

SUPPLEMENTARY MATERIALS

Incidence trends and burden of human papillomavirus-associated cancers among women in the United States, 2001-2017

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SUPPLEMENTARY METHODS

Data sources, case definition and tumor characteristics, demographic characteristics, definition of cancer incidence and burden, and statistical analysis

Data source

We analyzed the US Cancer Statistics dataset that comes from the two federally funded population-based source of cancer cases in the United States, the Centers for Disease Control and Prevention's (CDC's) National Program of Cancer Registries (NPCR) dataset and the National Cancer Institute's Surveillance, Epidemiology, and End Results Program dataset. This dataset includes cancer incidence data from central cancer registries reported to NPCR in 46 states, the District of Columbia, and to SEER in 4 states. Data about all new diagnoses of cancer from patient records at medical facilities such as hospitals, physicians' offices, therapeutic radiation facilities, freestanding surgical centers, and pathology laboratories are reported to central cancer registries, which collate these data and use state vital records to collect information about any cancer deaths that were not reported as cases. The central cancer registries use uniform data items and codes as documented by the North American Association of Central Cancer Registries. These data are submitted annually to CDC and NCI and combined into one dataset. Cancer registries demonstrate that data were of high quality by meeting U.S. Cancer Statistics publication criteria.

Case Definitions and Tumor Characteristics

This study includes new cases of primary invasive HPV associated (i.e., cervical, anal, oropharyngeal, vaginal, and vulvar epithelial) cancers identified based on *International Classification of Diseases for Oncology* (ICD-O)-Third Edition and histology codes. Cases were limited to invasive microscopically confirmed cancers. All epithelial carcinomas (histology codes 8010-8671 and 8940-8941) were included for cervical cancer (C53.0-53.9). For other cancer sites, we included squamous cell carcinomas (histology codes 8050-8084 and 8120-8131) for

sites in the vulva (C51.0-C51.9), vagina (C52.9), anus (C21.0-C21.2, C21.8), and certain subsites of the oropharynx in which HPV DNA is frequently detected (C01.9, C02.4, C02.8, C05.1, C05.2, C09.0 to C10.9, and C14.0 to C14.8). Supplementary Figure 1 provides a detailed step-by-step process that we followed to identify each HPV-associated cancer type.

Demographic characteristics

The demographic characteristics information submitted to each cancer registry were abstracted from patient medical records. We identified the age of cancer diagnosis. Race and ethnicity was classified into categories—non-Hispanic Whites, non-Hispanic Blacks, Hispanics, and non-Hispanic other races, including American Indian or Alaska Natives and Asian or Pacific Islanders. We categorized age into the groups <50 years, 50-64 years, 65-74 years, and ≥75 years. The justification for the creation of these categories is provided below:

- <50 years (age group in which the incidence of anal and oropharyngeal cancer has historically remained stable),
- 50-64 years (age-group that is seeing a marked increase in anal and oropharyngeal cancer incidence; the maximum age cutoff of cervical cancer screening recommendations),
- 65-74 years (the age group that is seeing a marked increase in anal cancer and a relatively slower increase in oropharyngeal cancer incidence rates; the group that could also be a potential target for screening)
- ≥75 years (the age group that is seeing a relatively slower increase in anal and oropharyngeal cancer incidence)

