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Prevalence of Human Papillomavirus Genotypes in High-Grade Cervical Precancer and Invasive Cervical Cancer From Cancer Registries Before and After Vaccine Introduction in the United States

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CONFLICT OF INTEREST DISCLOSURES

The authors made no disclosures.

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Abstract

Background: US population-based cancer registries can be used for surveillance of human papillomavirus (HPV) types found in HPV-associated cancers. Using this framework, HPV prevalence among high-grade cervical precancers and invasive cervical cancers were compared before and after HPV vaccine availability.

Methods: Archived tissue from 2 studies of cervical precancers and invasive cervical cancers diagnosed from 1993–2005 (prevaccine) were identified from 7 central cancer registries in Florida; Hawaii; Iowa; Kentucky; Louisiana; Los Angeles County, California; and Michigan; from 2014 through 2015 (postvaccine) cases were identified from 3 registries in Iowa, Kentucky, and Louisiana. HPV testing was performed using L1 consensus polymerase chain reaction analysis. HPV-type–specific prevalence was examined grouped by hierarchical attribution to vaccine types: HPV 16, 18, HPV 31, 33, 45, 52, 58, other oncogenic HPV types, and other types/HPV negative. Generalized logit models were used to compare HPV prevalence in the prevaccine study to the postvaccine study by patient age, adjusting for sampling factors.

Results: A total of 676 precancers (328 prevaccine and 348 postvaccine) and 1140 invasive cervical cancers (777 prevaccine and 363 postvaccine) were typed. No differences were observed in HPV-type prevalence by patient age between the 2 studies among precancers or invasive cancers.

Conclusions: The lack of reduction in vaccine-type prevalence between the 2 studies is likely explained by the low number of cases and low HPV vaccination coverage among women in the postvaccine study. Monitoring HPV-type prevalence through population-based strategies will continue to be important in evaluating the impact of the HPV vaccine.

Keywords

cervical cancer; human papillomavirus (HPV); United States; vaccine

INTRODUCTION

In the United States, there were 12,831 new cases of cervical cancer and 4,207 women who died from the disease in 2017.[1] The majority of cervical cancers are caused by the human papillomavirus (HPV), with most being attributed to oncogenic HPV types 16 and 18.[2] Since 2006, HPV vaccination has been routinely recommended for US female teens aged 11–12 years.[3] Although coverage was low at first introduction, HPV vaccination coverage has increased; coverage of ≥1 dose of HPV vaccine among female adolescents aged 13–17 years increased from 37% in 2008 to 73% in 2019.[4,5] The impact of HPV vaccine on cervical disease has been shown by decreasing incidence of cervical precancers and decreases in vaccine-type HPV prevalence in cervical precancer lesions in young women.[6–8] The HPV vaccine impact on invasive cervical cancer has not yet been fully shown because of the long duration for cancer development and a lower burden of invasive cervical cancer in younger women in whom HPV vaccination would have the most impact. However, recent studies have suggested that the HPV vaccine may be reducing the incidence of invasive cervical cancers.[9–11] In this study, we sought to examine the potential impact of HPV vaccine on HPV prevalence among cervical precancers and invasive cervical cancers using

data collected from select US population-based cancer registries before and after the HPV vaccine introduction.

MATERIALS AND METHODS

Study Design and Population

Population-based tracking of HPV types in HPV-associated cancers is not routinely conducted in the United States. However, the Centers for Disease Control and Prevention (CDC) has supported 2 multistate HPV-typing studies using central cancer registries (cancer registries), 1 of which was conducted before the availability of HPV vaccines (prevaccine), and another after HPV vaccines became available in the United States (postvaccine). In the prevaccine study, the CDC Cancer Registry Sentinel Surveillance System was developed in partnership with 7 cancer registries and provided the first population-based HPV typing prevalence data in the United States from 1993–2005.[2] This study included cases diagnosed from 1993–2005 from cancer registries in Florida (FL); Hawaii (HI); Iowa (IA); Kentucky (KY); Los Angeles County, California (CA); Louisiana (LA); and Michigan (MI). In the postvaccine study, CDC partnered with 3 cancer registries in IA, KY, and LA to collect HPV-typing information from select cancer sites diagnosed in 2014 and 2015. In both studies, histologically confirmed cervical intraepithelial neoplasia grade 3 or adenocarcinoma in situ (CIN3/AIS, referred to as CIN3+ going forward) and invasive cervical cancers (ICCs) were identified by cancer registries using the *International Classification of Diseases for Oncology, 3rd Edition* (*ICD-O-3*) site codes C53.0-C53.9.[12] CIN3+ were limited to ICD-O-3 behavior code 2.

