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Trends in HPV- and non-HPV-Associated Vulvar Cancer Incidence, United States, 2001–2017

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Abstract

Vulvar cancer incidence has been rising in recent years, possibly due to increasing exposure to human papillomavirus (HPV). We assessed incidence rates of HPV-associated and non-HPV-associated vulvar cancers diagnosed from 2001 to 2017 in the United States (US). Using population-based cancer registry data covering 99% of the US population, incidence rates were calculated and stratified by age, race/ethnicity, stage, geographic region, and histology. The annual percent change and average annual percent change in incidence per year were calculated using joinpoint regression. From 2001 to 2017, the incidence of HPV-associated vulvar cancers increased by 1.2% per year, most notably among women who were aged 50–59 years (2.6%), 60–69 years (2.4%), and ≥70 years (0.9%); of White (1.5%) and Black (1.1%) race; diagnosed at an early (1.3%) and late (1.8%) stage; and living in the Midwest (1.9%), Northeast (1.4%), and South (1.2%). Incidence increased each year for HPV-associated histologic subtypes including keratinizing (4.7%), non-keratinizing (6.0%), and basaloid (3.1%) squamous cell carcinomas (SCCs), while decreases were found in warty (2.7%) and microinvasive (5.5%) SCCs. HPV-associated vulvar cancer incidence increased overall and among women aged over 50 years while remaining stable among women younger than 50 years. The overall incidence for non-HPV-associated cancers was stable. Continued surveillance of HPV-associated cancers will allow us to monitor future trends as HPV vaccination coverage increases in the US.

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Disclaimer:

The findings and conclusions in this article are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Ethics:

This study used publicly available, anonymized population-based cancer registry data from USCS. Thus, it was exempt from ethical compliance.

Disclosures:

The authors report no conflict of interest.

Keywords

vulvar cancer; HPV; HPV-associated cancer; incidence; trends

1. Introduction

Vulvar cancer accounts for approximately 5% of gynecologic cancers and 0.6% of female cancers in the United States (US) (U.S. Department of Health and Human Services et al.). In 2018, 5,496 new cases occurred, with an age-adjusted incidence rate of 2.6 per 100,000 women (U.S. Department of Health and Human Services et al.). Although vulvar cancer is rare, its incidence has been rising over the past two decades in the US and other high-income countries in North America, Europe, and Asia (Kang et al., 2017; Van Dyne et al., 2018). This increase has been partially attributed to increasing HPV infection (Kang et al., 2017).

Vulvar cancer is caused by two main pathways—oncogenic human papillomavirus (HPV) infection and independent of HPV infection (Alkatout et al., 2015; Halec et al., 2017). In a study using data from seven US cancer registries, HPV DNA was found in approximately 69% of invasive vulvar cancers (approximately 68% were high-risk HPV types and approximately 48% were HPV 16) (Gargano et al., 2012). Warty and basaloid subtypes of vulvar squamous cell carcinoma (SCC) are most likely to be HPV-mediated, but other subtypes, such as keratinizing SCC, are also associated with HPV (de Sanjosé et al., 2013; Gargano et al., 2012). In the same registry study, HPV DNA was detected in approximately 92% of basaloid, 78% of warty, and 50% of keratinizing vulvar SCC cases (Gargano et al., 2012).

In this report, we examine incidence rates and trends for vulvar cancers by histologic subtypes known to be associated with oncogenic HPV infection, as well as vulvar cancers that are not thought to be associated with HPV. Assessing trends in vulvar cancer incidence differentiated by HPV-associated status will help us interpret the potential impact of HPV vaccination as vaccination coverage increases in the US.

