based surveillance of precancerous cervical lesions including cervical intraepithelial neoplasia (CIN) grade 2 and higher and adenocarcinoma in situ. To facilitate implementation of this surveillance system at the Connecticut Emerging Infections Program site, the Connecticut Department of Public Health added CIN 2 and higher and adenocarcinoma in situ to the list of statewide reportable diseases effective January 1, 2008.[10] Currently, all 34 pathology laboratories in the state that process cervical biopsy specimens and diagnose CIN 2 and higher and adenocarcinoma in situ are in compliance with this reporting requirement. Enhanced surveillance including patient interviews and medical record reviews were conducted for residents of New Haven County between 18 and 39 years of age. Medical records were reviewed at offices of the providers who performed the biopsy that resulted in the CIN 2 and higher or adenocarcinoma in situ diagnoses. First, Emerging Infections Program staff contacted these providers to verify basic reporting elements, obtain up-to-date patient contact information, and review patients' medical records to ascertain HPV vaccination and cervical cancer screening histories. Next, Emerging Infections Program staff conducted telephone interviews with case patients to collect similar information about HPV vaccination and cervical cancer screening histories. For screening history, the date of the abnormal cytology result based on a Pap test that preceded the CIN 2 and higher or adenocarcinoma in situ diagnosis was abstracted. When vaccine histories were missing from provider records and women reported a different vaccine provider, Emerging Infections Program staff reviewed those charts to verify history and dates of vaccination. Data for this analysis were collected for cases reported from January 1, 2008 to December 31, 2010, for women who had interviews and medical record reviews completed.

Patient demographics included age, race, ethnicity, and insurance status as reported in the interview. Age at diagnosis was dichotomized at the median of 23 years. Race was categorized as white, African American, and other, and ethnicity was categorized as Hispanic and non-Hispanic. Other races included Asian or Pacific Islander, Native American, and multiple races; these were combined into one category because of the low frequency. Insurance type was categorized as private, public, and none. History of HPV vaccination was the primary outcome of interest. Interviewers asked each woman the following about HPV vaccine: whether she had ever heard of an HPV vaccine, whether a health care provider had ever talked to her about the HPV vaccine, her HPV vaccination history, number and dates (month and year) of vaccine doses received, and name and type of health care provider that administered vaccine. Status of HPV vaccination was classified as yes (1 dose or more) or no (0 doses). Medical records often had no information about vaccination history recorded (45%); therefore, interview data were used as the basis for establishing vaccine history. Women who did not receive HPV vaccine were asked an open-ended question about their reason for not receiving the vaccine. Using data on provider name or type of practice from both the pathology reports and the interview, we compared the vaccine provider to the provider who performed the biopsy to determine whether it was the same provider. We also classified the vaccine providers according to specialty.

This analysis was restricted to women aged 27 years and younger at the time of their diagnosis because they were in the age-eligible range for catch-up vaccination. Logistic regression was used to estimate associations between age, race, ethnicity, and insurance type with vaccine history. Unadjusted and adjusted odds ratios were calculated with 95% confi-

dence intervals. The adjusted model included all four covariates.

The $\chi^2$ and Fisher exact tests were used to examine correlates of vaccine awareness among unvaccinated women, including age, race, ethnicity, and insurance type. To assess possible barriers, frequencies and percentages were calculated for all reported reasons for why women had not been vaccinated, and these responses were rank-ordered. Because "no provider recommendation" emerged as the most common reason, responses to a separate question of whether a provider had ever discussed vaccine with the patient were further analyzed. We used $\chi^2$ and Fisher exact tests to examine correlates of this measure, including age, race, ethnicity, and insurance type, in addition to the measure of vaccination history.

Dates of first dose of HPV vaccine and abnormal Pap test results that prompted the cervical biopsy were compared to establish timing of vaccination in relation to the diagnosis of CIN 2 and higher or adenocarcinoma in situ. Because we collected information about abnormal Pap test result dates from both interviews and medical record reviews, we first compared these two sources and determined that medical records were a more complete source of this information (100.0% compared with 70.8% nonmissing). Therefore, dates of abnormal Pap test results from medical records were used. Because data for vaccination history were found to be more complete in the interviews as previously described, we compared self-report of dates of first dose between interviews and the medical record with the vaccine history to determine the feasibility of using dates from the interview when missing from medical records. Information on date of first dose (month and year) was present in both interviews and medical charts for 41women. Of these, a majority (n=27, 65.9%) had a self-reported vaccination date that was within 3 months of the vaccination date listed in the medical record. Therefore, the primary source of HPV vaccination dates was medical records supplemented with dates from interview when missing in medical records. Women were categorized as having initiated vaccination before, after, or in the same month as the abnormal Pap test result. The amount of time between receiving the first dose and abnormal Pap test result was computed. Correlates of the timing measure were examined, including age, race, ethnicity, insurance type, provider type, and whether the vaccine provider was the same provider who performed the cervical biopsy. All data were analyzed using SAS 9.2. This project was reviewed by Centers for Disease Control and Prevention, Connecticut Department of Public Health, and Yale University Institutional Review Boards and deemed exempt from the need for approval.

