Prevalence of human papillomavirus types in invasive cervical cancers from seven US cancer registries prior to vaccine introduction

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Abstract

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

Objective—We conducted a baseline study of human papillomavirus (HPV) type prevalence in invasive cervical cancers (ICC) using data from seven cancer registries (CR) in the US. Cases were diagnosed between 1994 and 2005, before the implementation of the HPV vaccines.

Materials and Methods—CRs from Florida, Kentucky, Louisiana, Michigan, Hawaii, Iowa and Los Angeles, California identified eligible ICC cases, and obtained sections from representative blocks of archived tumor specimens for DNA extraction. All extracts were assayed by Linear Array and if inadequate or HPV negative, re-tested with INNO-LiPA Genotype test. Clinical and demographic factors were obtained from the CRs and merged with the HPV typing data to analyze factors associated with different types and with HPV negativity.

Results—A total of 777 ICCs were included in this analysis, with broad geographic, age and race distribution. Overall, HPV was detected in 91% of cases, including 51% HPV16, 16% HPV18 (HPV16 negative), and 24% other oncogenic and rare types. After HPV16 and 18, the most common types were 45, 33, 31, 35 and 52. Older age and non-squamous histology were associated with HPV negative typing.

Conclusions—This study provides baseline pre-vaccine HPV types for post-vaccine ICC surveillance in the future. HPV16 and/or 18 were found in 67% of ICCs, indicating the potential for vaccines to prevent a significant number of cervical cancers.

Keywords

Human Papillomavirus; HPV typing; HPV prevalence; invasive cervical cancer

Background

Invasive cervical cancer (ICC) is the third most common cancer among females worldwide, with an estimated 530,000 new cases in 2008.[1] In the same year, in the United States (US) there were 12,410 new cases diagnosed and 4,008 deaths attributable to ICC.[2] While incidence and mortality rates in the US have declined in recent decades due to the widespread use of the Papanicolaou (Pap) test and improved treatment, there are still disparities by race and geography.[3, 4]

Human papillomavirus (HPV) is an established risk factor for developing ICC.[5–7] While infection with HPV is common, and usually does not result in ICC, persistent infection with high-risk, or oncogenic, types of HPV increases a woman's risk of developing cancer. International prevalence studies estimate that about 70% of ICCs are attributed to HPV16 and HPV18.[8–11] A meta-analysis of 85 studies worldwide showed the overall detection rate for HPV in ICC was similar in all regions (83–89%); HPV16 was the predominant type in squamous cell carcinoma (46–63%) followed by HPV18 (10–14%), while for adenocarcinoma and adenosquamous carcinoma the predominant type was HPV18 (37–41%) followed by HPV16 (26–36%).[9]

There are currently two HPV vaccines available which protect against HPV16 and 18, targeted for girls before the onset of sexual activity (and HPV exposure), with catch-up vaccine approved to age 26.[12] It will be at least 10–30 years before the first vaccinated female cohorts reach the ages at greatest risk for cancer precursors such as cervical

intraepithelial neoplasia 3 (CIN-3) and adenocarcinoma in situ (AIS), and ICC.[13] It is of great public health importance to monitor the impact of these vaccines on the rates of ICC, as well as any changes in the HPV types responsible for future cases of ICC that might occur as a result of widespread use of the vaccines.[14] The high-quality cancer registries in the US, such as those included in the National Program of Cancer Registries (NPCR) and the Surveillance, Epidemiology, and End Results (SEER) Program, provide the infrastructure for a sentinel surveillance system to monitor these potential changes on a long-term basis.[13]

The burden of HPV-associated cancers in the US was recently assessed using 1998–2003 data from NPCR and the SEER Program, providing baseline rates and geographic distribution of ICC in the US in the pre-vaccine era.[4] Since HPV typing of cancers is not performed as part of clinical care, this information is not available to cancer registries. Recent studies have determined type-specific prevalence of HPV in ICC cases in various populations in the US,[15–19] but this is the first registry-based, multi-state assessment of HPV in ICC, prior to the approval of HPV vaccines.

Methods

NPCR registries in Kentucky, Louisiana, Michigan and Florida (Kentucky, Louisiana and Detroit, MI are also part of the SEER Program) requested stored tissue samples from a simple random statewide sample of women diagnosed with ICC during 2004–2005. For Florida, the sample included three counties in the southeast part of the state (Palm Beach, Broward, Miami-Dade). Three SEER residual tissue repositories (RTR) that store tissue specimens that would otherwise be discarded, submitted samples from ICC cases: Los Angeles County, California, 1994–1999; Iowa statewide, 1994–1999; Hawaii statewide, 2000–2004.