2. Materials and methods

2.1. Data source and cancer classification

We analyzed vulvar cancer incidence data from the United States Cancer Statistics (USCS) database, which includes population-based cancer registry data from the Centers for Disease Control and Prevention's National Program of Cancer Registries (NPCR) and the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program (Centers for Disease Control and Prevention). Cancer registries demonstrate that data were of high quality by meeting the USCS publication criteria (Centers for Disease Control and Prevention); from 2001 to 2017, data from all cancer registries (except Mississippi in 2002) met these criteria, covering 99% of the US population. We identified vulvar cancer cases using the *International Classification of Diseases for Oncology*, Third Edition (ICD-O-3), topography codes C51.0-C51.9 (Jack et al., 2000), excluding histology codes 9050–

9055 (mesothelioma), 9140 (Kaposi sarcoma), and 9590–9992 (lymphoma, myeloma, and leukemia).

Based on the definition of risk factor-associated cancers, HPV-associated cancers were defined as vulvar cancers with specific cell types in which HPV DNA is frequently found, including ICD-O-3 histology codes 8050–8084 and 8120–8131 restricted to squamous cell carcinomas (SCCs) (United States Cancer Statistics, 2022). We further categorized HPV-associated vulvar cancers into SCCs, not otherwise specified (8070); keratinizing SCC (8071); warty SCC (8051); basaloid SCC (8083); microinvasive SCC (8076); small cell and large cell non-keratinizing SCC (8072 and 8073); and other SCC types (8050, 8052–8060, 8074, 8075, 8077–8084, 8120–8131). Non-HPV-associated vulvar cancers included ICD-O-3 histology codes 8000–8049, 8085–8119, and 8132–9992. We categorized the histologies of non-HPV-associated vulvar cancers into basal cell carcinomas (8090–8098), glandular carcinomas (8140–8575), soft tissue cancers (8800–8912), melanocytic cancers (8720–8780), and miscellaneous (8000–8049, 8085–8089, 8099–8119, 8132–8139, 8576–8719, 8781–8799, 8913–9992). These groupings were based on the World Health Organization Classification guidelines and the ICD-O-3 SEER site/histology validation list (Kurman et al., 2014), which group subtypes of cancer by their site and histological characteristics. All cancers were microscopically confirmed.

2.2. Data analysis

We calculated age-adjusted incidence rates of vulvar cancer per 100,000 women, standardized to the 2000 US population, using SEER*Stat software version 8.3.6 (Calverton, MD). We examined incidence rates of HPV-associated and non-HPV-associated vulvar cancers by age, race/ethnicity groups, census region, tumor stage, histology, and HPV status. Data were suppressed for cells with fewer than six cases to ensure data confidentiality (U.S. Department of Health and Human Services et al.).

We stratified and presented vulvar cancer incidence rates by the following age groups: <30, 30–39, 40–49, 50–59, 60–69, and ≥70 years. We classified racial and ethnic groups as non-Hispanic White (White), non-Hispanic Black (Black), non-Hispanic American Indian and Alaska Native (AI/AN), non-Hispanic Asian and Pacific Islander (A/PI), and Hispanic. Information about race and Hispanic ethnicity was collected separately. To reduce misclassification of Hispanic persons, an algorithm was applied to the ethnicity data (NAACCR Race and Ethnicity Work Group, 2011). Similarly, to minimize the misclassification of AI/AN race, cases were linked with the Indian Health Service patient registration database and coded as AI/AN (Jim et al., 2014).

The tumor stage was classified using a variable that combined SEER Summary Stage 2000 (for cases diagnosed from 2001 to 2003) and Derived Summary Stage 2000 (for cases diagnosed in 2004 or later). The staging criteria characterized cancers as localized, regional, distant, or unknown stage. Localized cancer is confined to the primary site; regional cancer has spread directly beyond the primary site (regional extension) or to regional lymph nodes; and distant cancer has spread to other organs (distant extension) or remote lymph nodes (Young, 2001). We categorized tumor stage as early (localized), late (regional and distant), or unstaged.

