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Estimated prevalence and incidence of disease-associated HPV types among 15–59-year-olds in the United States

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Abstract

Introduction: Human papillomavirus (HPV) can cause anogenital warts and several types of cancer, including cervical cancers and precancers. We estimated the prevalence, incidence, and number of persons with prevalent and incident HPV infections in the United States in 2018.

Methods: Prevalence and incidence were estimated for infections with any HPV (any of 37 types detected using Linear Array) and disease-associated HPV, two types that cause anogenital warts plus 14 types detected by tests used for cervical cancer screening (HPV 6/11/16/18/31/33/35/39/45/51/52/56/58/59/66/68). We used the 2013–2016 National Health and Nutrition Examination Survey to estimate prevalence among 15–59-year-olds, overall and by sex. Incidences in 2018 were estimated per 10,000 persons using an individual-based transmission-dynamic type-specific model calibrated to US data. We estimated number of infected persons by applying prevalences and incidences to 2018 US population estimates.

Results: Prevalence of infection with any HPV was 40.0% overall, 41.8% in males and 38.4% in females; prevalence of infection with disease-associated HPV was 24.2% in males and 19.9% in females. An estimated 23.4 and 19.2 million males and females had a disease-associated HPV type infection in 2018. Incidences of any and disease-associated HPV infection were 1222 and 672 per 10,000 persons; incidence of disease-associated HPV infection was 708 per 10,000 males and 636

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per 10,000 females. An estimated 6.9 and 6.1 million males and females had an incident infection with a disease-associated HPV type in 2018.

Conclusions: We document a high HPV burden of infection in the United States in 2018, with 42 million persons infected with disease-associated HPV and 13 million persons acquiring a new infection. While most infections clear, some disease-associated HPV type infections progress to disease. The HPV burden highlights the need for continued monitoring of HPV-associated cancers, cervical cancer screening, and HPV vaccination to track and prevent disease.

Summary:

In 2018 in the United States, 42.5 million persons were infected with 1 HPV type that can cause HPV-associated precancers/cancers or anogenital warts; 13 million persons acquired a new infection.

Keywords

Human papillomavirus; prevalence; incidence; HPV-ADVISE; National Health and Nutrition Examination Survey

Introduction

Human papillomavirus (HPV) is the most common sexually transmitted infection in the United States and causes several diseases, including anogenital warts and cancers.(1–3) There are over 40 different types of mucosal HPV, and most HPV infections do not progress to disease.(4) However, two HPV types, HPV 6 and 11, cause nearly all cases of anogenital warts,(2) and high-risk (HR) types, defined based on their oncogenic potential, can cause cancer of the cervix, vulva, vagina, penis, anus, and oropharynx.(3) Cervical cancer is the most common HPV-associated cancer globally.(5) However, in the United States, oropharyngeal cancer is now the most common HPV-associated cancer as rates of oropharyngeal cancer are increasing while rates of cervical cancer are decreasing due to screening and treatment of cervical precancers.(6, 7)

Disease caused by HPV (e.g., genital warts, cancers) cause substantial morbidity and mortality in the United States, including approximately 196,000 cervical precancers (8) and 35,900 HPV-attributable cancers occurring annually. Understanding the epidemiology of infections with disease-associated HPV types (i.e., HPV types that can cause disease) can inform prevention and control efforts. Using nationally representative data and mathematical modeling, we provide updated estimates of the prevalence of infection, incidence of infection, and numbers of persons with prevalent and incident infections with any and disease-associated HPV types for US males and females.

Materials and Methods

Data source and analytic sample

The National Health and Nutrition Examination Survey (NHANES) is an ongoing cross-sectional survey administered by the National Center for Health Statistics (NCHS) at the Centers for Disease Control and Prevention (CDC) designed to be nationally representative

of the non-institutionalized, civilian population living in the United States. Data collection includes an in-home interview, where demographic data are collected, and a medical exam in the Mobile Examination Center (MEC), where participants self-collect a cervicovaginal or penile swab. Detailed methods are provided elsewhere.(10–12) Informed consent was obtained from all participants or their guardians. Data collection was approved by the NCHS Research Ethics Review Board.