## RESULTS

There were a total of 660 age-eligible cases (women 18–27 years old) reported in 2008–2010, and medical record reviews and interviews were initiated during this time period for 460 cases. Of these, 271 (59%) women completed interviews, 124 (27%) were unreachable, 61 (13%) refused to participate, 2 (less than 1%) were not contacted on provider request, and 2 (less than 1%) were deemed ineligible because of residence outside New Haven County. Two (less than 1%) of the 271 completed interviews were missing vaccine history and were excluded from the analysis. Comparison of women who completed interviews (n=269) with the women who could not be included (n=191) revealed no significant differences with respect to age or diagnosis, the two variables routinely available on the basic surveillance reports ($P>.30$ for both).

The median age was 23 years, and the sample was predominantly white (76.7%), non-Hispanic (83.1%), and privately insured (67.2%) (Table 1). Forty-three percent of women reported having received at least one dose of HPV vaccine, with mean age at vaccine initiation of 22 years (range 17–27 years). Among the 116 previously vaccinated women, 65.5% reported receiving vaccine from an obstetrician–gynecologist. The vaccine provider and the provider who performed the cervical biopsy were the same for 58.6% women and different for 33.6%; this could not be determined for 7.8% of women.

In unadjusted analyses, having public and no insurance were significantly associated with not having received vaccine compared with those who were privately insured (77.1% and 84.6% compared with 47.7%, $P<.05$ for both comparisons) (Table 1). After controlling for all other factors in the adjusted analysis, having public and no insurance remained statistically significantly associated with not being vaccinated (odds ratio 2.74, 95% confidence interval 1.32–5.69 and odds ratio 5.02, 95% confidence interval 1.06–23.81, respectively). There were no statistically significant associations for race or ethnicity with vaccination history after controlling for age and insurance type.

In the total sample, 9.4% reported they had not heard of HPV vaccine; among unvaccinated women, the proportion was 15.9% (Table 2). Among unvaccinated women, not being aware of HPV vaccine was significantly higher among Hispanic (31.0%), publicly

**Table 1. Correlates of No Vaccination History**

| | Vaccination History | No Vaccination History | Unadjusted Odds Ratio (95% CI) | Adjusted* Odds Ratio (95% CI) |
|---|---|---|---|---|
| Total (n=269) | 116 (43.1) | 153 (56.9) | NA | NA |
| Age (y) (n=269) | | | | |
| 18–22 | 61 (50.4) | 60 (49.6) | 1.00 | 1.00 |
| 23–27 | 55 (37.2) | 93 (62.8) | 1.72 (1.05–2.80)* | 1.81 (1.05–3.12)† |
| Race (n=249) | | | | |
| White | 91 (47.6) | 100 (52.4) | 1.00 | 1.00 |
| African American | 11 (30.6) | 25 (69.4) | 2.07 (0.96–4.44) | 1.31 (0.56–3.04) |
| Other | 6 (27.3) | 16 (72.7) | 2.43 (0.91–6.47) | 2.09 (0.65–6.76) |
| Ethnicity (n=266) | | | | |
| Non-Hispanic | 99 (44.8) | 122 (55.2) | 1.00 | 1.00 |
| Hispanic | 16 (35.6) | 29 (64.4) | 1.47 (0.76–2.86) | 0.96 (0.36–2.62) |
| Insurance type (n=253) | | | | |
| Private | 89 (52.3) | 81 (47.7) | 1.00 | 1.00 |
| Public | 16 (22.9) | 54 (77.1) | 3.66 (1.94–6.90)‡ | 2.74 (1.32–5.69)§ |
| None | 2 (15.4) | 11 (84.6) | 5.97 (1.28–27.73)† | 5.02 (1.06–23.81)† |

CI, confidence interval; NA, not applicable.
Data are n (%) unless otherwise specified.
* Adjusted for all covariates in the Table.
† $P<.05$.
‡ $P<.001$.
§ $P<.01$.

insured (26.4%), and uninsured women (36.4%) ($P<.05$ for each comparison). The most frequently reported reasons were no recommendation (25.0%), previous HPV diagnosis (19.7%), and being too old for vaccine (15.1%). Another 15.4% reported they were not sure why or did not give a reason, and all other reasons were reported infrequently (less than 6%).