We estimated the change in rates from 2001 to 2017 using joinpoint regression, which involves fitting a series of joined straight lines on a logarithmic scale to the trends in the annual age-standardized rates (Kim et al., 2000); up to 2 joinpoints (3 line segments) were allowed (Kim et al., 2000). The average annual percentage change (AAPC) for 2001 to 2017 was calculated using a weighted average of the slope coefficients of the underlying joinpoint regression line with the weights equal to the length of each segment over the interval. AAPC is a summary measure of the overall incidence trend from 2001 to 2017. To determine whether the AAPC was statistically different from zero at an alpha of 0.05, a two-sided *t*-test was used for 0 joinpoints, and a two-sided *z*-test was used for 1 or more joinpoints. Incidence rates were considered to increase if the AAPC was higher than zero ($P < 0.05$) and to decrease if the AAPC was less than zero ($P < 0.05$). Otherwise, rates were considered stable. We calculated trends using joinpoint regression program version 4.8.0.1.

This study used publicly available, anonymized population-based cancer registry data from USCS. Thus, it was exempt from ethical compliance.

3. Results

From 2001 to 2017, approximately 3,500 cases of HPV-associated and 1,000 cases of non-HPV-associated vulvar cancers occurred annually in the US. New cases of HPV-associated vulvar cancer increased from 2,711 cases in 2001 to 4,257 cases in 2017, increasing by 1.2% each year (Table 1). HPV-associated vulvar cancer incidence was stable among women aged 30 years and younger (0.2% per year), aged 30–39 years (−0.6% per year), and 40–49 years (−0.0% per year). However, incidence among women 50 years and older increased by 1.4% per year, with highest incidence rates among women aged 50–59 years (2.6% per year), followed by women aged 60–69 years (2.4% per year), and women aged 70 years and older (0.9% per year). The incidence of HPV-associated vulvar cancer increased by 1.5% per year among White women and 1.1% per year among Black women, but was stable among AI/AN, A/PI, and Hispanic women. Incidence also increased by 1.3% per year for localized cancers and 1.8% per year for regional and distant cancers. By census region, the incidence for HPV-associated vulvar cancer increased in the Midwest (1.9% per year), Northeast (1.4% per year), and South (1.2% per year) regions.

Among non-HPV-associated vulvar cancers, incidence trends were stable from 2001 to 2017 (−1.0% per year). Incidence of non-HPV-associated-vulvar cancers decreased in younger women, with a decline of 4.4% per year among women under 30 years, 2.8% among women aged 30–39 years, 1.5% among women aged 40–49 years, and 1.2% among women aged 50–59 years. Incidence rates decreased by 0.5% per year for White women but were stable for all other race and ethnicity groups examined. By stage, the incidence of localized tumors decreased by 0.9% per year for non-HPV-associated vulvar cancers. In addition, the incidence rate decreased by 1.1% per year in the Midwest region for non-HPV-associated cancers.

Among HPV-associated vulvar cancers, incidence increased for keratinizing (4.7% per year), nonkeratinizing (6.0% per year), and basaloid (3.1% per year) SCCs; however, incidence declined for microinvasive (5.5% per year) and warty (2.9% per year) SCCs

(Table 2). Among non-HPV-associated vulvar cancers, incidence decreased among basal cell carcinomas (1.5% per year), soft tissue cancers (1.5% per year), and other non-HPV-associated cancers (3.2% per year).

4. Discussion

In this study examining 19 years of data from the US, the incidence of HPV-associated vulvar cancers increased among women aged 50 years and older, but the incidence was stable among women younger than 50 years from 2001 to 2017. This stable trend in HPV-associated cancer incidence among younger women is encouraging as stabilization is a key step that often precedes and potentially signals the anticipated decline in the future.