All participating registries followed the same protocol for identifying and submitting the formalin-fixed paraffin-embedded (FFPE) tissue samples. Eligible cases had to be state residents of the participating registry and have a histologically-confirmed ICC (ICD-O-3 site codes C53.0, C53.1, C53.8, C53.9 and behavior code 3) diagnosed during the study years described above. Study coordinators in Kentucky, Louisiana, Michigan and Florida requested participation of hospitals and pathology laboratories where tissue blocks for eligible cases were stored. The criteria for selection of a representative diagnostic block from each case included the highest ratio of viable tumor to normal tissue and the best preservation (favoring use of biopsy rather than resection specimen). Participating laboratories prepared the samples according to the study protocol. In some cases, a central laboratory prepared the samples, and then the paraffin tissue blocks were returned to the donating facility. For the SEER RTRs, a laboratory at each site prepared the tissue samples. Materials for submitting and shipping the specimens were provided by CDC, and specimens were sent directly to the CDC for analysis. Selected demographic and clinical data from each registry were linked with HPV typing results to form a complete record.

CDC received IRB approval for the study, and each participating registry completed an IRB review with its own institution. In addition, some hospitals and pathology laboratories required an IRB review before participating.

Laboratory Methods

Blocks were cut using precautions to prevent polymerase chain reaction (PCR) contamination between cases, including single-use disposable microtome blades, cleaning microtome between samples, and direct transfer of sections for PCR from microtome to sterile tubes using clean single-use applicator. The first and last sections were stained with Hematoxylin and Eosin (H&E). Intervening sections were transferred into 2 ml conical screw cap tubes with tether cap, one 10-micron section or two 5-mciron sections per tube (Simport, Beloeil, Canada).

H&E sections were reviewed by a study pathologist to confirm that tumor was present. Samples that did not have representative material were not processed. For confirmed samples, DNA was extracted with the Chemagic Viral NA/gDNA Kit special (chemagen USA, Worcester MA) as previously described.[20] Briefly, sections were heated for 20 min at 120°C in 180 μl tissue lysis buffer, then incubated with Proteinase K overnight at 65°C and then purified using Chemagic MSM1 (chemagen USA). The DNA was eluted in a final volume of 100 μl.

All DNA extracts were tested with the Linear Array HPV Genotyping Test (LA, Roche Diagnostics, Indianapolis, IN). The test was performed according to the manufacturer's protocol except for a template volume of 10 μl in the PCR reaction and the use of Beeblot instrument (Bee Robotics, Caernarfon, UK) for automated hybridization and washing of the reverse line blot. The LA detects 37 HPV types (6, 11, 16, 18, 26, 31, 33, 35, 39, 40, 42, 45, 51, XR(52), 53, 54, 55, 56, 58, 59, 61, 62, 64, 66, 67, 68, 69, 70, 71, 72, 73, 81, 82, 83, 84, 89, IS39). Samples positive for the XR probe that were also positive for HPV33, 35 and 58 required further evaluation to confirm or exclude the presence of HPV52. An HPV52 quantitative PCR assay was used to determine the status of HPV52 in these cases.[21]

Samples with negative or inadequate LA results were re-tested with the INNO-LiPA HPV Genotyping Assay (LiPA, Innogenetics, Gent, Belgium) following the manufacturer's specifications. LiPA 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). Samples failing both assays were considered inadequate and excluded from analysis (N=9). H&E slides of negative samples were reviewed to see if sampling or preservation could have contributed to false negative results.

Statistical Analysis

The descriptive analysis presented here includes tabulation of HPV typing results by registry, race, age, histology, stage, grade, and urban/rural residence, and distribution of HPV types alone and in combinations. Statistical analysis was conducted using Stata 10 software.[22]

We used the hierarchical categories for HPV types as suggested by Wheeler et al.[15] with HPV16 as the most oncogenic type: HPV16 positive; HPV18 positive, HPV16 negative; HPV16 and HPV18 negative, positive for other oncogenic HPV types (31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68); negative for major oncogenic HPV types, but positive for other HPV types, both oncogenic and non-oncogenic; negative for all HPV. Rates of positive and

negative results were compared by race, age, histology, stage and grade using bivariate analysis and as well as logistic regression to elucidate factors associated with HPV negativity.