Because "no recommendation" was identified as the most common self-reported barrier to vaccination, we examined correlates of not having discussed vaccine with a provider among the entire sample (Table 2). As expected, women who received HPV vaccine were more likely to have a provider who had discussed HPV vaccine with them than women who

**Table 2. Vaccine Awareness and Provider Discussion About Human Papillomavirus Vaccine**

| | Ever Heard of HPV Vaccine (n=151 Unvaccinated Women) | | | Provider Has Talked With Patient About Vaccine (n=261) | | |
|---|---|---|---|---|---|---|
| | Yes | No | P* | Yes | No | P* |
| Total | 127 (84.1) | 24 (15.9) | NA | 196 (75.1) | 65 (24.9) | NA |
| Age (y) | | | | | | |
| 18–22 | 54 (90.0) | 6 (10.0) | | 97 (83.6) | 19 (16.4) | |
| 23–27 | 73 (80.2) | 18 (19.8) | .108 | 99 (68.3) | 46 (31.7) | .004 |
| Race | | | | | | |
| White | 90 (90.9) | 9 (9.1) | | 143 (78.1) | 40 (21.9) | |
| African American | 19 (76.0) | 6 (24.0) | .078† | 26 (72.2) | 10 (27.8) | .439 |
| Other | 9 (60.0) | 6 (40.0) | .005† | 13 (59.1) | 9 (40.9) | .048 |
| Ethnicity | | | | | | |
| Non-Hispanic | 105 (87.5) | 15 (12.5) | | 165 (77.1) | 49 (22.9) | |
| Hispanic | 20 (69.0) | 9 (31.0) | .023† | 28 (63.6) | 16 (36.4) | .061 |
| Insurance type | | | | | | |
| Private insurance | 75 (93.7) | 5 (6.3) | | 138 (81.7) | 31 (18.3) | |
| Public insurance | 39 (73.6) | 14 (26.4) | .001 | 41 (59.4) | 28 (40.6) | <.001 |
| None | 7 (63.6) | 4 (36.4) | .011† | 8 (61.5) | 5 (38.5) | .138† |

HPV, human papillomavirus; NA, not applicable.
Data are n (%) unless otherwise specified.
* $P$ for $\chi^2$ test unless otherwise noted.
† Fisher exact test.




**Table 3. Timing of Vaccine Initiation (n=109)**

| | Vaccination Before Abnormal Pap Test Result | Vaccination in Same Month as Abnormal Pap Test Result | Vaccination After Abnormal Pap Test Result | *P** |
|---|---|---|---|---|
| Total | 62 (56.9) | 9 (8.3) | 38 (34.9) | NA |
| Age (y) | | | | |
| 18–22 | 28 (49.1) | 6 (10.5) | 23 (40.4) | |
| 23–27 | 34 (65.4) | 3 (5.8) | 15 (28.8) | .138 |
| Race | | | | |
| White | 54 (61.4) | 8 (9.1) | 26 (29.5) | |
| African American | 2 (20.0) | 0 | 8 (80.0) | .005† |
| Other | 3 (50.0) | 1 (16.7) | 2 (33.3) | .999† |
| Ethnicity | | | | |
| Non-Hispanic | 55 (55.6) | 9 (9.1) | 35 (35.4) | |
| Hispanic | 7 (77.8) | 0 | 2 (22.2) | .477† |
| Insurance type | | | | |
| Private | 51 (59.3) | 7 (8.1) | 28 (32.6) | |
| Public | 6 (50.0) | 1 (8.3) | 5 (41.7) | .523† |
| None | 1 (50.0) | 0 (0) | 1 (50.0) | .999† |
| Provider type | | | | |
| Obstetrician–gynecologist | 39 (53.4) | 8 (11.0) | 26 (35.6) | |
| Other | 22 (68.8) | 1 (3.1) | 9 (28.1) | .515 |
| Same vaccine and biopsy provider | | | | |
| Yes | 34 (53.1) | 6 (9.4) | 24 (37.5) | |
| No | 24 (64.9) | 3 (8.1) | 10 (27.0) | .254 |

NA, not applicable.
Data are n (%) unless otherwise specified.
* *P* for $\chi^2$ test unless otherwise noted.
† Fisher exact test.

reported not having been vaccinated (98.2% compared with 58.0%, $P<.001$). Providers were more likely to discuss HPV vaccine with women aged 18–22 years compared with women aged 23–27 years (83.6% compared with 68.3%, $P=.004$), as well as with privately insured women compared with publicly insured women (81.7% compared with 59.4%, $P<.001$).