Among women aged 50 years and older, the incidence of HPV-associated vulvar cancers increased, most notably among women aged 50–59 years and 60–69 years, by an average of approximately 2.5% annually. This increase in incidence among women over aged 50 years has been reported in a prior publication covering the US data (Van Dyne et al., 2018). Possible explanations of the higher incidence rate among older women include higher cumulative high-risk HPV exposure (González et al., 2010), increased HPV persistence (Castle et al., 2005), or reactivation of latent HPV infection among older women (Gravitt et al., 2013). Consistent with previous reports (Centers for Disease Control and Prevention; Hu et al., 2010), White women had the highest incidence of HPV-associated vulvar cancer and the highest average annual increase in the incidence of HPV-associated vulvar cancer compared with the other racial groups examined.

To understand the stabilization of HPV-associated vulvar cancer incidence in the youngest population, it is important to consider the decline in vulvar precancer incidence, decrease in HPV prevalence, and increase in HPV vaccination coverage. In a recent analysis of SEER data, the incidence of vulvar precancers declined among women aged 15–29 years after the introduction of the HPV vaccine (Mix et al., 2022). Due to the latency period and delays in diagnosis of vulvar cancer (Goodman, 2021), the analogous decline in the incidence of HPV-associated vulvar cancers among younger women is anticipated in the future. Also, the prevalence of HPV has decreased since the HPV vaccination program was introduced in the US. From 2015 to 2018, the prevalence of HPV vaccine-type infections declined by 88% among females aged 14–19 years and by 81% among females aged 20–24 years when compared with the pre-vaccine era (Rosenblum et al., 2021). Furthermore, data from the National Immunization Survey-Teen showed that the HPV vaccination coverage with ≥1 dose among adolescent females increased from approximately 25% in 2007 to 77% in 2020 (Pingali et al., 2021). Similarly, in 2018, 52.8% of women aged 19–26 years reported receiving ≥1 dose of the HPV vaccine in the National Health Interview Survey (Lu et al., 2021), an increase from 34.5% reported in 2012 (Williams et al., 2014), and a further increase from 10.5% reported in 2008 (Schiller & Euler, 2009). The continued decline in the prevalence of HPV types and the increase in the coverage of HPV vaccination could contribute to the stabilization of HPV-associated vulvar cancer incidence among younger women in this study.

The overall incidence of non-HPV-associated vulvar cancers remained stable from 2001 to 2017. However, the incidence rates decreased in women who were White, at an early stage, and from the Midwest region. Previous studies from high-income countries have reported an increasing incidence of vulvar cancer among younger women (Barlow et al., 2015; Bray et al., 2020; Buttmann-Schweiger et al., 2015). However, we observed a decline in non-HPV-associated cancer incidence for each age group under 60 years and stabilization for HPV-associated cancer incidence for each group under 50 years. The reasons for the decline in incidence of non-HPV-associated vulvar cancer are not clearly understood. Some possible factors include the increased recognition of differentiated vulvar intraepithelial neoplasia as a precursor lesion to HPV-independent vulvar cancer (Eva et al., 2020). Also, improved treatment options for vulvar lichen sclerosus, which decrease malignancy, may partly explain the decline in new cases (Lorenz et al., 1998). Histologic trends for non-HPV-associated cancers revealed a decreasing trend of basal cell carcinoma and soft tissue cancers. For HPV-associated vulvar cancer subtypes, the incidence of warty decreased, and basaloid increased from 2001 to 2017. The reasons for these opposite trends are unknown but merit further consideration.

Currently, no recommended screening strategies are available for the early detection of vulvar cancer in the general population (Committee on Gynecologic Practice at the American College of Obstetricians and Gynecologists, 2016). Given the lack of screening recommendations, CDC has the *Inside Knowledge About Gynecologic Cancer* campaign to increase awareness of the signs and symptoms of vulvar and other gynecologic cancers and promote HPV vaccine uptake (Centers for Disease Control and Prevention, 2021). HPV vaccination is recommended for the primary prevention of vulvar cancers as well as other HPV-associated cancers. Vaccination is routinely recommended for all persons aged 11–12 years, with catch-up vaccination through 26 years (Meites et al., 2019). In 2020, over half of adolescents aged 13–17 years were up to date with the HPV vaccine series (Pingali et al., 2021). Increasing coverage of the HPV vaccine could prevent most HPV-associated vulvar cancers in the future.