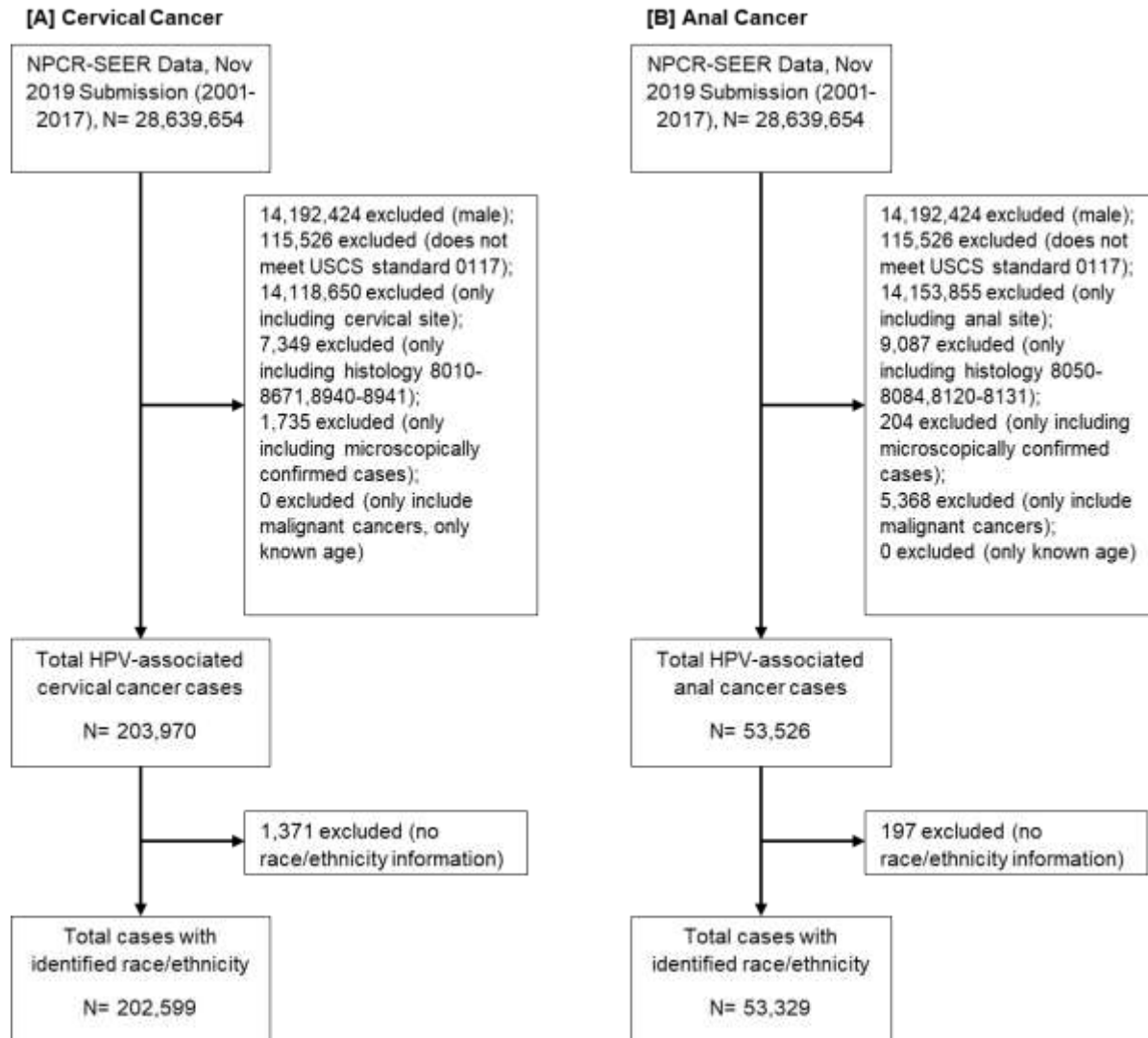
Definition of cancer incidence and burden

As defined by the US NCI SEER program, a cancer incidence rate was defined as the number of new cancers of a specific site/type occurring in a specified population during a year,

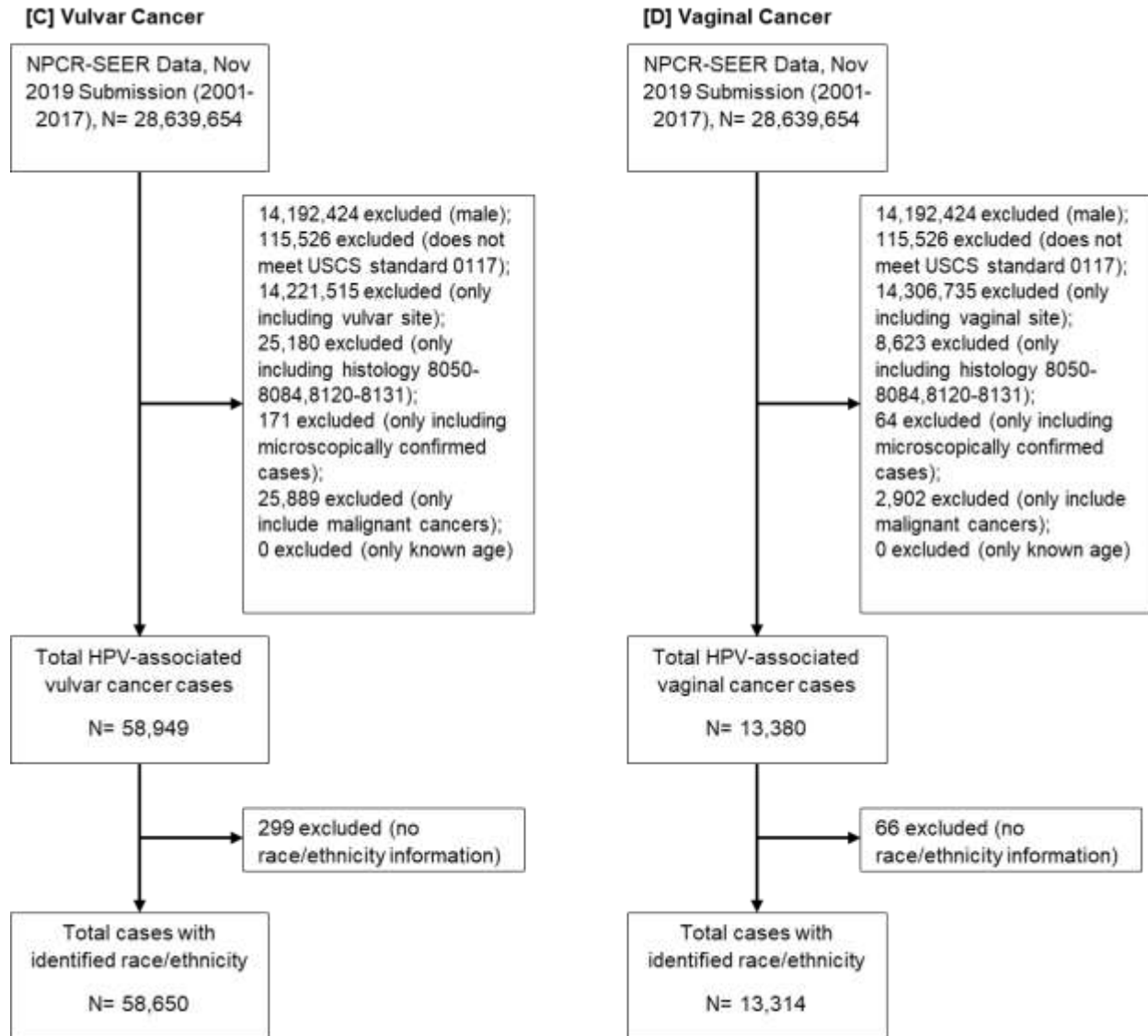
expressed as the number of cancers per 100,000 population at risk. The numerator of the incidence rate is the number of new cancers; the denominator is the size of the population. The population used depends on the rate (e.g., specific to age and race/ethnicity) to be calculated. The burden was defined as the annual number of new cancer cases diagnosed in a specific population and is a function of both incidence and population composition (i.e., age and race/ethnicity). The number of new cancers may include multiple primary cancers occurring in one patient.

