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# Racial and ethnic disparities in human papillomavirus (HPV)-associated cancer burden with first- and second-generation HPV vaccines

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## Abstract

**Background—**In the United States, the burden of human papillomavirus (HPV)-associated cancers varies by racial/ethnic group. HPV vaccination may provide opportunities for primary prevention of these cancers. We projected changes in HPV-associated cancer burden among racial/ethnic groups under various coverage assumptions with the available first-generation and second-generation HPV vaccines in order to evaluate changes in racial/ethnic disparities.

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**Author contributions:** EAB, KL, and JJK participated in the study conception and design, data synthesis and analysis, and interpretation of the results. TT, MS, LM, and HC participated in the analysis design, acquisition of data, and interpretation of the results. EAB drafted the original manuscript; all authors reviewed and edited the manuscript. All authors provided approval of the final draft of the report.

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

**Methods—**Cancer-specific mathematical models simulated the burden of six HPV-associated cancers. Models parameters, informed using national registries and epidemiological studies, reflected sex-, age- and racial/ethnic-specific heterogeneities in HPV type distribution, cancer incidence, stage detection and mortality. Model outcomes included the cumulative lifetime risks of developing and dying from six HPV-associated cancers. The level of racial/ethnic disparities was evaluated under each alternative HPV vaccine scenario using several metrics of social-group disparity.

**Results—**HPV vaccination is expected to reduce the risks of developing and dying from HPV-associated cancers in all racial/ethnic groups and reduce the absolute degree of disparities. However, alternative metrics suggested that relative disparities would persist and in some scenarios worsen. For example, when assuming high uptake with the second-generation HPV vaccine, the lifetime risk of dying from an HPV-associated cancer for males decreased by ~60%, yet the relative disparity increased from 3.0 to 3.9.

**Conclusions—**HPV vaccines are expected to reduce the overall burden of HPV-associated cancers for all racial/ethnic groups and to reduce the absolute disparity gap. However, even with the second-generation vaccine, relative disparities will likely still exist and may widen if the underlying causes of these disparities remain unaddressed.

### Keywords

Health Status Disparities; Human Papilloma Virus; Vaccines; Neoplasms

## INTRODUCTION

Persistent infection with high-risk human papillomavirus (HPV), the most common sexually transmitted infection, is responsible for several anogenital and oropharyngeal cancers among both women and men. The incidence and mortality rates of each HPV-associated cancer differs by racial and ethnic group, with disproportionately higher rates often occurring among Hispanics, Blacks and American Indian/Alaska Natives.[1] For example, not only do Black women have the second-highest incidence rate of cervical cancer compared with other racial/ethnic groups (i.e., 9.8 per 100,000 women), but cancers in these women are also more likely to be detected at a later stage with a poorer stage-specific probability of surviving, resulting in the highest cervical cancer mortality rate among all racial/ethnic groups.[2] Reasons for such inequalities may include differences in socially controllable factors (e.g., participation in screening, health-seeking behavior), as well as differential access to health services, including cancer treatment.[3,4] Genetic and other “non-modifiable” biological factors (e.g., genetic markers) may also contribute to existing inequalities between racial/ethnic groups; however, interactions between inherent biologic factors of individuals and environmental exposures do not allow these factors to be viewed in isolation.

The advent of the first-generation HPV vaccines, which protect against two of the most carcinogenic HPV genotypes (16 and 18), provides opportunities for primary prevention of HPV-associated cancers, and may also alleviate existing disparities. However, while guidelines for HPV vaccination have been in place since 2007, less than half of U.S. girls aged 13–17 years have received all three doses of the HPV vaccine series, a coverage rate

that is considerably lower than other currently recommended pre-adolescent vaccines in the U.S.[5] In addition, initiation and completion of the HPV vaccine series also differs by racial/ethnic group.[5,6]

Improving population health and reducing health disparities continue to be priorities for several U.S. agencies (e.g., National Cancer Institute (NCI), the Centers for Disease Control and Prevention (CDC)).[7,8] However, while the HPV vaccines have been projected to reduce the overall population burden of HPV-associated cancers,[9] it is unknown how the racial/ethnic-specific burden of HPV-associated cancers will change as cohorts of vaccinated individuals age. In addition, there may be opportunities to further reduce inequalities under scenarios of improved vaccination coverage or with the newly approved second-generation HPV vaccine, which protects against an additional five cancer-causing HPV genotypes (i.e., HPV-31, -33, -45, -52, and -58).