In the prevaccine study, random sampling was used to identify CIN3+ and ICCs from the cancer registries. Only MI, CA, and IA submitted CIN3+ samples. In the postvaccine study, the sampling design was a stratified random sample with strata based on age and racial/ethnic group; CIN3+ cases were only available from KY and LA cancer registries. The sampling strategy for the postvaccine study focused on precancer cases only among women aged <35 years, and invasive cervical cancer cases among women aged <35 years, 35–50 years, and ≥50 years. Younger age groups and minority race/ethnicity groups were oversampled to obtain more precise estimates. Sampling weights were calculated based on the probability of selection within each cancer registry to weight analyses to the age and racial/ethnic group distributions in the underlying registry populations. We excluded 153 CIN3+ cases who were aged >35 years from the prevaccine study to match the inclusion criteria of the postvaccine study.

Tissue processing, histology review, and laboratory methods—Tissue processing, histology review, and laboratory methods have been described previously.[2] Briefly, formalin-fixed paraffin-embedded tissue blocks were identified by cancer registries with the following criteria: 1) representative histology from primary site, 2) highest ratio of tumor to nontumor tissue in block, 3) minimal necrosis, 4) best preservation, and 5) sufficient residual tissue for the six 5-μm sections required for study. Hematoxylin and eosin slides of the first and last sections along with the bracketed unstained tissue sections were sent to the CDC laboratory for histologic review and HPV typing.

Histologic review was performed by a study patholo-gist to provide confirmation of a representative sample in slides before and after sections to be tested. Samples passing histologic review were extracted for DNA as previously described.[3] All samples were tested with Linear Array (LA; Roche Diagnostics), which detects 37 HPV types (6, 11, 16, 18, 26, 31, 33, 35, 39, 40, 42, 45, 51, 52(XR), 53, 54, 55, 56, 58, 59, 61, 62, 64, 66, 67, 68, 69, 70, 71, 72, 73, 81, 82, 83, 84, 89, IS39). In the prevaccine study, inadequate and HPV–negative samples were retested with the INNO-PA HPV typing assay (LiPA; Innogenetics), which detects 29 HPV types (6, 11, 16, 18, 26, 31, 33, 35, 39, 40, 43, 44, 45, 51, 52, 53, 54, 56, 58, 59, 66, 68, 69, 70, 71, 73, 74, 81, 82). In the postvaccine study, samples that were inadequate or HPV–negative were retested with the RHA kit HPV SPF-10-LiPA25, version 1 (Labo Biomedical Products B.V.) that detects 25 HPV types (6, 11, 16, 18, 31, 33, 34, 35, 39, 40, 42–45, 51–54, 56, 58, 59, 66, 68, 70, 74). Cancer registries provided demographic and clinical data for cases, including sex, race/ethnicity, age at diagnosis, and surveillance, epidemiology, and end results (SEER) summary tumor stage at diagnosis. All protocols were reviewed and approved by the institutional review boards of all participating organizations and the CDC.