Statistical analysis

We used the SEER*Stat version 8.3.5 to estimate incidence rates. Person-years were estimated by summing population sizes across calendar years. Incidence estimates were age-adjusted to the 2000 US standard population and were expressed per 100 000 person-years. To quantify trends in incidence rates over time and to calculate annual percentage changes (APCs) and average APCs (AAPCs), we used the National Cancer Institute's Joinpoint Regression Analysis program (version 4.7.0). The APC characterizes trend, a single regression line on a log scale fitted over a fixed interval, whereas the AAPC is a weighted average of the APCs from the joinpoint model with the weights equal to the length of the APC interval. The joinpoint program selected the best-fitting log-linear regression model to identify calendar years (i.e., the joinpoints) when APCs changed significantly, allowing for the minimum number of joinpoints necessary to fit the data. To determine the number of significant joinpoints, Monte Carlo permutation test was used. To determine whether the trends were different from 0, a t test was used for zero join-points, and a z test was used for one or more join-points. Statistical significance was assessed at a level of $P < .05$, and all hypotheses were two-sided.

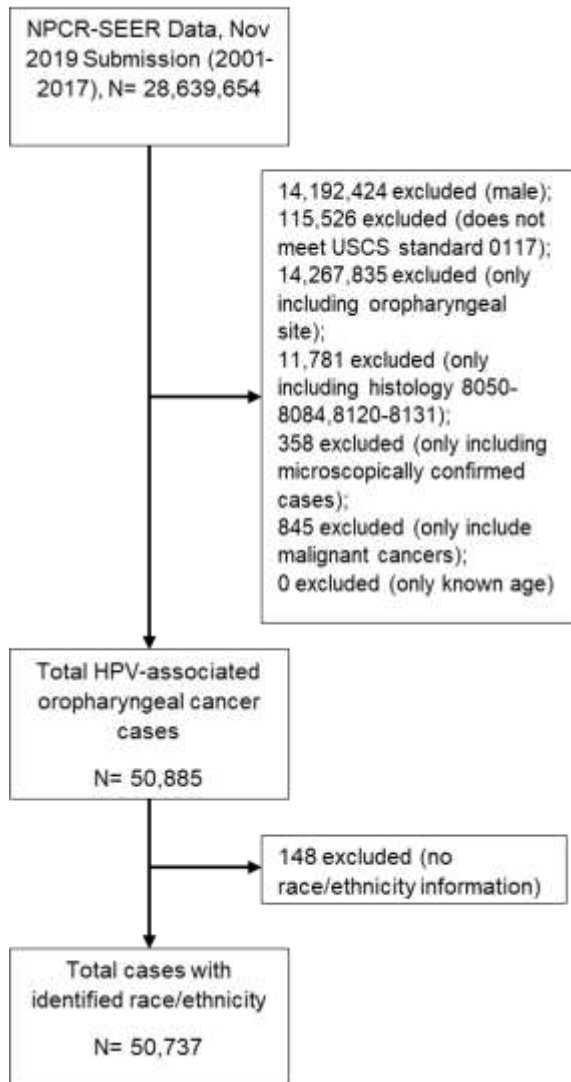


Supplementary Figure 1. Diagram depicting the sample flow of the study population



Supplementary Figure 1 (Cont). Diagram depicting the sample flow of the study population

[E] Oropharyngeal Cancer



Supplementary Figure 1 (Cont). Diagram depicting the sample flow of the study population