Decades of observations are required to monitor the impact of HPV vaccination on long-term health consequences of HPV such as cancer incidence and mortality. In the absence of such data, disease simulation models provide a formal framework that can project changes in HPV-associated cancer burden in the overall population, as well as important subgroups. These model projections can be used to guide pressing cancer control policies and decisions in a timely manner. Our objective was to use mathematical modeling to synthesize primary epidemiological data by racial/ethnic group and project the changes in HPV-associated cancer burden under current and optimistic coverage assumptions with both the first- and second-generation HPV vaccines. In this context, we evaluated the level of racial/ethnic disparities under each HPV vaccine scenario using common metrics of social-group disparity.

## METHODS

### Analytic approach

We developed a series of mathematical models to project the lifetime risks of developing and dying from six HPV-associated cancers (i.e., cervical, anal, vaginal, vulvar, oropharyngeal and penile) under current levels of HPV vaccination coverage, and high levels vaccination coverage for the first-generation (HPV-16/18) and second-generation (9-valent) HPV vaccines. The models simulate a birth cohort from age eleven until death, where each year, individuals are at risk for developing an HPV-associated cancer, governed by age-, sex-, and cancer-specific incidence rates. Individuals with cancer face stage-specific cancer mortality, while all individuals are at risk of dying from other causes. When available, model inputs reflected heterogeneities across five racial/ethnic subgroups: 1) Non-Hispanic White, 2) Non-Hispanic Black, 3) Hispanic, 4) American Indian/Alaska Native (AI/AN), and 5) Asian, Pacific-Islander (API). The HPV vaccine was assumed to reduce the proportion of cases attributed to the oncogenic HPV genotypes included in the vaccine for each HPV-associated cancer.

## Model input parameters

We synthesized data from epidemiological studies and cancer registries to inform model input parameters (Table 1). For racial/ethnic-specific parameters such as cancer incidence and stage of detection, we used population-based data from CDC's National Program of Cancer Registries (NPCR) and NCI's Surveillance, Epidemiology, and End Results (SEER) program for cancer registries that met the United States Cancer Statistics (USCS) data quality criteria, for years 2007–2011.[10] The registries included cover 99.1% of the U.S. population. The 5-year cancer survival probabilities by race/ethnicity, sex, and stage were extracted from SEER for 2000–2011. The proportions of each cancer attributed to vaccine-targeted HPV genotypes was informed using primary HPV genotyping data from the CDC, specified by sex and racial/ethnic group.[11] When data for a given racial/ethnic group were not available (e.g., suppressed due to confidentiality or stability), we assumed the "all race" value. For a given subgroup, we accounted for racial/ethnic-specific background mortality using CDC's National Center for Health Statistics' National Vital Statistics System for 2010.[12]

The 3-dose HPV vaccination coverage rates by sex and racial/ethnic subgroup were based on the published 2013 National Immunization Survey-Teen (NIS-Teen) results.[5] We assumed 100% lifelong efficacy against the HPV genotypes targeted by the vaccine and no cross-protection. For cervical cancer, we did not model screening practice explicitly; rather, we used the current cervical cancer incidence rates reported in the population-based registries that reflect current screening participation.

## Measuring disparities

We relied on multiple disparity indicator metrics to summarize changes in racial/ethnic cancer burden under the alternative HPV vaccine scenarios. For a given HPV vaccine and coverage assumption, we identified the racial/ethnic groups with the highest and lowest cumulative lifetime risks of developing or dying from an HPV-associated cancer, and calculated the absolute and relative differences between the two extreme groups. We refer to these calculations as the absolute and relative disparity measures, respectively. To capture the internal variability and distribution of the group-specific risk we calculated the Index of Disparity (ID). The ID is a composite measure of relative disparity that summarizes the average absolute deviation of the group risk from the average population risk relative to the average population risk, expressed as a percentage.[13] The absolute, relative and ID metrics were evaluated for each HPV-associated cancer individually and cumulatively (Supplementary Material). To assess the stability in the trends of the disparity metrics, we calculated three additional composite measures of disparity: the population attributable proportion (PAP), the Gini coefficient and a weighted version of the ID (weighted by population size of the racial/ethnic groups) for the cumulative lifetime risks (Supplementary Material).[14]