Statistical Analysis

We summarized descriptive characteristics of the participating women by histology (squamous cell carcinoma, adenocarcinoma, and other) and study period (Table 1). In the prevaccine study, unweighted frequencies were calculated, but in the postvaccine study, weighted frequencies were calculated using sampling weights to account for the stratified sampling by age and racial/ethnic group. HPV type–specific prevalence was grouped by the hierarchical attribution to oncogenic types targeted by HPV vaccines: HPV 16, 18 (targeted by all HPV vaccines), HPV 31, 33, 45, 52, 58 (5 additional oncogenic types targeted by HPV 9–valent vaccine), other oncogenic HPV types (35, 39, 51, 56, 59, 66, 68), other HPV types, and HPV negative. We descriptively compared demographics using unweighted frequencies in the prevaccine study to frequencies weighted for oversampling in the postvaccine study but did not perform statistical testing because of the differences in the cancer registries included in the comparison and the nonrepresentative distribution of racial/ethnic groups in the prevaccine study. In the prevaccine study, the proportion of cases that were classified as non-Hispanic White was lower among typed cases compared with nontyped cases.[2] In the postvaccine study, the racial/ethnic distribution was representative of the study population by design through stratification and sampling weights.

We compared HPV-type prevalence between the prevaccine and postvaccine studies by cancer status and age group. CIN3+ patients were stratified by age: 15–24 years, 25–29 years, and 30–34 years; among the patients with ICCs, the age groups were <35 years, 35–50 years, and ≥50 years. Other HPV and HPV negative cases were combined into a single group because of the small number of cases. We descriptively compared unweighted estimates from the prevaccine study with the weighted estimates in the postvaccine study. Statistical testing for differences across HPV groups was performed using generalized logit models adjusting for sampling factors (age and/or race/ethnicity group). If the overall *P* value for any differences across the HPV groups was significant, pair-wise comparisons were tested. Sixty patients with CIN3+ and 5 patients with an ICC in the prevaccine study

were excluded from the models because of missing race/ethnicity. As a subset of the cancer registries collected ICC data from the same registries during both studies (IA, KY, and LA), we performed a sensitivity analysis among invasive cancers to evaluate any bias caused by comparison including different cancer registries. All analyses were performed using SAS version 9.4 (Cary, NC).

RESULTS

A total of 676 patients with CIN3+ (328 in the prevaccine study; 348 in the postvaccine study) and 1,140 patients with ICC (777 in the prevaccine study; 363 in the postvaccine study) were successfully genotyped and included in our analytic sample. Study characteristics of CIN3+ and ICC by study are reported in Table 1. Among women with CIN3+, the age distribution varied between the 2 studies, with an overall lower number of younger women in the second study. In both studies, the majority of the CIN3+ cases were non-Hispanic White (83.2% prevaccine, 79.0% postvaccine) and diagnosed with squamous cell histology (86.6% prevaccine, 95.1% postvaccine). Among women with ICC, most women were aged 50–94 years (44.4% prevaccine, 43.4% postvaccine) and non-Hispanic White (53.0% prevaccine, 70.9% postvaccine), and diagnosed with squamous cell carcinoma (73.4% prevaccine, 66.6% postvaccine).

HPV-type prevalence among women with CIN3+ by age group and study period are reported in Table 2. In the total sample, approximately two-thirds of cases were attributed to HPV 16, 18 both in the prevaccine and postvaccine study. When comparing HPV-type prevalence in the prevaccine to the postvaccine study, a statistically significant difference was found in the distribution among all age groups ($P = .03$). There was increased positive HPV 31, 33, 45, 52, 58 compared with both other oncogenic HPV ($P = .029$) and other HPV/HPV negative ($P = .019$) in the postvaccine study compared with the prevaccine study. However, no differences were observed between HPV-type prevalence by age. Notably, among women aged 15–24 years, the proportion attributed to HPV 31, 33, 45, 52, 58 was 14.2% in the prevaccine study versus 21.4% in the postvaccine study, but the difference was not statistically significant.

HPV-type prevalence among women with ICC by age group and study period are reported in Table 3. Among women aged 19–34 years, the proportion attributed to HPV 16, 18 was somewhat higher in the postvaccine period compared with the prevaccine period (84.4% vs 74.4%). However, no significant differences were observed in HPV-type prevalence between the prevaccine and postvaccine studies in any age strata. When we limited the analysis to the subset of cancer registries collecting data in both studies, similar results were observed but sample sizes within stratum of age and HPV type became very small for these comparisons (see supporting information).