Specimen collection and laboratory methods

Cervicovaginal and penile self-collected swabs were shipped to and analyzed at CDC using Research Use Only Roche Linear Array Assay (Roche Diagnostics, Indianapolis, IN). This assay uses L1 consensus PCR followed by type-specific hybridization for qualitative detection of 37 HPV types (HPV 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) and β -globin, an internal control for specimen adequacy.(13, 14) The analysis was restricted to participants with adequate samples (samples positive for HPV and/or β -globin).

HPV type categories

Twelve HPV types are defined as carcinogenic to humans (HPV 16/18/31/33/35/39/45/51/52/56/58/59, also known as Group 1) by the International Agency for Research on Cancer (IARC).(3) Commercially-available HPV tests used for clinical cervical cancer screening detect these 12 types, as well as HPV 66 (defined as possibly carcinogenic) and HPV 68 (defined as probably carcinogenic).(3, 15) Other disease-associated types, such as HPV 6/11 which cause most genital warts, are not carcinogenic. Due to type-specific associations with different HPV-associated diseases, we analyzed prevalence and incidence in several different type categories including: any HPV (any of 37 types detected using Linear Array), HPV 6/11, IARC Group 1, 14HR (types detected by clinical HPV tests, IARC Group 1 plus HPV 66/68), and disease-associated HPV (14HR plus HPV 6/11). For the purpose of this analysis, infection was defined as positivity for least one type in the respective HPV type category.

Statistical analysis

Prevalence—Weighted prevalence of infection and corresponding confidence intervals (CI) were estimated overall and by sex for 15–59- and, for a subset of that age group, 15–24-year-olds, for each HPV category using MEC weights and complex survey analytic methods.(16, 17) The most recent NHANES data available to estimate national prevalence are from 2013–2016; these were used for all prevalence estimates. To provide estimates for 2018, consistent with an initiative to estimate overall national burden of STIs in that year,(18) we assumed the HPV prevalence in 2013–2016 is comparable to prevalence in 2018 as suggested by previous research.(19, 20) Numbers of infected persons (in millions) per year and CIs were estimated by multiplying 2013–2016 prevalence and CIs by 2018 population totals for the entire US population based on the American Community Survey (ACS).(21) Because this analysis is part of an effort to estimate national burden of STIs

overall, rather than presenting conventional 95% CIs, 50% CIs were calculated to improve comparability with methods used to estimate other infections. (18)

Data management and analysis were performed in SAS 9.4 (SAS Institute, Cary, NC) and SAS-callable SUDAAN 11.0 (RTI International, Research Triangle Park, NC). Prevalence estimates were noted as unstable if the relative standard error (RSE) was >30%.

Incidence—Incidence of infection among 15–59- and 15–24-year-olds was estimated using the HPV-ADVISE model, an individual-based transmission-dynamic type-specific model of multi-type HPV infection. Originally developed to model HPV transmission in Canada,(22) it has since been calibrated to model transmission in the United States using sexual behavior data from national surveys and HPV prevalence data from NHANES.(23, 24) This model has been used to inform HPV vaccination policy decisions in the United States.(24–26) The HPV-ADVISE model performed 20 runs for 50 parameter sets, for a total of 1000 runs; results for each parameter set were averaged. Mean incidence (mean of the parameter set averages) and a 50% uncertainty interval (UI) per 10,000 persons in 2018 were estimated for HPV 6/11, IARC Group 1, 14HR types, and disease-associated HPV. HPV-ADVISE was not designed to model all 37 HPV types (any HPV) detected using Linear Array. To estimate the incidence of any HPV infection, disease-associated HPV infection incidence and the 50% UI bounds were multiplied by sex-age group-specific adjustment factors equal to the ratio of prevalence point estimates of any HPV to disease-associated HPV estimated using NHANES data. All modeled incidences and 50% UIs were multiplied by the 2018 ACS-based population totals to estimate the number of US persons in 2018 with an incident infection.