Results

Tissue samples for 786 cases of ICC were eligible for testing, 777 of which (98.9%) were adequate for evaluation. Selected demographic variables are presented by registry in Table 1. Overall, 53% of cases were non-Hispanic white; however, the racial/ethnic distribution varied considerably by state, as expected. Most cases were non-Hispanic white in Iowa, Kentucky and Michigan, while in Louisiana the cases were distributed evenly between non-Hispanic white and non-Hispanic black. Florida and Los Angeles had the largest proportion of Hispanic cases, and in Hawaii, 68% were Asian-Pacific Islander. Overall, less than half of the cases were aged 50 years and older, and almost one-third were among young women under age 40. The majority of the cases resided in urban counties. Because of their classification as urban counties, Los Angeles County and the three-county area in Florida did not contribute any cases from a rural residence.

Overall, HPV16 was detected in 51% of cases, followed by HPV18 (with HPV16 negative) which was detected in 16% of the cases (Table 1). In addition, 21% of cases were negative for HPV16 and 18 but positive for other oncogenic types, 3.2% were positive for other HPV types, and 9.4% tested negative for HPV. Among those positive for HPV16 and/or HPV18, 9.5% were also positive for other HPV types (data not shown).

Table 2 presents the HPV categories by selected demographic and clinical variables for the seven registries combined. HPV16 was detected in over half the women in the younger age groups but was less common in older women. Overall, HPV18 was detected in 16% of cases; however, it varied greatly among the age groups with young women under age 30 having the highest proportion and women aged 70 and older having the lowest. Women aged 70 and older were less likely to be positive for HPV16 and HPV18, and more likely to be positive for other oncogenic HPV types. The majority of squamous cell carcinomas were positive for HPV16 (56%), followed by 25% which were negative for HPV16 and 18 but positive for other oncogenic types. For adenocarcinomas, 36% were HPV16 positive, followed by 32% HPV18 positive, while 20% were negative for HPV. Most cases in the histologic category of "All other" were HPV16 positive (46%), followed by 32% which were negative for HPV. About half of the local, regional and distant cases were positive for HPV16, but HPV types varied considerably for the remaining half in each category. A higher percentage of cases in the local (21%) and regional (22%) stages were positive for types other than HPV16 and 18, compared to distant stage (12%).

Negative results for oncogenic HPV types were more common among women who were older and non-Hispanic white, and among tumors that were adenocarcinomas, and cancers that were more advanced stage and grade. When all these variables were included in a logistic model, only age and histology were found to be statistically significant independent predictors: older women were more likely than younger to have HPV negative results (OR=3.2 for 50–69 and OR=5.8 for 70+, compared with 40–49 years old); and

adenocarcinomas (OR=5.1) and "all others" (OR=6.3) were more likely to be HPV negative than squamous tumors.

The H&E slides of the 73 samples with negative results were reviewed to see if sampling or preservation could have contributed to false negative results. Only seven were limited by extremely small foci of tumor (9.6%) and all appeared to be adequately preserved. Nearly 60% were adeno- or adenosquamous carcinomas that could not be distinguished histologically from endometrial cancers.

HPV types (single and combinations) by the hierarchical categories are shown in Table 3. Single-type HPV16 was found in 44% of tumor samples, and single-type HPV18 was found in 15%. With respect to the current vaccine coverage, 67% of cases were positive for HPV16 and/or 18; 7% of these also had additional HPV types detected. Among cases negative for HPV16 and 18, the five types with the highest frequency were HPV45 (5.3%), HPV33 (3.2%), HPV31 (1.9%), HPV35 (1.9%) and HPV52 (1.8%). We also examined HPV types among just HPV-positive samples (N=704), as in a study of 17 countries in Europe,[23] and found 342 (49%) were HPV16 only; 116 (16%) were HPV18 only; 182 (26%) were other single HPV types; 64 (9%) were multiple types (of which 10, or 1.4%, were HPV16 and 18).

Discussion

In our registry-based study including seven geographical regions of the US, 67% of ICC were positive for HPV16 and/or 18, and 24% for other types. This is generally in agreement with other studies and meta-analyses that have found that about 70% of cervical cancers can be attributed to HPV16 and 18.[8–11] In our study, HPV16, HPV18 and HPV45 were most commonly detected, similar to studies from New Mexico and Washington.[15, 16] We found substantial differences in HPV types by histology, with squamous cell having the highest percentage of HPV16, but the lowest percentage of HPV18.