DISCUSSION

In this population-based cancer registry study, we did not find a reduction in vaccine-type HPV prevalence among patients with CIN3+ or ICC from the prevaccine to the postvaccine study by age group. Although an overall significant difference was observed among all

women with CIN3+, this difference appears to be driven by larger differences in the proportion attributed to HPV 31, 33, 45, 52, 58 compared with both other oncogenic HPV types and other HPV/HPV negative observed in the postvaccine study versus the prevaccine study. Vaccine impact would be expected to first be observed in the type distribution of CIN3+ detected in the age groups most likely to have been vaccinated. The lack of significant change in HPV 16, 18-type prevalence among patients with CIN3+ and ICC by age in this study could be explained by the low number of cases captured by the study (particularly in the youngest age groups), suboptimal HPV vaccination coverage in the postvaccine period of data collection, and that the time point of the postvaccine study collection may be too early in the natural history of ICC to observe this association fully.

Early evidence of population-level HPV vaccine impact on cervical cancer in the United States has been shown by the decreasing prevalence of vaccine-type HPV infections after vaccine introduction and the decreasing prevalence of cervical precancers. Analyses of large national data sets of cervicovaginal specimens have shown a 56% reduction in the prevalence of HPV types targeted by the 4-valent vaccine within 4 years of HPV vaccine introduction among women aged 14–19 years.[13] Greater reductions in the prevalence of HPV types targeted by the 4-valent vaccine occurred 6 and 8 years after vaccine introduction as well as the observation of decreases in prevalence among women aged 20–24 years, which reflects increasing HPV vaccination coverage in these age groups over time.[14,15] Evidence of decreased vaccine-type HPV prevalence has also been observed in both vaccinated and unvaccinated women screened for cervical cancer in a large managed health care network 9 to 10 years after HPV vaccine introduction, which highlights the direct impact of HPV vaccine as well as herd protection.[16] In the New Mexico HPV Pap Registry, which linked population-based cancer registry and screening data, significant declines from 2007–2014 among CIN grades 1–3 were observed among women aged 15–19 years and also among women with CIN2 aged 20–24 years.[17] Findings from the CDC's Human Papillomavirus Vaccine Impact Monitoring Project conducted in 5 US catchment areas showed significant declines in CIN2+ from 2008–2015 among screened women aged 18–24 years,[7] and in adenocarcinoma in situ cases among women aged 21–24 years.[6] In addition, this project found that the proportion of HPV 16, 18–positive CIN2+ cases declined from 2008–2014, with larger decreases among vaccinated women and younger age groups. However, these declines were limited to CIN2 and CIN 2/3 cases. With additional follow-up of these HPV-typing cohorts, it is reasonable to expect a reduction in CIN3+ to reflect increasing HPV-vaccination coverage.

The lack of reduction in vaccine-type HPV prevalence among patients with ICC in our study is not unexpected. First, there are a low number of cases in the United States, let alone among a subset of US cancer registries, and especially among younger age groups. Because of the long amount of time between HPV infection and development of ICC, more follow-up time is likely needed to observe vaccine effects on these more distal end points. Although some evidence suggests that HPV impact can be observed earlier in young women,[18] vaccine coverage is likely quite low in the postvaccine study. Few studies have examined vaccine effectiveness on invasive cancers, but a recent Swedish study found a 63% reduction in ICC incidence among vaccinated women compared with unvaccinated women after HPV vaccine implementation (2006–2017), with an 88% greater reduction among

women vaccinated before 17 years of age.[9] In addition, studies in the United States using population-based cancer registry data suggest that incidence rates of ICCs have declined in the youngest age groups of women after the HPV vaccination program began.[11,19] Given these findings, we might expect to see an impact on the prevalence of HPV types targeted by HPV vaccines with additional years of follow-up.