Results

Estimated Prevalence

HPV infection prevalences and number of persons with prevalent HPV infection are presented overall and by sex for 15–59- and 15–24-year-olds in Table 1. Because prevalences were calculated overall and separately by sex, estimates for females and males may not sum to exactly to estimates for the total population. Among 15–59-year-olds, 2013–2016 prevalence of any HPV infection was 40.0% overall, 41.8% among males, and 38.4% among females. These prevalences correspond to 77.3 million persons overall, or 40.5 million males and 37.0 million females, with a prevalent HPV infection in 2018. Prevalence of disease-associated HPV infection was 22.0% overall, 24.2% in males and 19.9% in females corresponding to 42.5 million persons, 23.4 million males, and 19.2 million females with an infection of at least one disease-associated HPV type in 2018. Prevalence point estimates of infections with all HPV categories in males were somewhat higher than females in 15–59-year-olds. Prevalence of 14HR infection was about 2.5 percentage points higher than estimates of IARC Group 1 infection prevalence overall and among males and females.

In contrast to what was found in 15–59-year-olds, in the younger age group of 15–24-year-olds, most prevalence of infection point estimates were lower among males than females. Among 15–24-year-olds, prevalence of any HPV infection was 32.8% overall, 25.6% among males, and 40.1% among females, corresponding to 14.2, 5.7, and 8.4 million infected

persons, males, and females, respectively, in 2018. Prevalence of disease-associated HPV infection was 20.9% overall, corresponding to 9.0 million infected persons in 2018 (3.6 million males and 5.4 million females). Prevalence of IARC Group 1 infection was 13.6% in males and 21.2% in females and differed from 14HR infection prevalence by about 2–4 percentage points.

Estimated Incidence

HPV infection incidence and number of persons with incident HPV infection in 2018 are presented overall and by sex for 15–59- and 15–24-year-olds in Table 2. Patterns in incidence by type categories, sex, and age group were similar to patterns in prevalence. Among 15–59-year-olds, incidence of any HPV infection was 1222 per 10,000 persons, with 23.6 million persons acquiring any HPV infection in 2018. Incidence of disease-associated HPV infection was 672, 708, and 636 per 10,000 persons, males, and females, corresponding to 13.0, 6.9, and 6.1 million persons, males, and females with an incident infection. Similar to the pattern observed for prevalence among the same age group, 15–59-year-olds, males had somewhat higher incidence than females for most HPV categories.

Among 15–24-year-olds, all incidence estimates were higher than among 15–59-year-olds, and females had higher incidence than males for all HPV categories. Incidence of any HPV infection was 2566 per 10,000 persons, equating to 11.1 million persons with an incident infection. Incidences of disease-associated HPV infection were 1635, 1491, and 1783 per 10,000 persons, males, and females. In 2018, 7.1 million persons (3.3 million males and 3.8 million females) acquired a disease-associated HPV type infection.

Discussion

We provide national HPV infection prevalence estimates using data from both males and females and show that HPV is a common sexually transmitted infection with a prevalence of 40% among persons aged 15–59 years in the United States. We estimated that, in 2018, over 77 million persons had a prevalent infection. Disease-associated types were common with an estimated 23.4 million males and 19.2 million females having a prevalent infection with at least one disease-associated type in 2018. In addition, using a transmission-dynamic model of HPV,(25, 26) we estimated that in 2018 approximately 13 million persons in the United States (6.9 million males and 6.1 million females) acquired an HPV infection with a disease-associated HPV type.

The burden of each HPV category should be interpreted with respect to the potential sequelae caused by specific HPV types in each category. Burden of the 12 HR types in Group 1 designated as human carcinogens by IARC can be interpreted as the burden of HPV that causes almost all HPV-attributable cancers. Burden of 14HR types reflects HPV that, in addition to causing almost all HPV-attributable cancers, would require follow-up in the clinical setting of cervical cancer screening; we note that the additional types detected by clinical HPV tests, which can cause cervical lesions but seldom cause cancer, contribute 2–4 percentage points to the prevalence estimates.(15) HPV 6/11 reflects the burden of infections that cause most anogenital warts.(2) Therefore, the category of disease-associated HPV, which includes the HPV types detected during cervical cancer screening and that cause

genital warts, encompasses the types responsible for a vast majority of HPV-associated diseases. Measures of prevalence of any HPV infection depend on the biologic sample and collection method, sensitivity of the assay used, and number of types detected by the assay. This should be taken into consideration when comparing prevalence estimates of any HPV infection across research studies.