Our findings are subject to at least four limitations. First, we used histology as an indicator of vulvar cancers likely attributable to HPV, based upon the cell types in which HPV DNA is most frequently found. Although cancer registry data are useful for tracking broad histologic categories, pathology reports from the cancer registries often lack information on vulvar cancer subtypes. In this study, we observed a high proportion of cases reported as not otherwise specified (NOS). The lack of specific histological classification limits our ability to look at subtypes such as warty or basaloid, which are most strongly associated with HPV infection (Siegel et al., 2017). Second, there is variability in the prevalence of HPV by histologic subtypes. For instance, the prevalence of HPV positive keratinizing tumor varied between studies, from approximately 50% (Gargano et al., 2012) to 33% (Brusen Villadsen et al., 2021), but was reported to be as low as 13% (Faber et al., 2017). Third, the number of cases and corresponding incidence rates for some racial and ethnic groups, such as AI/AN, A/PI, or Hispanic populations, could potentially be misclassified or undercounted. Fourth, the rates or trends based on small numbers, such as fewer than 16 cases, could raise statistical issues concerning stability. In our study, the small number of annual cases for some racial groups and histologic subtypes may lead to unstable trends. Despite these

limitations, this study used high-quality, population-based surveillance data covering 99% of the US population.

5. Conclusions

In an analysis based on classification of histologic subtypes, the incidence of HPV-associated vulvar cancer increased overall and more prominently among women aged over 50 years; however, incidence remained stable for women younger than 50 years. Continued surveillance of HPV-associated vulvar cancer is important as HPV vaccination coverage increase in the US.

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HIGHLIGHTS

- The overall incidence of HPV-associated vulvar cancers in the United States increased by 1.2% each year from 2001 to 2017.
- The overall incidence of non-HPV-associated vulvar cancers remained stable from 2001 to 2017 (−1.0% per year).
- HPV-associated vulvar cancer incidence increased among women aged ≥50 years but was stable among women <50 years.
- Incidence of HPV-associated subtypes such as keratinizing, non-keratinizing, and basaloid SCCs increased.
- Incidence of non-HPV-associated vulvar cancer subtypes such as basal cell and soft tissue cancers decreased.

Table 1.

Incidence of HPV- and non-HPV-associated Vulvar Cancer–United States Cancer Statistics, 2001–2017