## Analysis

We projected the changes in the cumulative lifetime risks of developing and dying from any HPV-associated cancer by racial/ethnic group under the current 3-dose coverage level, as well as for a "high coverage" scenario that assumes that current immunization rates for the

Tetanus, diphtheria & acellular pertussis (Tdap) vaccine in adolescents can be achieved for HPV vaccines.[5] We repeated model simulations to project changes in cancer disparities assuming protection against the seven oncogenic HPV types targeted by the second-generation (9-valent) vaccine. Since not all HPV-associated cancers are attributable to HPV and because the percent attributable to HPV varies by anatomic site and sex, in sensitivity analysis, we isolated the potential impact of excluding HPV-negative cancers on the cumulative lifetime risks and disparity metrics. In addition, lifetime risks reflect racial/ethnic differences in life expectancy (i.e., background mortality due to other causes than HPV-associated cancers); therefore, in sensitivity analysis we standardized background mortality to be equal across all racial/ethnic groups.

## RESULTS

### Cumulative lifetime risk of developing HPV-associated cancers

In the absence of HPV vaccination, the cumulative lifetime risk of developing an HPV-associated cancer among women was the highest for Hispanics (1.63%) and Non-Hispanic Blacks (1.46%), and lowest for Asian/Pacific Islanders (0.83%), where cervical cancer contributed to 40–70% of the HPV-associated cancer burden (Figure 1a). For unvaccinated men, the lifetime risk of developing an HPV-associated cancer was overall 30–60% lower compared with females, where oropharyngeal cancer consistently contributed the largest proportion of the burden (Figure 1b). Among men, the highest risk of developing HPV-associated cancers was among Non-Hispanic Whites. While the absolute disparity was lower for males compared with females, the magnitude of relative racial/ethnic disparities was consistently greater for males compared with females across multiple metrics (Table 2; Supplementary Material Tables 1–2).

Under current HPV vaccination coverage levels that are variable by race/ethnicity, the first-generation HPV-16/18 vaccines were projected to reduce the cumulative lifetime risk of developing an HPV-associated cancer for both sexes, and across all racial/ethnic groups (Figure 1), resulting in declines in the absolute disparities (Table 2). However, at current coverage levels, HPV vaccination was not projected to markedly impact existing relative or composite racial/ethnic disparities. For example, under current coverage rates, the ID was projected to decrease by <0.5% for both females and males.

Under improved vaccination coverage assumptions (i.e., Tdap vaccination coverage), the reductions in cumulative lifetime risk of developing an HPV-associated cancer were more pronounced (Figure 1), leading to further declines in the absolute disparity gap for both women and men, compared with HPV vaccination at current levels. However, the current levels of relative racial/ethnic disparities continued to persist (Table 2). Of note, four out of six disparity metrics increased for males under this scenario (Supplementary Material Table 2), and Non-Hispanic Black males had the highest cumulative lifetime risk of developing an HPV-associated cancer, exceeding that of Non-Hispanic White males.

Compared with the first-generation HPV vaccines under current coverage levels, the second-generation (9-valent) vaccine was projected to further reduce the disease burden for all racial/ethnic groups under both vaccination coverage scenarios (Figure 1); yet, relative

racial/ethnic disparities continued to persist. When we evaluated each HPV-associated cancer separately, oropharyngeal cancer was a primary contributor to the projected increases in male relative disparities under the high-coverage vaccination scenarios (Supplementary Material Figure 2).

### Cumulative lifetime risk of dying from HPV-associated cancers

For the individuals not vaccinated against HPV, the average population risk of dying from an HPV-associated cancer was 0.24% for females and 0.20% for males, where Non-Hispanic Black individuals faced the highest burden for both sexes (i.e., 0.32% and 0.25%, respectively) (Figure 2). In the absence of HPV vaccination, the relative and composite disparity metrics for females indicated greater racial/ethnic disparity associated with the risk of dying compared with risk of developing an HPV-associated cancer (Table 2; Supplementary Material Table 1).