In the overall age group of 15–59-year-olds, prevalences of infection with most HPV categories were 3–4 percentage points higher in males than females. In the younger group of 15–24-year-olds, most prevalences were 7–14 percentage points higher in females than males. We previously conducted more detailed analyses of sex-specific genital prevalence in different age groups in the United States, showing that males have higher prevalence overall, but that sex differences vary by age group. From the teens through mid-20s, females have higher HPV prevalences than males, but after the mid-20s, prevalences are higher among males than females.⁽²⁷⁾ Similar age- and sex-specific differences were also seen in HPV infection incidence estimates in the present analysis. Sex differences in natural history and sexual behavior may contribute to the different sex-specific patterns found in prevalence and incidence among 15–59- and 15–24-year-olds.^(28, 29)

In 2006, the quadrivalent HPV vaccine that protects against HPV 6/11/16/18 was licensed in the United States and routinely recommended as a 3-dose series for females at ages 11 or 12 years (but could be started at age 9 years) with catch-up vaccination for 13–26-year-olds.⁽³⁰⁾ Since the initiation of the national vaccination program, additional HPV vaccines have been licensed, the program has been expanded to males, and the recommended number of doses for some age groups has changed.^(31s-35s) Currently in the United States, vaccination is routinely recommended for both males and females at ages 11 or 12 years, with catch-up through age 26 years. Shared clinical decision-making is recommended regarding vaccination of persons aged 27 through 45 years. Since the end of 2016, all vaccine used in the United States has been the 9-valent vaccine, protecting against HPV 6/11/16/18/31/33/45/52/58 (2 HPV types that cause anogenital warts and 7 HR types that cause a majority of HPV-attributable cancers).^(35s) Significant reductions in the prevalence of HPV types in the quadrivalent vaccine (HPV 6/11/16/18) have already been observed among adolescent and young adult females,⁽²⁰⁾ which may explain the comparable prevalence of HPV 6/11 infection in male and female 15–24-year-olds where prevalences of infections with other HPV categories (which include HR types not targeted by the quadrivalent vaccine) were higher in females than males. As vaccinated persons age, vaccination coverage will increase among 15–59-year-olds, vaccine-type incidence and prevalence are expected to decrease, and sex differences will be attenuated.

We present HPV infection burden estimates for 2018, with updated data and methods compared to a published estimate for 2008. In this analysis, using 2013–2016 national data from both males and females, we estimated 77.3 million people in the United States had a prevalent HPV infection in 2018, including approximately 42.5 million people with at least one disease-associated HPV type. Previously, Satterwhite and colleagues,⁽¹⁾ using 2003–2006 NHANES data from females only with the assumption that prevalence among males was comparable to females, estimated 79.1 million people had a prevalent HPV infection in 2008, a figure similar to our estimate for 2018. On the other hand, our estimate of 23.6

million people with an incident infection with any HPV in 2018 is notably higher than the 14.1 million estimated by the Satterwhite study for 2008. However, these incidence results are not directly comparable due to differences in the models used. Our 2018 incidence was estimated using the HPV-ADVISE model, while the 2008 incidence estimates from the Satterwhite study were generated using age-specific HPV incidence rates from a different mathematical model of cervical HPV infection published by Canfell.(36s) That model produced estimates found to be consistent with US data for prevalence of 13 oncogenic HPV types.(37s, 38s) Therefore, the Satterwhite estimate of 14.1 million persons with an incident infection in 2008 is more comparable to our estimate for 14 HR (12.9 million persons with an incident infection in 2018). Using these comparisons, our results are reasonably consistent with, but slightly lower than, previous estimates for HPV incidence.