	HPV-associated[1]					Non-HPV-associated[1]				
	2001		2017		2001–2017	2001		2017		2001–2017
	No.	rate*	No.	rate*	AAPC (95% CI)[1]	No.	rate*	No.	rate*	AAPC (95% CI)[2]
Total	2,711	1.73	4,257	2.08	1.2† (0.9 to 1.5)	935	0.61	1,083	0.52	−1.0 (−2.4 to 0.5)
Age (years) [3]										
<30	15	0.03	19	0.02	0.2 (−3.1 to 3.5)	28	0.05	19	0.03	−4.4† (−7.6 to −1.0)
30–39	147	0.70	129	0.62	−0.6 (−1.4 to 0.3)	38	0.18	27	0.13	−2.8† (−5.2 to −0.3)
40–49	410	1.88	394	1.89	−0.0 (−0.8 to 0.8)	85	0.39	60	0.29	−1.5† (−2.6 to −0.3)
50–59	424	2.56	810	3.70	2.6† (2.1 to 3.1)	146	0.88	175	0.78	−1.2† (−2.3 to −0.1)
60–69	388	3.58	1,043	5.46	2.4† (2.0 to 2.9)	185	1.70	264	1.39	−1.3 (−3.2 to 0.7)
≥70	1,327	8.44	1,865	9.52	0.9† (0.7 to 1.2)	517	3.27	557	2.82	−0.5 (−1.8 to 0.8)
Race/ethnicity [4]										
White	2,339	1.88	3,533	2.40	1.5† (1.2 to 1.9)	878	0.69	879	0.57	−0.5† (−1.1 to −0.0)
Black	213	1.37	377	1.74	1.1† (0.3 to 1.8)	56	0.37	57	0.26	−1.4 (−2.8 to 0.0)
AI/AN	11	1.54	16	1.21	1.3 (−1.7 to 4.3)	--	--	--	--	--
A/PI	18	0.39	51	0.48	1.1 (−0.5 to 2.8)	14	0.27	48	0.42	0.3 (−1.4 to 1.9)
Hispanic	116	1.27	238	1.16	−0.5 (−1.1 to 0.1)	36	0.37	88	0.42	−0.5 (−2.1 to 1.2)
Stage [5]										
Early	1,695	1.09	2,718	1.35	1.3† (0.3 to 2.2)	660	0.42	698	0.33	−0.9† (−1.6 to −0.3)
Late	855	0.54	1,336	0.64	1.8† (0.1 to 3.5)	164	0.10	202	0.10	0.0 (−1.2 to 1.1)
Unknown	161	0.10	203	0.10	−0.9 (−2.7 to 0.8)	154	0.10	178	0.08	−0.4 (−1.6 to 0.9)
Census Region [6]										
Northeast	622	1.84	888	2.27	1.4† (0.9 to 1.8)	231	0.69	237	0.58	0.0 (−0.6 to 0.6)
Midwest	686	1.86	1,060	2.41	1.9† (1.3 to 2.5)	261	0.69	228	0.49	−1.1† (−1.8 to −0.5)
South	947	1.75	1,553	2.08	1.2† (0.8 to 1.5)	325	0.59	400	0.52	−0.7 (−1.5 to 0.1)
West	456	1.42	756	1.62	0.4 (−0.1 to 1.0)	182	0.57	237	0.51	−0.4 (−1.1 to 0.3)

Data Sources: Center for Disease Control and Prevention's National Program of Cancer Registries and the National Cancer Institute's Surveillance, Epidemiology, and End Results Program. Cancer incidence compiled from cancer registries that meet the data quality criteria for all invasive cancer sites combined for each year from the period 2001–2017 (covering 99% of the US population).

Abbreviations: AAPC, average annual percent change; AI/AN, American Indian and Alaska Native; A/PI, Asian and Pacific Islander; CI, confidence interval; HPV, human papillomavirus; SCC, squamous cell carcinoma.

[1]Vulvar cancers were microscopically confirmed and identified with International Classification of Diseases for Oncology, Third Edition [ICD-O-3] site codes C53.0–C53.9, excluding histology codes 9050–9055, 9140, and 9590–9992. HPV-associated vulvar cancers were limited to squamous cell carcinomas (ICD-O-3 histology codes 8050–8084, 8120–8131); SCC, NOS (8070), keratinizing (8071), non-keratinizing (8072, 8073), warty (8051), basaloid (8083), microinvasive (8076), and other SCC (8050, 8052–8060, 8074, 8075, 8077–8084, 8120–8131). Non-HPV associated histologic subtypes included BCC (8090–8098), glandular carcinomas (8140–8575), soft tissue cancers (8800–8912), melanocytic cancers (8720–8780), and other (8000–8049, 8085–8089, 8099–8119, 8132–8139, 8576–8719, 8781–8799, 8913–9992).

[2]Trends were measured with AAPC in age-adjusted rates and were considered to increase or decrease if $P < 0.05$; otherwise, trends were considered stable.

[3]Median age at diagnosis from 2001 to 2017 was 67 years for HPV-associated vulvar cancers and 71 years for non-HPV-associated cancers.

[4]Limited to cases without unknown or other race or unknown ethnicity (n = 75,918). White = non-Hispanic White; Black = non-Hispanic Black; AI/AN = non-Hispanic American Indian and Alaska Native; and A/PI = non-Hispanic Asian and Pacific Islander.