Our results are also consistent with a joint analysis of two recent multi-center studies in Europe, which included 17 countries and about 2,900 cases of ICC.[23] However, direct comparisons are hard to make as they only presented an analysis of HPV-positive cases; among those with single HPV infections (80% of their HPV-positive cases), 79% were either HPV16 or HPV18, which is similar to our results if we exclude the negatives (73%, analysis not shown). Among the 704 HPV-positive cases in our analysis, 9% had multiple HPV types (2 or more), compared with 17.4% in the European study, but because of how the data were presented we cannot analyze what factors may account for this difference.

Although it has been accepted that HPV is a necessary factor in the causal pathway to ICC,[5] HPV is not always detected in tumor specimens from women diagnosed with ICC. Overall, we found 91% of cases tested positive for HPV, which is consistent with other studies, and similar to results of a recent meta-analysis including over 40,000 ICC cases worldwide where 89% tested positive for HPV,[24] and another meta-analysis of 1,503 cases from studies dating from 1994 to 2007.[25] We observed substantial variation in the proportion of negative HPV results across the variables considered, but only older age and adenocarcinomas

remained significant in the multivariate logistic regression. Similar findings for age and histology were reported in a large study in Spain.[26] Nearly 60% of the HPV negative cases could not be distinguished from endometrial primaries on the basis of histology alone. Attributing lower-uterine segment endometrial to endocervical primaries may be one explanation for HPV negative results. As endometrial cancers are more likely to occur in older women, the higher prevalence of HPV negative tumors in older age groups and with non-squamous histology raises the possibility that some tumors were of non-cervical origin. False negative results due to limitations of HPV detection and typing methods cannot be ruled out.

With respect to the reach of the current vaccines, our results suggest that 67% of the cases could potentially be covered, as they were positive for HPV16 and/or 18 either alone or in combination with other types. A nonavalent vaccine is being developed which will cover HPV31, 33, 45, 52 and 58 in addition to HPV16, 18, 6 and 11. Based on the distribution of HPV types in our study, the coverage of such a vaccine would increase another 18%.

This study demonstrates the effectiveness of using a registry-based approach to sample and determine HPV type distribution in cervical cancer. The strength of this approach is that the data for the submitted cases were very complete except for stage, and seven different regions of the US were included. Not all cases could be included as not all facilities agreed to participate and some tissue blocks could not be located or did not have an adequate sample. Another limitation was the restriction in lifestyle or behavioral variables available in the data routinely and uniformly collected by the cancer registries, such as smoking, co-morbidities, number of sexual partners and other risky health factors that would allow a more comprehensive characterization of the factors associated with the different HPV types.