Timing of vaccination in relation to diagnosis could be determined for 109 women (94% of those vaccinated) based on having complete dates for first dose (Table 3). Sixty-two (56.9%) received their first dose before their Pap test (with abnormal result) date, nine (8.3%) in the same month as their Pap test (with abnormal result), and 38 (34.9%) after their Pap test (with abnormal result). For those who received vaccine before their abnormal Pap test result, the median number of months between abnormal Pap test result and vaccine initiation was 16 (range 1–31 months). For those who received vaccine after their abnormal Pap test result, the median number of months between was 3 (range 1–22). African American women were significantly more likely than white women to have been vaccinated after their abnormal Pap test result (80.0% compared with 29.5%, $P<.01$). There were no significant differences by age, ethnicity, insurance type, or provider characteristics. Because of the strong effect of race on timing of vaccination, we conducted post hoc analyses to examine whether there were disparities in vaccination before diagnosis compared with no or late history of vaccination. The difference for race was statistically significant in the adjusted model (6% of African Americans vaccinated before diagnosis compared with 29% of whites, $P<.05$).

## DISCUSSION

The proportion of women in this sample who reported history of vaccination with at least one dose, 43.1%, is substantially higher than the 11.7% estimate recently reported in a similar age group from a national survey[11] but comparable to estimates from select population studies.[12–14] Differences may reflect variation in access to health care, including insurance coverage for vaccination in the populations surveyed. Although vaccine coverage in this age group has increased since 2006,[15–17] less than half of women age-eligible for catch-up vaccination have initiated the three-dose series. Efforts are currently needed to raise this suboptimal level.

The strong and significant associations between having public and no health insurance and reporting

no history of vaccination, consistent with previous reports,[16,18–20] may reflect that the cost of HPV vaccine (approximately $120 per dose) is a barrier for this population. Women older than age 18 years do not qualify to receive free vaccine from the Vaccines for Children program; therefore, providing vaccine to women in this age group will be challenging. Achieving optimal coverage of low-income women before age 19 years, when vaccine is available for eligible women through Vaccines for Children, may help to reduce disparities in the catch-up age group in the future. Difference by race and ethnicity were less clear with not significant but lower estimates of vaccination history among African American and Hispanic women. Certainly, income, race, and ethnicity are inter-related in complex ways and assessing their independent effects of vaccine uptake should be a priority for future research.

Lack of provider recommendation, the most commonly cited reason for not having received vaccine, coupled with the finding that publicly insured women were less likely to report discussion of HPV vaccine with providers than privately insured women may reflect that providers are reluctant to discuss vaccine with patients who may not be able to afford it. It is also noteworthy that previous diagnosis of HPV and being too old were the next most commonly reported reasons for not having been previously vaccinated, although an HPV diagnosis is not a contraindication for vaccination and none of the women in this age group was beyond the age-eligible range for catch-up vaccination. Providers who care for women who missed vaccination at the target ages should discuss and offer vaccines to all age-eligible women while recognizing that cost may be a challenge for some patients.

Importantly, many women (approximately one-third) with a history of vaccination received vaccine after an abnormal cytology result that prompted the cervical biopsy resulting in the CIN 2 and higher or adenocarcinoma in situ diagnoses, suggesting that the abnormal cytology result triggered vaccination for some of these women. Vaccination timing differed significantly by race, with African American women being more likely to have initiated vaccination after the abnormal cytology result compared with white women. Although vaccination of women after a diagnosis can provide protection against infection with HPV types they have not previously acquired, HPV vaccines are not therapeutic and it is preferable to vaccinate women before sexual debut and certainly before any diagnosis of abnormal cervical changes, and special efforts may be needed to reach African American women earlier.

These data cannot be used to make any inference about vaccine effectiveness. Although approximately half of women in the sample were vaccinated before their abnormal cytology result, the median time between vaccination and diagnosis was less than the average time between infection and development of precancerous lesions,[21] suggesting that most if not all of these women were vaccinated after infection but before diagnosis. There are possible limitations to this study, including selection bias that may have occurred related to participation of women who were reachable by telephone and agreed to the interview, reliance on self-reported data for some measures, and lack of statistical power related to our sample size for some associations. An important strength of this study was the use of several data sources (interviews and multiple medical records when indicated) for our measure of vaccination history.

Overall, socioeconomic, racial, and ethnic disparities exist in history of vaccination, vaccine awareness, and provider discussions, and timing of vaccine initiation. These data are troubling because of known disparities in cervical cancer incidence. Providers should be encouraged to recommend HPV vaccine to all women eligible for catch-up vaccination and efforts should be made to vaccinate all girls at the recommended target age.

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