There were several limitations to our study for consideration in the interpretation of these findings. First, almost all cancer registries discontinued the routine reporting of cervical cancer precursors in 1996 because of concerns about appropriate case definitions, changes in diagnostic terminology,[20] and increased diagnosis and treatment in outpatient settings. Since 2006, several additional cancer registries have collected cervical precancer incidence, but they did not contribute to the prevaccine period prevalence. Second, we were unable to collect postvaccine data from all 7 cancer registries that participated in the prevaccine study, resulting in the inclusion of different cancer registries when comparing HPV prevalence in patients with CIN3+ and ICC. Among ICC, we performed a sensitivity analysis including only the cancer registries that collected data during both periods and found similar results; however, sample sizes were limited for these comparisons. Third, the postvaccine study oversampled by age and racial/ethnic group, which required weighting the sample back to the total population. Differences in the racial/ethnic group distribution between the prevaccine and postvaccine study may have resulted from the oversampling strategy employed in the postvaccine study. In addition, the pre- and postvaccine samples were drawn from different states with different underlying distributions of race/ethnicity. To account for these sampling differences, statistical testing was based on regression models that adjusted for stratification factors. Finally, we were limited in the variables we could analyze to those collected routinely by the cancer registries; HPV vaccination status, cancer screening, and human immunodeficiency virus status are variables that are not collected. Some state health departments including Michigan and New Mexico have been working to link vaccination and screening information to cancer registry data, but the process is complex and takes collaboration with several stakeholders to build the infrastructure and capacity. Linking these data sources more routinely could help further determine the impact of HPV vaccine on HPV-associated cancers including cervical cancer.

The major strength of our study was the systematic, population-based framework for evaluating HPV-type prevalence using cancer registries. The framework that was developed for this study is novel, robust, and could be expanded for the purpose of monitoring the impact of HPV vaccination on cervical precancers and invasive cancers in younger US women. Although we were not able to detect differences in HPV-type prevalence between our studies, our sampling methodology was refined in the postvaccine study and could be used in future studies with a larger sampling frame. Nearly 15 years have passed since the HPV vaccine was introduced, and other US studies have noted declines in precancers.[6,7,17] A study of HPV-type prevalence using population-based cancer registries including larger geographical representation using the methodologies developed through these studies could help to further show HPV vaccine impact in precancers and early impact of HPV vaccine in invasive cancers among young women with generalizability to the US population.

In conclusion, in this study of high-grade cervical precancers and invasive cervical cancers, we did not find differences in HPV-type prevalence by age in prevaccine and postvaccine studies. These findings could be explained by the postvaccine study data being too early to observe cancer outcomes and the lagging coverage of HPV vaccine, particularly with regard to series completion. However, the methodologic framework developed by these studies could be used to develop a routine, population-based system for monitoring HPV-type prevalence using central cancer registry data with linkage to HPV vaccination data. Monitoring HPV-type prevalence of precancer and invasive cervical cancers will continue to be important in the coming years as HPV vaccine coverage improves, especially for the youngest age groups of women.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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TABLE 1.

Characteristics of Prevaccine and Postvaccine Study Samples From the CDC Cancer Registry Sentinel Surveillance System

Characteristics	CIN3+				ICC			
	Prevaccine 1993–2005[a] (n = 328)		Postvaccine 2014–2015[b] (n = 348)		Prevaccine 1993–2005[c] (n = 777)		Postvaccine 2014–2015[d] (n = 363)	
Age, y	No. of Patients	%	No. of Patients	%	No. of Patients	%	No. of Patients	%
<35[e]	—	—	—	—	123	15.8	96	20.5
15–24	162	49.4	71	21.8	—	—	—	—
25–29	108	32.9	154	47.0	—	—	—	—
30–34	58	17.7	123	31.1	—	—	—	—
35–49	—	—	—	—	309	39.8	134	36.1
50–94	—	—	—	—	345	44.4	133	43.4
Race/ethnicity								
Non-Hispanic White	223	83.2	195	79.0	409	53.0	263	70.9
Non-Hispanic Black	24	9.0	86	17.5	129	16.7	67	23.4
Hispanic	17	6.3	51	2.6	124	16.1	23	3.8
Non-Hispanic other races	4	1.5	16	0.9	110	14.3	10	1.8
Missing	60		0		5		0	
Histology								
Squamous cell	284	86.6	331	95.1	570	73.4	248	66.6
Adenocarcinoma	7	2.1	11	2.8	145	18.7	95	27.6
Other	37	11.3	6	2.1	62	8.0	20	5.8
HPV type[f]								
HPV 16, 18	217	66.2	227	67.8	517	66.5	262	69.3
HPV 31, 33, 45, 52, 58	58	17.7	83	21.7	112	14.4	37	10.4
Other oncogenic HPV	34	10.4	29	7.4	50	6.4	17	5.8
Other HPV	15	4.6	4	1.3	25	3.2	14	3.7
HPV negative	4	1.2	5	1.8	73	9.4	33	10.8