Acknowledgements

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Table 1

Demographics and HPV types for invasive cervical cancer cases by cancer registry

	Los Angeles County	Hawaii	Iowa	Kentucky	Florida[a]	Louisiana	Michigan	TOTAL
Number of cases contributed	70	116	66	159	169	93	104	777
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)
Race								
White, non-Hispanic	20 (28.6)	19 (16.3)	59 (89.4)	135 (84.9)	51 (30.2)	45 (48.4)	80 (76.9)	409 (52.6)
Black, non-Hispanic	4 (5.7)	1 (0.9)	4 (6.1)	21 (13.2)	43 (25.4)	43 (46.2)	13 (12.5)	129 (16.6)
Hispanic	38 (54.3)	1 (0.9)	0 (0.0)	2 (1.3)	73 (43.2)	2 (2.2)	8 (7.7)	124 (16.0)
Asian, Pacific Islander	7 (10.0)	79 (68.1)	3 (4.5)	0 (0.0)	0 (0.0)	3 (3.2)	1 (1.0)	93 (12.0)
All other or unknown	1 (1.4)	16 (13.8)	0 (0.0)	1 (0.6)	2 (1.2)	0 (0.0)	2 (1.9)	22 (2.8)
Age								
<30	4 (5.7)	10 (8.6)	5 (7.5)	7 (4.4)	9 (5.3)	6 (6.5)	4 (3.9)	45 (5.8)
30–39	20 (28.6)	20 (17.2)	27 (40.9)	19 (11.9)	39 (23.1)	23 (24.7)	35 (33.6)	183 (23.5)
40–49	14 (20.0)	35 (30.2)	10 (15.2)	51 (32.1)	47 (27.8)	23 (24.7)	24 (23.1)	204 (26.3)
50–69	21 (30.0)	32 (27.6)	14 (21.2)	59 (37.1)	49 (29.0)	26 (28.0)	29 (27.9)	230 (29.6)
70+	11 (15.7)	19 (16.4)	10 (15.2)	23 (14.5)	25 (14.8)	15 (16.1)	12 (11.5)	115 (14.8)
County of residence[b]								
Urban	70 (100.0)	90 (77.6)	28 (42.4)	86 (54.1)	169 (100.0)	74 (79.6)	76 (73.8)	593 (76.4)
Rural	0 (0.0)	26 (22.4)	38 (57.6)	73 (45.9)	0 (0.0)	19 (20.4)	27 (26.2)	183 (23.6)
HPV Type[c]								
HPV16 positive	34 (48.6)	54 (46.6)	35 (53.0)	84 (52.8)	88 (52.1)	45 (48.4)	55 (52.9)	395 (50.8)
HPV18 positive, HPV16 negative	9 (12.9)	18 (15.5)	11 (16.7)	28 (17.6)	17 (10.1)	17 (18.3)	22 (21.2)	122 (15.7)
Positive for other oncogenic types[d]	17 (24.3)	30 (25.9)	11 (16.7)	25 (15.7)	41 (24.3)	22 (23.6)	16 (15.4)	162 (20.9)
Positive for other types	2 (2.9)	6 (5.1)	2 (3.0)	6 (3.8)	3 (1.8)	4 (4.3)	2 (1.9)	25 (3.2)
Negative for HPV	8 (11.3)	8 (6.9)	7 (10.6)	16 (10.1)	20 (11.8)	5 (5.4)	9 (8.6)	73 (9.4)

[a] Palm Beach, Broward, Miami-Dade Counties.

[b] Rural-Urban Continuum Codes (1–3 for urban, 4–9 for rural).[27] There was one unknown urban-rural code in Michigan.

[c] See Methods section for further explanation of HPV Type hierarchical groups.

[d]HPV31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68

Table 2

HPV types for invasive cervical cancers by selected demographic and clinical variables, and odds ratios comparing HPV positive and negative cases

	Total	HPV16 positive No. (%)	HPV18 positive, HPV16 negative No. (%)	Positive for other oncogenic types No. (%)	Positive for other rare types No. (%)	Negative for HPV No. (%)	Odds Ratio[a]	Odds Ratio 95% CI
Total	777	395 (50.8)	122 (15.7)	162 (20.9)	25 (3.2)	73 (9.4)	--	--
Race/Ethnicity[b]								
White, non-Hispanic	409	213 (52.1)	64 (15.7)	72 (17.6)	12 (2.9)	48 (11.7)	2.53	1.0–6.41
Black, non-Hispanic	129	64 (49.6)	24 (18.6)	32 (24.8)	3 (2.3)	6 (4.7)	1.0	(--)
Hispanic	124	63 (50.8)	16 (12.9)	30 (24.2)	5 (4.0)	10 (8.1)	2.01	0.65–6.19
Asian, Pacific Islander	93	40 (43.0)	16 (17.2)	24 (25.8)	5 (5.4)	8 (8.6)	1.97	0.62–6.89
All other	17	11 (64.7)	1 (5.9)	4 (23.5)	0 (0.0)	1 (5.9)	2.67	0.28–25.69
Age								
<30	45	25 (55.6)	10 (22.2)	7 (15.6)	0 (0.0)	3 (6.6)	1.72	0.41–7.22
30–39	183	108 (59.0)	27 (14.7)	39 (21.3)	1 (0.6)	8 (4.4)	1.02	0.36–2.86
40–49	204	111 (54.4)	42 (20.6)	38 (18.6)	5 (2.5)	8 (3.9)	1.0	(--)
50–69	230	104 (45.2)	32 (13.9)	51 (22.2)	13 (5.7)	30 (13.0)	3.18	1.37–7.38
70+	115	47 (40.8)	11 (9.6)	27 (23.5)	6 (5.2)	24 (20.9)	5.80	2.40–13.97
Histology[c]								
Squamous	570	317 (55.6)	61 (10.7)	141 (24.7)	23 (4.0)	28 (5.0)	1.0	(--)
Adenocarcinoma	179	65 (36.3)	58 (32.4)	19 (10.6)	1 (0.6)	36 (20.1)	5.10	2.88–9.04
All other	28	13 (46.4)	3 (10.7)	2 (7.1)	1 (3.6)	9 (32.1)	6.25	2.31–16.91
Stage								
Local	367	191 (52.0)	66 (17.9)	78 (21.3)	9 (2.5)	23 (6.3)	1.0	(--)
Regional	246	127 (51.6)	27 (10.9)	55 (22.4)	10 (4.1)	27 (11.0)	1.57	0.83–2.99
Distant	74	37 (50.0)	13 (17.6)	9 (12.1)	3 (4.1)	12 (16.2)	1.94	0.83–4.56
Unknown	90	40 (44.4)	16 (17.8)	20 (22.2)	3 (3.3)	11 (12.2)	1.92	0.82–4.53
Tumor grade								
Grade I	66	38 (57.6)	16 (24.2)	4 (6.1)	3 (4.5)	5 (7.6)	1.0	(--)
Grade II	237	122 (51.5)	30 (12.7)	57 (24.0)	8 (3.4)	20 (8.4)	1.66	0.54–5.10