While our estimates are based on the first four years of nationally representative data from both males and females as well as a well published mathematical model, this study is subject to some limitations. First, we assumed prevalence of infection was comparable in 2013–2016 and 2018. In the 8–10 years following vaccine introduction in 2006, while vaccine-type HPV prevalence decreased dramatically in younger females, non-vaccine-type HPV prevalence remained stable in most age groups.(19, 20) This suggests there have not been substantial changes in the risk of HPV acquisition during this time period. Second, to provide estimates of persons with a prevalent infection in the United States, we assumed the prevalence among the non-institutionalized population (which excludes active duty military personnel, families of active duty military personnel living overseas, and all persons in supervised care or custody in institutional settings [e.g., nursing facilities, prisons]) is similar to prevalence in the total population. Because HPV is common and a small proportion of Americans constitute the excluded populations, it is unlikely that these excluded populations would have a significant effect on national prevalence. Finally, presented incidences are modeled estimates and are not from empirical data.

This report includes our most recent estimates of HPV infection prevalence and incidence in the United States using data from national surveys and a mathematical model. While most HPV infections will become undetectable, a portion of infections with disease-associated HPV types will progress to disease.(4) This substantial burden of HPV highlights the need for continued monitoring of HPV-associated cancers through registries, monitoring of other HPV-associated diseases, cervical cancer screening, and HPV vaccination to monitor and prevent HPV-associated disease among persons in the United States.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1:

Prevalence in 2013–2016 and estimated number of persons with prevalent infection in 2018, any HPV and disease-associated HPV type categories, NHANES

Age / HPV type group	Total	Males	Females
Age 15–59 years	N = 8005	N = 3784	N = 4221
Weighted prevalence (50% CI), 2013–2016			
Any HPV	40.0 (39.2, 40.9)	41.8 (40.6, 42.9)	38.4 (37.6, 39.2)
6/11	1.9 (1.7, 2.0)	2.6 (2.4, 2.9)	1.1 (1.0, 1.3)
IARC Group 1	18.5 (18.0, 19.0)	20.3 (19.6, 20.9)	16.9 (16.3, 17.5)
14HR	21.0 (20.4, 21.6)	22.8 (22.1, 23.5)	19.3 (18.8, 19.9)
Disease-associated	22.0 (21.4, 22.6)	24.2 (23.5, 25.0)	19.9 (19.4, 20.5)
Estimated number of persons with infection, in millions (50% CI), 2018			
Any HPV	77.3 (75.7–79.0)	40.5 (39.3–41.5)	37.0 (36.3–37.8)
6/11	3.7 (3.3–3.9)	2.5 (2.3–2.8)	1.1 (1.0–1.3)
IARC Group 1	35.7 (34.8–36.7)	19.7 (19.0–20.2)	16.3 (15.7–16.9)
14HR	40.6 (39.4–41.7)	22.1 (21.4–22.7)	18.6 (18.1–19.2)
Disease-associated	42.5 (41.4–43.7)	23.4 (22.7–24.2)	19.2 (18.7–19.8)
Age 15–24 years	N = 2118	N = 1056	N = 1062
Weighted prevalence (50% CI), 2013–2016			
Any HPV	32.8 (31.9, 33.8)	25.6 (24.4, 26.8)	40.1 (38.7, 41.5)
6/11	1.0 (0.9, 1.2)	1.0 (0.8, 1.3) [†]	1.0 (0.7, 1.2) [†]
IARC Group 1	17.4 (16.6, 18.3)	13.6 (12.7, 14.5)	21.2 (19.9, 22.6)
14HR	20.5 (19.6, 21.5)	15.8 (14.9, 16.9)	25.2 (23.9, 26.6)
Disease-associated	20.9 (19.9, 21.9)	16.3 (15.3, 17.3)	25.5 (24.1, 26.8)
Estimated number of persons with infection, in millions (50% CI), 2018			
Any HPV	14.2 (13.8–14.6)	5.7 (5.4–5.9)	8.4 (8.2–8.7)
6/11	0.4 (0.4–0.5)	0.2 (0.2–0.3)	0.2 (0.1–0.3)
IARC Group 1	7.5 (7.2–7.9)	3.0 (2.8–3.2)	4.5 (4.2–4.8)
14HR	8.8 (8.5–9.3)	3.5 (3.3–3.7)	5.3 (5.0–5.6)
Disease-associated	9.0 (8.6–9.5)	3.6 (3.4–3.8)	5.4 (5.1–5.6)