Figure 2a. Incidence trends of HPV-associated cancers among women, 2001-2017

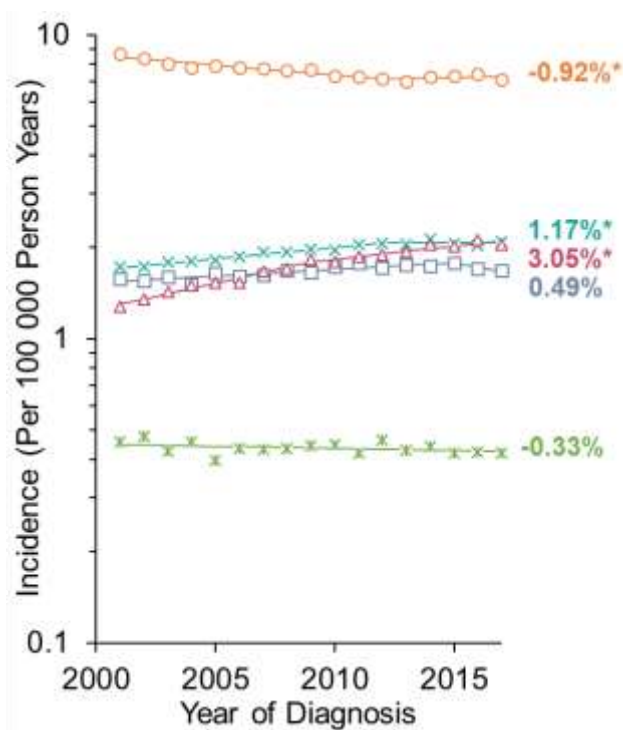
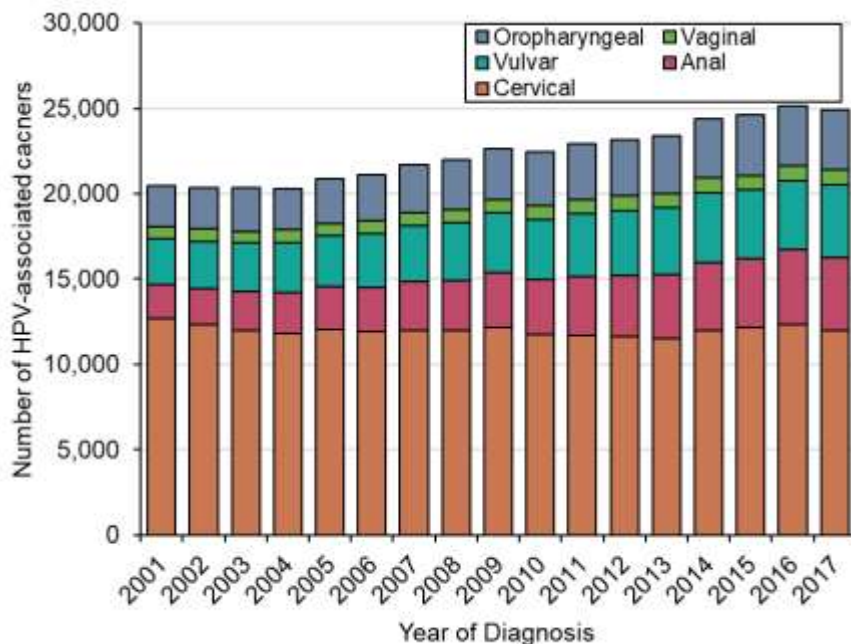


Figure 2b. Burden of HPV-associated cancers among US women, 2001-2017



Supplementary Figure 2. Incidence trends and burden of HPV-associated (cervical, anal, vulvar, vaginal, and oropharyngeal) cancers among US women: NPCR and SEER (2001-2017)

Abbreviations: NPCR, National Program of Cancer Registries; SEER, Surveillance Epidemiology, and End Results program

Supplementary Table 1. Cervical and non-cervical (collective) and by anatomic sites (anal, vulvar, vaginal, and oropharyngeal) cancer incidence rates* among US women by age at diagnosis, race/ethnicity, and year of diagnosis during 2001-2017 in the United States