Abbreviations: CA, Los Angeles County, California; CDC, Centers for Disease Control; CIN3+, cervical intraepithelial neoplasia grade 3 and adenocarcinoma in situ; FL, Florida; HI, Hawaii; HPV, human papillomavirus; IA, Iowa; ICC, invasive cervical cancer; KY, Kentucky; LA, Louisiana; MI, Michigan.

The sampling strategy for obtaining cases differed between the prevaccine and postvaccine study; hence, the percentages were not directly comparable. Please refer to the Materials and Methods section for more details. The data source was the CDC Cancer Registry Sentinel Surveillance System.

[a] Cases from cancer registries in IA, CA, and MI; 9.5% of cases diagnosed in 1994, 22.9% in 1995, 34.8% in 2004, and 32.9% in 2005.

[b] Cases from cancer registries in IA, KY, and LA; 47.4% of cases diagnosed in 2014 and 52.6% in 2015. Weighted percentages take into account sampling frame for age and race/ethnicity.

[c] Cases from cancer registries in FL, HI, IA, KY, CA, LA, and MI; 30.1% of cases diagnosed from 1993–2003; 34.4% in 2004, and 35.5% in 2005.

[d] Cases from cancer registries in IA, KY, and LA; 54.8% of cases diagnosed in 2014 and 45.2% in 2015. Weighted percentages take into account sampling frame for age and race/ethnicity.

[e] Minimum age in prevaccine study was 19 y; for the postvaccine study it was 22 y.

[f] Other oncogenic types include HPV 35, 39, 51, 56, 59, 66, and 68.

TABLE 2.

HPV Type Prevalence Among CIN3+ in Prevaccine and Postvaccine Studies From the CDC Cancer Registry Sentinel Surveillance System

		Prevaccine 1993–2005[a]			Postvaccine 2014–2015[b]			
Age y	HPV Type[c]	No. of Patients	Unweighted %	95% CI	No. of Patients	Weighted %	95% CI	*p* [d]
Total			n = 268			n = 348		.03*
	HPV 16, 18	180	67.2	61.3–72.5	227	67.8	61.3–73.7	
	HPV 31, 33, 45, 52, 58	42	15.7	11.8–20.5	83	21.7	16.7–27.7	
	Other oncogenic HPV	31	11.6	8.3–16.0	29	7.4	4.7–11.5	
	Other HPV/HPV negative	15	5.6	3.4–9.0	9	3.1	1.3–7.0	
15–24			n = 134			n = 71		.27
	HPV 16, 18	93	69.4	61.2–76.6	43	67.6	54.0–78.8	
	HPV 31, 33, 45, 52, 58	19	14.2	9.3–21.1	21	21.4	12.7–33.7	
	Other oncogenic HPV	13	9.7	5.8–15.9	5	8.4	3.1–21.0	
	Other HPV/HPV negative	9	6.7	3.6–12.3	2	2.6	0.7–9.5	
25–29			n = 87			n = 154		.47
	HPV 16, 18	58	66.7	56.2–75.7	106	72.1	62.4–80.0	
	HPV 31, 33, 45, 52, 58	16	18.4	11.6–27.8	33	16.3	10.6–24.2	
	Other oncogenic HPV	10	11.5	6.4–19.9	11	7.2	3.6–13.7	
	Other HPV/HPV negative	3	3.4	1.2–9.7	4	4.5	1.5–12.9	
30–34			n = 47			n = 123		.21
	HPV 16, 18	29	61.7	47.4–74.2	78	61.5	49.7–72.0	
	HPV 31, 33, 45, 52, 58	7	14.9	7.4–27.7	29	30.2	20.2–42.4	
	Other oncogenic HPV	8	17.0	8.9–30.1	13	7.1	3.7–13.1	
	Other HPV/HPV negative	3	6.4	2.2–17.2	3	1.2	0.3–5.1	

Abbreviations: CDC, Centers for Disease Control; CIN3+, cervical intraepithelial neoplasia grade 3 and adenocarcinoma in situ; FL, Florida; HI, Hawaii; HPV, human papillomavirus; IA, Iowa; ICC, invasive cervical cancer; KY, Kentucky; LA, Louisiana; MI, Michigan.