Under current HPV vaccination coverage, the first-generation vaccines were projected to reduce the cumulative lifetime risk of dying from an HPV-associated cancer for all racial/ethnic groups and for both sexes (Figure 2), yielding declines in the absolute disparity. However, similar to the risk of developing HPV-associated cancers, relative measures of racial/ethnic disparities persisted, and in certain vaccination scenarios, were exacerbated (Table 2). For example, when assuming high vaccination coverage (i.e., Tdap) with the second-generation HPV vaccine, the average male population cumulative lifetime risk of dying from an HPV-associated cancer was projected to decrease by ~60%, but the ID was estimated to increase by nearly 75% (i.e., from 21.8% to 37.8%). When disaggregated by HPV-associated cancer, oropharyngeal cancer-related death was a key contributor to the relative disparities, for both sexes (Supplementary Material Figure 3).

### Sensitivity analysis

When we conditioned cancer incidence and HPV type distribution on HPV-positive cancers, we found that the absolute disparity gaps narrowed for both sexes; in addition, the magnitude of the relative disparity and composite ID metrics uniformly decreased for males (Table 3; Supplementary Material). Conversely, when we standardized background mortality to that of the total U.S. population, the absolute disparity gaps for the cumulative lifetime risk of dying increased for both sexes compared with the base case analysis; however, the general disparity trends across the vaccination scenarios remained consistent.

## DISCUSSION

Using several metrics of health disparity, we projected the magnitude of unequal cancer burden across five racial/ethnic groups under two plausible scenarios of vaccination coverage for both the first- and second-generation HPV vaccines. Our model-based analysis, parameterized using data from national population-based cancer registries covering nearly the entire U.S. population, suggests that with the adoption of the first- or second-generation HPV vaccines, the risks of developing and dying from an HPV-associated cancer are expected to decline for all racial/ethnic groups. In addition, the absolute disparity gaps between the best- and worst-off racial/ethnic groups are expected to narrow. However, we

find that even under favorable vaccination coverage scenarios, the relative and composite indicators of disparity suggest that racial/ethnic disparities in cancer burden, especially with respect to risk of dying, are likely to persist and may even widen.

This analysis is the first to leverage U.S. population-based registry data to project changes in HPV-associated cancer burden and racial/ethnic disparities associated with HPV vaccination. The adoption of HPV vaccines has the potential to not only reduce the HPV-associated cancer burden, but also compensate for the disparities resulting from differential access to healthcare services for cancer screening, diagnosis and treatment that is experienced across different subgroup populations. This analysis, which synthesized the available data on HPV-associated cancer epidemiology and vaccine uptake by racial/ethnic group, projected that while the absolute cancer burden (and absolute disparities) will decrease overall, HPV vaccination may not reduce existing relative disparities. In fact, we found that the relative differences in cancer burden across racial/ethnic groups were most pronounced under scenarios of high vaccination coverage, particularly for men, where relative disparities were generally greater compared with women (Table 2). The greater magnitude of relative disparities for men under the HPV vaccination scenarios is likely due in part to the lower proportion of HPV-positive oropharyngeal cancers among Non-Hispanic Black individuals, coupled with the larger contribution oropharyngeal cancers have in the overall male HPV-associated cancer burden. When we restricted the analysis to HPV-positive cancers, the racial/ethnic disparities among men under all vaccination scenarios decreased. For women, the relative and composite measures of disparities with and without vaccination were the widest in terms of the risk of dying from an HPV-associated cancer and were disproportionately higher than those related to risk of developing an HPV-associated cancer. This may be due in part to differences in access to and quality of care following cancer diagnosis.

Summary measures of health disparity encompass simple pairwise metrics (e.g., absolute and relative disparity between extreme groups), as well as composite metrics (e.g., ID[13]).[14] As there is little agreement for a single comprehensive measure of health disparity (two metrics may contradict changes in health disparity), we elected to report multiple metrics as they each fundamentally provide unique and complementary information about the magnitude and direction of changes in health disparity. Declines in both the absolute and relative disparity metrics provide the best evidence for progress in disparity elimination. We found that the changes in absolute disparity signaled improvements in health disparity as a result of vaccination, while the relative disparity metric, which adjusts for changes in the reference point over the vaccination scenarios, did not correspond. The four composite disparity measures generally agreed with the direction of the relative disparity metric. Our finding that the relative and summary metrics signaled persistent or even exacerbating health disparity should be tempered by the fact that the cumulative lifetime risks of developing and dying from HPV-associated cancers are small.