	Cervical		Non-cervical		Non-cervical anatomic sites							
	Cases No. (%)	Rate	Cases No. (%)	Rate	Anal		Vulvar		Vaginal		Oropharyngeal	
	Cases No. (%)	Rate	Cases No. (%)	Rate	Cases No. (%)	Rate	Cases No. (%)	Rate	Cases No. (%)	Rate	Cases No. (%)	Rate
Age at diagnosis												
<50	106102 (52.02)	6.21 (6.18-6.25)	26814 (15.17)	1.54 (1.52-1.56)	8440 (15.77)	0.48 (0.47-0.49)	10150 (17.22)	0.59 (0.58-0.60)	1659 (12.40)	0.10 (0.09-0.10)	6565 (12.90)	0.37 (0.37-0.38)
50-64	58773 (28.81)	12.14 (12.04-12.24)	66693 (37.74)	13.57 (13.46-13.67)	23709 (44.29)	4.83 (4.77-4.89)	17028 (28.89)	3.48 (3.42-3.53)	3883 (29.02)	0.79 (0.76-0.81)	22073 (43.38)	4.47 (4.41-4.53)
65-74	22337 (10.95)	11.06 (10.91-11.20)	39272 (22.22)	19.57 (19.37-19.76)	11610 (21.69)	5.76 (5.66-5.87)	11571 (19.63)	5.80 (5.69-5.90)	3166 (23.66)	1.59 (1.53-1.64)	12925 (25.40)	6.43 (6.32-6.54)
≥75	16758 (8.22)	8.92 (8.78-9.05)	43961 (24.87)	22.88 (22.66-23.10)	9767 (18.25)	5.16 (5.06-5.27)	20200 (34.27)	10.28 (10.14-10.43)	4672 (34.92)	2.40 (2.33-2.47)	9322 (18.32)	5.03 (4.93-5.14)
Race/ethnicity												
NH White	126883 (62.63)	6.96 (6.92-7.00)	146365 (83.15)	6.44 (6.41-6.48)	44676 (83.77)	1.99 (1.97-2.01)	49854 (85.00)	2.19 (2.17-2.21)	9693 (72.80)	0.41 (0.41-0.42)	42142 (83.06)	1.85 (1.83-1.87)
NH Black	30527 (15.07)	9.56 (9.45-9.67)	16262 (9.24)	5.07 (4.99-5.15)	4336 (8.13)	1.34 (1.30-1.39)	4795 (8.18)	1.51 (1.47-1.55)	1949 (14.64)	0.63 (0.60-0.66)	5182 (10.21)	1.58 (1.54-1.62)
Hispanic	33575 (16.57)	10.25 (10.14-10.36)	10140 (5.76)	3.89 (3.81-3.97)	3543 (6.64)	1.33 (1.28-1.37)	3065 (5.23)	1.24 (1.19-1.28)	1229 (9.23)	0.48 (0.46-0.51)	2303 (4.54)	0.84 (0.80-0.87)
Others†	11614 (5.73)	7.13 (7.00-7.26)	3263 (1.85)	2.16 (2.08-2.23)	774 (1.45)	0.50 (0.46-0.54)	936 (1.60)	0.64 (0.60-0.68)	443 (3.33)	0.30 (0.27-0.33)	1110 (2.19)	0.72 (0.68-0.76)
2001	12704 (6.23)	8.68 (8.53-8.83)	7780 (3.84)	5.03 (4.92-5.15)	1950 (3.64)	1.28 (1.22-1.33)	2703 (4.59)	1.72 (1.66-1.79)	721 (5.39)	0.46 (0.42-0.49)	2406 (4.73)	1.58 (1.51-1.64)
2002	12341 (6.05)	8.34 (8.19-8.49)	7981 (3.94)	5.10 (4.99-5.21)	2090 (3.90)	1.35 (1.29-1.41)	2736 (4.64)	1.72 (1.66-1.79)	758 (5.67)	0.48 (0.44-0.51)	2397 (4.71)	1.55 (1.49-1.61)
2003	11988 (5.88)	8.02 (7.88-8.17)	8335 (4.12)	5.23 (5.11-5.34)	2254 (4.21)	1.42 (1.37-1.48)	2869 (4.87)	1.78 (1.72-1.85)	693 (5.18)	0.43 (0.40-0.46)	2519 (4.95)	1.59 (1.53-1.66)
2004	11807 (5.79)	7.82 (7.68-7.97)	8497 (4.20)	5.25 (5.14-5.37)	2402 (4.49)	1.50 (1.44-1.56)	2922 (4.96)	1.79 (1.73-1.86)	751 (5.61)	0.46 (0.43-0.49)	2422 (4.76)	1.51 (1.45-1.57)
2005	12027 (5.90)	7.91 (7.77-8.05)	8872 (4.38)	5.38 (5.27-5.50)	2505 (4.68)	1.53 (1.47-1.59)	3025 (5.13)	1.82 (1.75-1.88)	663 (4.96)	0.40 (0.37-0.43)	2679 (5.26)	1.64 (1.58-1.70)
2006	11948 (5.86)	7.78 (7.64-7.92)	9145 (4.52)	5.44 (5.33-5.55)	2570 (4.80)	1.53 (1.47-1.59)	3147 (5.34)	1.87 (1.80-1.93)	735 (5.49)	0.43 (0.40-0.47)	2693 (5.29)	1.61 (1.55-1.67)
2007	12007	7.74	9667	5.65	2846	1.66	3299	1.93	751	0.43	2771	1.62