The data source was the CDC Cancer Registry Sentinel Surveillance System.

[a] Includes cases diagnosed from 1993–2005 from cancer registries in IA, LA, and MI; unweighted frequencies.

[b] Includes cases diagnosed from 2014–2015 from KY and LA cancer registries. Frequencies weighted for age and race/ethnicity.

[c] Other oncogenic types include HPV 35, 39, 51, 56, 59, 66, and 68.

[d] *P* values derived from generalized logit models adjusting for race/ethnicity.

[*] *P* values considered statistically significant at $P < .05$.

TABLE 3.

HPV-Type Prevalence Among ICC in Prevaccine and Postvaccine Studies From the CDC Sentinel Surveillance Study

		Prevaccine 1993–2005[a]			Postvaccine 2014–2015[b]			
Age y	HPV Type[c]	No. of Patients	Unweighted %	95% CI	No. of Patients	Weighted %	95% CI	*P*[d]
Total			n = 772			n = 363		.32
	HPV 16, 18	512	66.3	62.9–69.6	262	69.3	62.9–75.1	
	HPV 31, 33, 45, 52, 58	112	14.5	12.2–17.2	37	10.4	6.9–15.2	
	Other oncogenic HPV	50	6.5	4.9–8.4	17	5.8	3.3–9.9	
	Other HPV/HPV negative	98	12.7	10.5–15.2	47	14.5	10.3–20.0	
19–34			n = 121			n = 96		.38
	HPV 16, 18	90	74.4	65.9–81.3	81	84.4	75.2–90.6	
	HPV 31, 33, 45, 52, 58	19	15.7	10.3–23.2	6	5.7	2.5–12.2	
	Other oncogenic HPV	6	5.0	2.3–10.4	3	3.5	1.1–10.6	
	Other HPV/HPV negative	6	5.0	2.3–10.4	6	6.4	2.8–14.0	
35–50			n = 309			n = 134		.46
	HPV 16, 18	231	74.8	69.6–79.3	101	75.0	65.3–82.8	
	HPV 31, 33, 45, 52, 58	36	11.7	8.5–15.7	14	12.0	6.6–20.8	
	Other oncogenic HPV	23	7.4	5.0–10.9	7	7.7	3.6–16.0	
	Other HPV/HPV negative	19	6.1	4.0–9.4	12	5.3	2.6–10.4	
50–94			n = 342			n = 133		.89
	HPV 16, 18	191	55.8	50.5–61.0	80	57.5	46.2–68.0	
	HPV 31, 33, 45, 52, 58	57	16.7	13.1–21.0	17	11.2	6.0–20.0	
	Other oncogenic HPV	21	6.1	4.1–9.2	7	5.3	2.1–12.8	
	Other HPV/HPV negative	73	21.3	17.3–26.0	29	26.0	17.3–37.0	

Abbreviations: CA, Los Angeles County, California; CDC, Centers for Disease Control; CIN3+, cervical intraepithelial neoplasia grade 3 and higher; FL, Florida; HI, Hawaii; HPV, human papillomavirus; IA, Iowa; ICC, invasive cervical cancer; KY, Kentucky; LA, Louisiana; MI, Michigan.

The data source was the CDC Cancer Registry Sentinel Surveillance System.

[a] Includes cases from cancer registries in FL, HI, IA, KY, CA, LA, and MI; unweighted frequencies.

[b] Includes cases from cancer registries in IA, KY, and LA. Frequencies weighted for age and race/ethnicity.

[d] *P* values derived from generalized logit models adjusting for age and race/ethnicity.

[c]Other oncogenic types include HPV 35, 39, 51, 56, 59, 66, and 68.