	Total	HPV16 positive No. (%)	HPV18 positive, HPV16 negative No. (%)	Positive for other oncogenic types No. (%)	Positive for other rare types No. (%)	Negative for HPV No. (%)	Odds Ratio[a]	Odds Ratio 95% CI
Grade III	252	121 (47.8)	44 (17.4)	48 (19.0)	8 (3.2)	31 (12.6)	1.85	0.61–5.59
Grade IV	12	1 (8.3)	4 (33.3)	4 (33.3)	0 (0.0)	3 (25.0)	2.30	0.37–14.02
Unknown	210	113 (53.8)	28 (13.3)	49 (23.3)	6 (2.9)	14 (6.7)	1.14	0.35–3.71

[a] Odds ratios correspond to a logistic regression model to examine factors associated with HPV negative results (binary outcome). All the variables in this table were included in the model. For each variable, the category with the lowest percentage of HPV negatives was selected as the reference group (OR=1).

[b] 5 cases were missing race/ethnicity data and were not included here

[c] Coded as squamous cell carcinoma, adenocarcinoma (including adenosquamous and glassy cell), and all other (including small cell, neuroendocrine and other rare types), as in Watson et al, 2008.[4]

Table 3

HPV type distribution among invasive cervical cancer cases by hierarchical group

HPV Types	Number	Percent
HPV16 positive	395	50.8
HPV16	342	44.0
HPV16, 18	10	1.4
HPV16, 33	6	0.8
HPV16, 45	5	0.6
HPV16, 58	5	0.6
HPV16, 52	4	0.5
HPV16, 59	4	0.5
HPV16, 31	2	0.3
HPV16, 39	2	0.3
HPV16, 56	2	0.3
HPV16, 18, 31	1	0.1
HPV16, 18, 33	1	0.1
HPV16, 18, 33, 45	1	0.1
HPV16, 18, 45, 52	1	0.1
HPV16, 18, 51, 55, 73	1	0.1
HPV16, 26	1	0.1
HPV16, 35, 52, 55, 71, 72, 83	1	0.1
HPV16, 42	1	0.1
HPV16, 51, 68	1	0.1
HPV16, 54	1	0.1
HPV16, 61	1	0.1
HPV16, 66	1	0.1
HPV16, is39	1	0.1
HPV18 positive, HPV16 negative	122	15.7
HPV18	116	14.9
HPV18, 33	1	0.1
HPV18, 35, 70, 73	1	0.1
HPV18, 45	1	0.1
HPV18, 52	1	0.1
HPV18, 70	1	0.1
HPV18, 72	1	0.1
HPV16/18 negative, positive for other oncogenic types	162	20.9
HPV45	41	5.3
HPV33	25	3.2
HPV31	15	1.9
HPV35	15	1.9
HPV52	14	1.8
HPV39	13	1.7

HPV Types	Number	Percent
HPV58	13	1.7
HPV56	6	0.8
HPV59	6	0.8
HPV68	4	0.5
HPV51	3	0.4
HPV66	2	0.3
HPV33, 58	2	0.3
HPV39, 45	1	0.1
HPV53, 56	1	0.1
HPV11, 31	1	0.1
Other rare HPV types[a]	25	3.2
Negative for HPV	73	9.4

[a] Includes 6,11,26,40,54,62,67,69,70,73,82, is 39 and four cases detected but not typed.