	(5.89)	(7.60-7.88)	(4.77)	(5.53-5.76)	(5.32)	(1.60-1.73)	(5.60)	(1.86-2.00)	(5.61)	(0.40-0.46)	(5.45)	(1.56-1.68)
2008	11972 (5.87)	7.62 (7.49-7.76)	10005 (4.94)	5.74 (5.62-5.85)	2963 (5.54)	1.71 (1.64-1.77)	3351 (5.68)	1.92 (1.86-1.99)	769 (5.75)	0.44 (0.41-0.47)	2922 (5.74)	1.67 (1.61-1.73)
2009	12143 (5.95)	7.69 (7.55-7.83)	10473 (5.17)	5.89 (5.75-6.01)	3261 (6.09)	1.83 (1.76-1.89)	3472 (5.89)	1.97 (1.90-2.03)	792 (5.92)	0.44 (0.41-0.48)	2948 (5.79)	1.65 (1.59-1.71)
2010	11735 (5.75)	7.33 (7.20-7.47)	10716 (5.29)	5.90 (5.79-6.02)	3234 (6.04)	1.78 (1.72-1.84)	3535 (6.00)	1.96 (1.89-2.02)	819 (6.12)	0.45 (0.42-0.48)	3128 (6.15)	1.72 (1.661.78)
2011	11686 (5.73)	7.25 (7.12-7.39)	11238 (5.55)	6.08 (5.97-6.20)	3439 (6.42)	1.86 (1.79-1.92)	3724 (6.32)	2.04 (1.97-2.10)	780 (5.83)	0.42 (0.39-0.45)	3295 (6.48)	1.77 (1.71-1.83)
2012	11620 (5.70)	7.15 (7.07-7.28)	11552 (5.71)	6.12 (6.01-6.24)	3576 (6.68)	1.89 (1.82-1.95)	3836 (6.51)	2.06 (1.99-2.13)	872 (6.52)	0.46 (0.43-0.50)	3268 (6.42)	1.71 (1.65-1.77)
2013	11527 (5.65)	7.02 (6.89-7.16)	11871 (5.86)	6.15 (6.04-6.27)	3736 (6.98)	1.93 (1.86-1.99)	3897 (6.61)	2.05 (1.68-2.11)	836 (6.25)	0.43 (0.40-0.46)	3402 (6.69)	1.75 (1.69-1.81)
2014	11953 (5.86)	7.25 (7.12-7.39)	12425 (6.14)	6.34 (6.23-6.45)	4015 (7.50)	2.04 (1.97-2.10)	4099 (6.95)	2.12 (2.06-2.19)	867 (6.48)	0.44 (0.41-0.47)	3444 (6.77)	1.74 (1.68-1.80)
2015	12144 (5.95)	7.33 (7.19-7.46)	12492 (6.17)	6.24 (6.13-6.35)	4054 (7.57)	2.01 (1.94-2.07)	4036 (6.85)	2.05 (1.98-2.11)	842 (6.29)	0.42 (0.39-0.45)	3560 (7.00)	1.77 (1.71-1.83)
2016	12358 (6.06)	7.41 (7.27-7.54)	12793 (6.32)	6.27 (6.16-6.38)	4366 (8.16)	2.12 (2.05-2.18)	4055 (6.88)	2.03 (1.97-2.10)	867 (6.48)	0.42 (0.40-0.45)	3505 (6.89)	1.70 (1.64-1.76)
2017	12010 (5.89)	7.10 (6.97-7.24)	12898 (6.37)	6.20 (6.09-6.31)	4265 (7.97)	2.03 (1.97-2.10)	4243 (7.20)	2.08 (2.01-2.14)	864 (6.46)	0.42 (0.39-0.45)	3526 (6.93)	1.67 (1.62-1.73)

Abbreviations: NH, Non-Hispanic

* Rates were calculated as number of cases per 100 000 person-year and age-adjusted to the 2000 US standard population.

† Others include Asian/Pacific Islander, American Indian/Alaskan Native, and others.

Supplementary Table 2. Trends in HPV-associated Cancers Incidence Rates* by Race and Age diagnosis during 2001-2017 in the United States

	Trend†										
	1			2			3			Overall (2001-2017)	
	Year	APC (95% CI)	P Value	Year	APC (95% CI)	P Value	Year	APC (95% CI)	P Value	AAPC (95% CI)	P Value
Cervical											
Overall	2001-2012	-1.48 (-1.89 to -1.08)	<0.001	2012-2017	0.35 (-1.05 to 1.77)	0.60				-0.92 (-1.38 to -0.45)	<0.001
Race/Age											
NH White	2001-2017	-0.51 (-0.80 to -0.22)	0.002							-0.51 (-0.80 to -0.22)	0.002
<50	2001-2017	-0.15 (-0.48 to 0.18)	0.35							-0.15 (-0.48 to 0.18)	0.35
50-64	2001-2003	-6.00 (-10.27 to -1.54)	0.01	2003-2017	-0.10 (-0.31 to 0.11)	0.33				-0.86 (-1.40 to -0.31)	0.002
65-74	2001-2017	-1.76 (-2.20 to -1.31)	<0.001							-1.76 (-2.20 to -1.31)	<0.001
≥75	2001-2012	-3.32 (-4.09 to -2.55)	<0.001	2012-2017	-0.18 (-3.06 to 2.78)	0.89				-2.35 (-3.28 to -1.41)	<0.001
NH Black	2001-2017	-2.44 (-2.77 to -2.12)	<0.001							-2.44 (-2.77 to -2.12)	<0.001
<50	2001-2017	-1.87 (-2.21 to -1.52)	<0.001							-1.87 (-2.21 to -1.52)	<0.001
50-64	2001-2017	-2.09 (-2.72 to -1.46)	<0.001							-2.09 (-2.72 to -1.46)	<0.001
65-74	2001-2017	-3.58 (-4.30 to -2.86)	<0.001							-3.58 (-4.30 to -2.86)	<0.001
≥75	2001-2017	-4.03 (-4.69 to -3.37)	<0.001							-4.03 (-4.69 to -3.37)	<0.001
Hispanic	2001-2011	-4.04 (-4.77 to -3.30)	<0.001	2011-2017	-0.72 (-2.27 to 0.85)	0.34				-2.81 (-3.47 to -2.14)	<0.001
<50	2001-2012	-3.41 (-4.37 to -2.44)	<0.001	2012-2017	1.27 (-1.94 to 4.58)	0.41				-1.97 (-3.04 to -0.89)	<0.001
50-64	2001-2011	-4.31 (-4.98 to -3.63)	<0.001	2011-2017	-1.12 (-2.50 to 0.28)	0.11				-3.12 (-3.72 to -2.52)	<0.001
65-74	2001-2017	-4.63 (-5.22 to -4.04)	<0.001							-4.63 (-5.22 to -4.04)	<0.001
≥75	2001-2017	-3.78 (-4.59 to -2.96)	<0.001							-3.78 (-4.59 to -2.96)	<0.001
Anus											
Overall	2001-2009	4.09 (3.22 to 4.97)	<0.001	2009-2017	2.02 (1.33 to 2.73)	<0.001				3.05 (2.55 to 3.56)	<0.001
Race/Age											