[5]Cancer stage derived using SEER Summary Stage guidelines. Early = localized, late = regional and distant, unknown = unknown or unstaged cancers. Limited to cases that were not diagnosed only by death certificate or autopsy (n = 76,029).

[6]Northeast: Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, and Vermont. Midwest: Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, and Wisconsin. South: Alabama, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, and West Virginia. West: Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, and Wyoming.

[†]Average annual percent change (AAPC) is significant at $P < 0.05$.

[*]Rates are per 100,000 women and are age-adjusted to the 2000 US standard population.

Table 2.

Age-adjusted Incidence Rates and Trends of Vulvar Cancers by Histology and HPV-associated Status–United States Cancer Statistics, 2001–2017

	2001			2017			2001–2017
	n	%	rate*	n	%	rate*	AAPC (95% CI)
HPV-associated [1]							
SCC, NOS	1,979	73.21	1.27	2,580	60.81	1.26	−0.1 (−0.6 to 0.4)
Keratinizing	484	17.91	0.30	1,352	31.86	0.66	4.7† (4.4 to 4.9)
Non-keratinizing	41	1.52	0.03	139	3.28	0.07	6.0† (4.9 to 7.2)
Warty	71	2.63	0.04	56	1.32	0.03	−2.9† (−4.7 to −1.0)
Basaloid	40	1.48	0.03	62	1.46	0.03	3.1† (1.3 to 5.0)
Microinvasive	68	2.52	0.05	28	0.66	0.01	−5.5† (−7.3 to −3.6)
Other SCC	20	0.74	0.01	26	0.61	0.01	−0.8 (−2.9 to 1.4)
Non-HPV-associated [1]							
BCC	278	29.26	0.17	269	26.02	0.13	−1.5† (−2.4 to −0.5)
Glandular carcinomas	292	30.74	0.19	355	34.33	0.17	−0.0 (−0.6 to 0.6)
Soft tissue cancers	49	5.16	0.03	48	4.64	0.03	−1.5† (−2.6 to −0.3)
Melanocytic cancers	226	23.79	0.14	285	27.56	0.14	0.4 (−0.3 to 1.1)
Other	105	11.05	0.07	77	7.45	0.04	−3.2† (−3.9 to −2.4)

Data Sources: Center for Disease Control and Prevention's National Program of Cancer Registries and the National Cancer Institute's Surveillance, Epidemiology, and End Results Program. Cancer incidence compiled from cancer registries that meet the data quality criteria for all invasive cancer sites combined for each year from the period 2001–2017 (covering 99% of the US population).

Abbreviations: AAPC, average annual percent change; BCC, basal cell carcinoma; CI, confidence interval; HPV, human papillomavirus; NOS, not otherwise specified; SCC, squamous cell carcinoma.

[1] Vulvar cancers were microscopically confirmed and identified with International Classification of Diseases for Oncology, Third Edition [ICD-O-3] site codes C53.0–C53.9, excluding histology codes 9050–9055, 9140, and 9590–9992. HPV-associated vulvar cancers were limited to squamous cell carcinomas (ICD-O-3 histology codes 8050–8084, 8120–8131); SCC, NOS (8070), keratinizing (8071), non-keratinizing (8072, 8073), warty (8051), basaloid (8083), microinvasive (8076), and other SCC (8050, 8052–8060, 8074, 8075, 8077–8084, 8120–8131). Non-HPV associated histologic subtypes included BCC (8090–8098), glandular carcinomas (8140–8575), soft tissue cancers (8800–8912), melanocytic cancers (8720–8780), and other (8000–8049, 8085–8089, 8099–8119, 8132–8139, 8576–8719, 8781–8799, 8913–9992).

† Significant at $P < 0.05$. Trends were measured with AAPC in rates and were considered to increase or decrease if $P < 0.05$; otherwise, rates were considered stable.

* Rates are per 100,000 women and are age-adjusted to the 2000 US standard population.