NHANES, National Health and Nutrition Examination Survey; HPV, human papillomavirus; CI, confidence interval; HR, high risk HPV types; IARC (International Agency for Research on Cancer) Group 1: HPV 16/18/31/33/35/39/45/51/52/56/58/59; 14HR, IARC Group 1 and HPV 66/68; disease-associated, HPV 6/11/16/18/31/33/35/39/45/51/52/56/58/59/66/68. Estimates for males and females may not sum to estimates for the total population.

Table 2:

Model-based estimates of annual incidence per 10,000 persons and number of persons with an incident infection of any HPV and disease-associated HPV type categories in 2018, HPV-ADVISE

Age / HPV type group	Total	Males	Females
Age 15–59 years			
Incidence per 10,000 persons (50% UI)			
Any HPV	1222 (969, 1436)	1223 (983, 1332)	1227 (942, 1478)
6/11	18 (12, 23)	17 (12, 21)	18 (11, 25)
IARC Group 1	587 (466, 681)	623 (501, 688)	552 (428, 657)
14HR	669 (530, 784)	706 (567, 770)	632 (486, 763)
Disease-associated	672 (533, 790)	708 (569, 771)	636 (488, 766)
Number of persons with incident infection, in millions (50% UI)			
Any HPV	23.6 (18.7, 27.8)	11.8 (9.5, 12.9)	11.8 (9.1, 14.3)
6/11	0.3 (0.2, 0.4)	0.2 (0.1, 0.2)	0.2 (0.1, 0.2)
IARC Group 1	11.3 (9.0, 13.2)	6.0 (4.8, 6.7)	5.3 (4.1, 6.3)
14HR	12.9 (10.2, 15.1)	6.8 (5.5, 7.5)	6.1 (4.7, 7.4)
Disease-associated	13.0 (10.3, 15.3)	6.9 (5.5, 7.5)	6.1 (4.7, 7.4)
Age 15–24 years			
Incidence per 10,000 persons (50% UI)			
Any HPV	2566 (2130, 2833)	2342 (2004, 2613)	2804 (2331, 3309)
6/11	37 (26, 47)	25 (18, 32)	50 (33, 71)
IARC Group 1	1432 (1186, 1559)	1308 (1108, 1474)	1559 (1303, 1831)
14HR	1632 (1354, 1800)	1489 (1274, 1663)	1779 (1478, 2099)
Disease-associated	1635 (1357, 1805)	1491 (1276, 1664)	1783 (1482, 2104)
Number of persons with incident infection, in millions (50% UI)			
Any HPV	11.1 (9.2, 12.2)	5.2 (4.4, 5.8)	5.9 (4.9, 7.0)
6/11	0.2 (0.1, 0.2)	0.1 (0.0, 0.1)	0.1 (0.1, 0.1)
IARC Group 1	6.2 (5.1, 6.7)	2.9 (2.4, 3.3)	3.3 (2.7, 3.9)
14HR	7.0 (5.8, 7.8)	3.3 (2.8, 3.7)	3.7 (3.1, 4.4)
Disease-associated	7.1 (5.9, 7.8)	3.3 (2.8, 3.7)	3.8 (3.1, 4.4)

HPV, human papillomavirus; UI, uncertainty interval; HR, high risk HPV types; IARC (International Agency for Research on Cancer) Group 1: HPV 16/18/31/33/35/39/45/51/52/56/58/59; 14HR, IARC Group 1 and HPV 66/68; disease-associated, HPV 6/11/16/18/31/33/35/39/45/51/52/56/58/59/66/68.

Note: Incidence of any HPV was calculated by multiplying the disease-associated HPV incidence and the 50% UI bounds by sex-age group-specific adjustment factors equal to the ratio of prevalence point estimates of any HPV to disease-associated HPV. Any HPV incidence among total population may not reflect weighted average of incidence among males and females.