NH White	2001-2009	4.65 (3.64 to 5.68)	<0.001	2009-2017	2.67 (1.85 to 3.50)	<0.001				3.66 (3.07 to 4.25)	<0.001
<50	2001-2008	2.33 (0.33 to 4.38)	0.03	2008-2017	-0.89 (-2.27 to 0.52)	0.19				0.51 (-0.54 to 0.95)	0.34
50-64	2001-2007	9.07 (6.14 to 12.08)	<0.001	2007-2017	3.49 (2.56 to 4.42)	<0.001				5.55 (4.44 to 6.66)	<0.001
65-74	2001-2017	5.05 (4.57 to 5.54)	<0.001							5.05 (4.57 to 5.54)	<0.001
≥75	2001-2017	2.55 (2.11 to 3.00)	<0.001							2.55 (2.11 to 3.00)	<0.001
NH Black	2001-2017	2.27 (1.55 to 3.00)	<0.001							2.27 (1.55 to 3.00)	<0.001
<50	2001-2017	0.92 (-0.73 to 2.61)	0.26							0.92 (-0.73 to 2.61)	0.26
50-64	2001-2017	3.06 (2.18 to 3.94)	<0.001							3.06 (2.18 to 3.94)	<0.001
65-74	2001-2017	2.74 (1.38 to 4.12)	0.001							2.74 (1.38 to 4.12)	0.001
≥75	2001-2017	1.94 (-0.28 to 4.21)	0.08							1.94 (-0.28 to 4.21)	0.08
Hispanic	2001-2017	0.48 (-0.17 to 1.13)	0.14							0.48 (-0.17 to 1.13)	0.14
<50	2001-2017	-1.58 (-3.26 to 0.12)	0.07							-1.58 (-3.26 to 0.12)	0.07
50-64	2001-2017	1.35 (0.27 to 2.45)	0.02							1.35 (0.27 to 2.45)	0.02
65-74	2001-2017	0.52 (-1.32 to 2.40)	0.56							0.52 (-1.32 to 2.40)	0.56
≥75	2001-2017	0.22 (-1.82 to 2.31)	0.82							0.22 (-1.82 to 2.31)	0.82
Vulva											
Overall	2001-2012	1.71 (1.40 to 2.01)	<0.001	2012-2017	0.00 (-0.89 to 0.90)	1.00				1.17 (0.85 to 1.49)	<0.001
Race/Age											
NH White	2001-2014	2.09 (1.89 to 2.30)	<0.001	2014-2017	-0.79 (-2.52 to 0.98)	0.35				1.55 (1.21 to 1.88)	<0.001
<50	2001-2017	0.45 (-0.12 to 1.02)	0.11							0.45 (-0.12 to 1.02)	0.11
50-64	2001-2012	4.22 (3.51 to 4.93)	<0.001	2012-2017	1.60 (-0.26 to 3.49)	0.09				3.39 (2.71 to 9.79)	<0.001
65-74	2001-2017	2.11 (1.73 to 2.49)	<0.001							2.11 (1.73 to 2.49)	<0.001
≥75	2001-2014	1.50 (1.17 to 1.83)	<0.001	2014-2017	-2.05 (-4.92 to 0.90)	0.15				0.82 (0.27 to 1.39)	0.004

NH Black	2001-2017	1.07 (0.34 to 1.82)	0.007							1.07 (0.34 to 1.82)	0.007
<50	2001-2017	0.86 (-0.26 to 1.99)	0.12							0.86 (-0.26 to 1.99)	0.12
50-64	2001-2017	1.48 (0.25 to 2.73)	0.02							1.48 (0.25 to 2.73)	0.02
65-74	2001-2017	0.57 (-1.16 to 2.33)	0.50							0.57 (-1.16 to 2.33)	0.50
≥75	2001-2017	1.01 (-0.53 to 2.57)	0.18							1.01 (-0.53 to 2.57)	0.18
Hispanic	2001-2017	-0.49 (-1.07 to 0.10)	0.10							-0.49 (-1.07 to 0.10)	0.10
<50	2001-2017	-1.69 (-3.63 to 0.28)	0.09							-1.69 (-3.63 to 0.28)	0.09
50-64	2001-2017	1.45 (-0.16 to 3.09)	0.08							1.45 (-0.16 to 3.09)	0.08
65-74	2001-2017	-0.87 (-2.14 to 0.41)	0.17							-0.87 (-2.14 to 0.41)	0.17
≥75	2001-2017	-0.85 (-1.86 to 0.17)	0.10							-0.85 (-1.86 to 0.17)	0.10
Vagina											
Overall	2001-2017	-0.33 (-0.77 to 0.11)	0.13							-0.33 (-0.77 to 0.11)	0.13
Race/Age											
NH White	2001-2017	-0.02 (-0.66 to 0.62)	0.95							-0.02 (-0.66 to 0.62)	0.95
<50	2001-2017	-0.24 (-1.67 to 1.20)	0.72							-0.24 (-1.67 to 1.20)	0.72
50-64	2001-2017	0.47 (-0.70 to 1.66)	0.41							0.47 (-0.70 to 1.66)	0.41
65-74	2001-2017	0.52 (-0.21 to 1.26)	0.15							0.52 (-0.21 to 1.26)	0.15
≥75	2001-2017	-0.59 (-1.23 to 0.05)	0.07							-0.59 (-1.23 to 0.05)	0.07
NH Black	2001-2017	-1.18 (-1.75 to -0.60)	0.001							-1.18 (-1.75 to -0.60)	0.001
<50	2002-2017§	0.97 (-1.13 to 3.12)	0.33							0.97 (-1.13 to 3.12)	0.33
50-64	2001-2017	0.02 (-1.24 to 1.29)	0.97							0.02 (-1.24 to 1.29)	0.97
65-74	2001-2017	-1.12 (-2.89 to 0.49)	0.15							-1.12 (-2.89 to 0.49)	0.15
≥75	2001-2017	-2.61 (-3.82 to -1.39)	<0.001							-2.61 (-3.82 to -1.39)	<0.001

Hispanic	2001-2017	-1.71 (-2.76 to -0.65)	0.004							-1.71 (-2.76 to -0.65)	0.004
<50	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
50-64	2002-2017	-1.51 (-4.31 to 1.37)	0.27							-1.51 (-4.31 to 1.37)	0.27
65-74	2001-2017	-4.73 (-6.25 to -3.19)	<0.001							-4.73 (-6.25 to -3.19)	<0.001
≥75	2001-2017	-2.63 (-4.39 to -0.83)	0.008							-2.63 (-4.39 to -0.83)	0.008
Oropharynx											
Overall	2001-2015	1.02 (0.70 to 1.34)	<0.001	2015-2017	-3.31 (-9.16 to 2.92)	0.26				0.47 (-0.28 to 1.22)	0.22
Race/Age											
NH White	2001-2015	1.70 (1.36 to 2.03)	<0.001	2015-2017	-2.80 (-8.93 to 3.74)	0.36				1.12 (0.34 to 1.91)	0.005
<50	2001-2017	0.74 (-0.12 to 1.60)	0.09							0.74 (-0.12 to 1.60)	0.09
50-64	2001-2017	2.29 (1.91 to 2.67)	<0.001							2.29 (1.91 to 2.67)	<0.001
65-74	2001-2017	1.74 (0.16 to 1.33)	0.02							1.74 (0.16 to 1.33)	0.02
≥75	2001-2017	1.12 (0.47 to 1.76)	0.002							1.12 (0.47 to 1.76)	0.002
NH Black	2001-2017	-1.91 (-2.35 to -1.48)	<0.001							-1.91 (-2.35 to -1.48)	<0.001
<50	2001-2017	-3.94 (-5.65 to -2.20)	<0.001							-3.94 (-5.65 to -2.20)	<0.001
50-64	2001-2017	-1.15 (-1.92 to -0.37)	0.007							-1.15 (-1.92 to -0.37)	0.007
65-74	2001-2017	-1.93 (-2.81 to -1.05)	<0.001							-1.93 (-2.81 to -1.05)	<0.001
≥75	2001-2017	-1.44 (-2.89 to 0.02)	0.05							-1.44 (-2.89 to 0.02)	0.05

										0.02)	
Hispanic	2001-2017	0.60 (-0.33 to 1.54)	0.19							0.60 (-0.33 to 1.54)	0.19
<50	2001-2017	-0.07 (-2.54 to 2.47)	0.96							-0.07 (-2.54 to 2.47)	0.96
50-64	2001-2006	10.36 (1.70 to 19.76)	0.02	2006-2017	0.59 (-1.07 to 2.27)	0.46				3.54 (0.97 to 6.18)	0.007
65-74	2001-2017	0.66 (-1.19 to 2.53)	0.46							0.66 (-1.19 to 2.53)	0.46
≥75	2001-2017	-2.38 (-5.33 to 0.67)	0.11							-2.38 (-5.33 to 0.67)	0.11

Abbreviations: APC, annual percentage change; AAPC, average annual percentage change; NH, Non-Hispanic

* Rates were calculated as number of cases per 100 000 person-year and age-adjusted to the 2000 US standard population.

† The calendar period of each segment was defined based on the identification of calendar years when a statistically significant change in the APC occurred (ie, the joinpoint)