## Limitations

Data stratified by each racial/ethnic group were limited or suppressed in some cases due to the small number of observations. Combining the NPCR and SEER registries for model

parameters such as cancer incidence and stage detection minimized the need for data assumptions; nevertheless, several model parameters reflected the average population value. In addition, cancer-specific survival data that reflected HPV-positive cancers stratified by racial/ethnic group were unavailable. Therefore, we could not account for the better prognosis associated with some HPV-positive cancers (e.g., oropharyngeal cancer[15]), and may have overestimated the benefit of the HPV vaccines on cancer mortality. Observed racial/ethnic disparities may mask underlying heterogeneity within certain racial/ethnic subgroups. For example, preventive health care varies by immigrant status[16]; therefore, projected racial/ethnic disparities may be confounded by immigrant-specific differences within sub-groups that are linked to access to care—both related to vaccination and screening uptake.

Our analysis reflects several simplifying assumptions. For example, we assumed that the HPV vaccines prevented the proportion of each cancer attributed to vaccine-targeted HPV genotypes (i.e., HPV type distribution) without cross protection. Excluding the potential benefits of cross-protection may be relatively more important for females than males, since the contribution of non-HPV-16/18 types to cervical cancers is larger; however, the durability of the HPV vaccines on other high-risk types not targeted by the vaccines is less certain.[17] In addition, current evidence suggests that the incidence of several HPV-associated cancers may be increasing;[1,18] subsequently, we may have underestimated the future burden of HPV-associated cancers by assuming the underlying burden remains constant over time in the absence of vaccination. This assumption only impacts our projected changes in racial/ethnicities disparities to the extent that the racial/ethnic-specific incidence rates are differentially changing. Our models captured direct vaccination benefit and did not include the herd effects vaccinated individuals may provide to unvaccinated individuals; therefore, the decreases in HPV-associated cancer burden – and the absolute declines in disparity – may be greater than we estimated. Australia, a country that has achieved HPV vaccination coverage rates (for ≥1 dose) similar to the Tdap coverage rates in the U.S., has documented important herd effects among unvaccinated individuals.[19] However, it is not clear how the inclusion of herd effects would impact our assessment of changes in relative disparities. Conversely, we assumed the HPV vaccines provide 100% lifelong efficacy against the targeted HPV genotypes, which may overestimate the protective effects the HPV vaccines have on reducing cancer burden. Similarly, our “high coverage” scenario, which assumes that current immunization rates for the Tdap vaccine in adolescents can be achieved with HPV vaccines, may be overly-optimistic. Unlike the Tdap vaccine, which requires a single dose, a 3-dose schedule is recommended for HPV vaccine in the United States. However, several countries are revisiting HPV vaccine schedules as several studies have shown that receiving fewer than three doses yields comparably high benefit.[20]

## CONCLUSION

The adoption of HPV vaccines has the potential to reduce the cumulative lifetime risks of developing and dying from an HPV-associated cancer for all racial/ethnic groups, and will likely reduce the absolute degree of disparities in these outcomes. However, even with the second generation HPV vaccine, relative disparities will likely still exist and may widen if

underlying causes of these disparities (e.g., differential access to preventive health services and cancer therapies by race/ethnicity) remain unaddressed.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## Abbreviations

| | |
|---|---|
| **AI/AN** | American Indian, Alaska Native |
| **API** | Asian, Pacific Islander |
| **CDC** | Centers for Disease Control and Prevention |
| **HPV** | Human papillomavirus |
| **MMWR** | Morbidity and Mortality Weekly Report |
| **NCI** | National Cancer Institute |
| **NIS-Teen** | National Immunization Survey-Teen |
| **NPCR** | National Program of Cancer Registries |
| **SEER** | Surveillance, Epidemiology, and End Results |
| **Tdap** | Tetanus, diphtheria & acellular pertussis |

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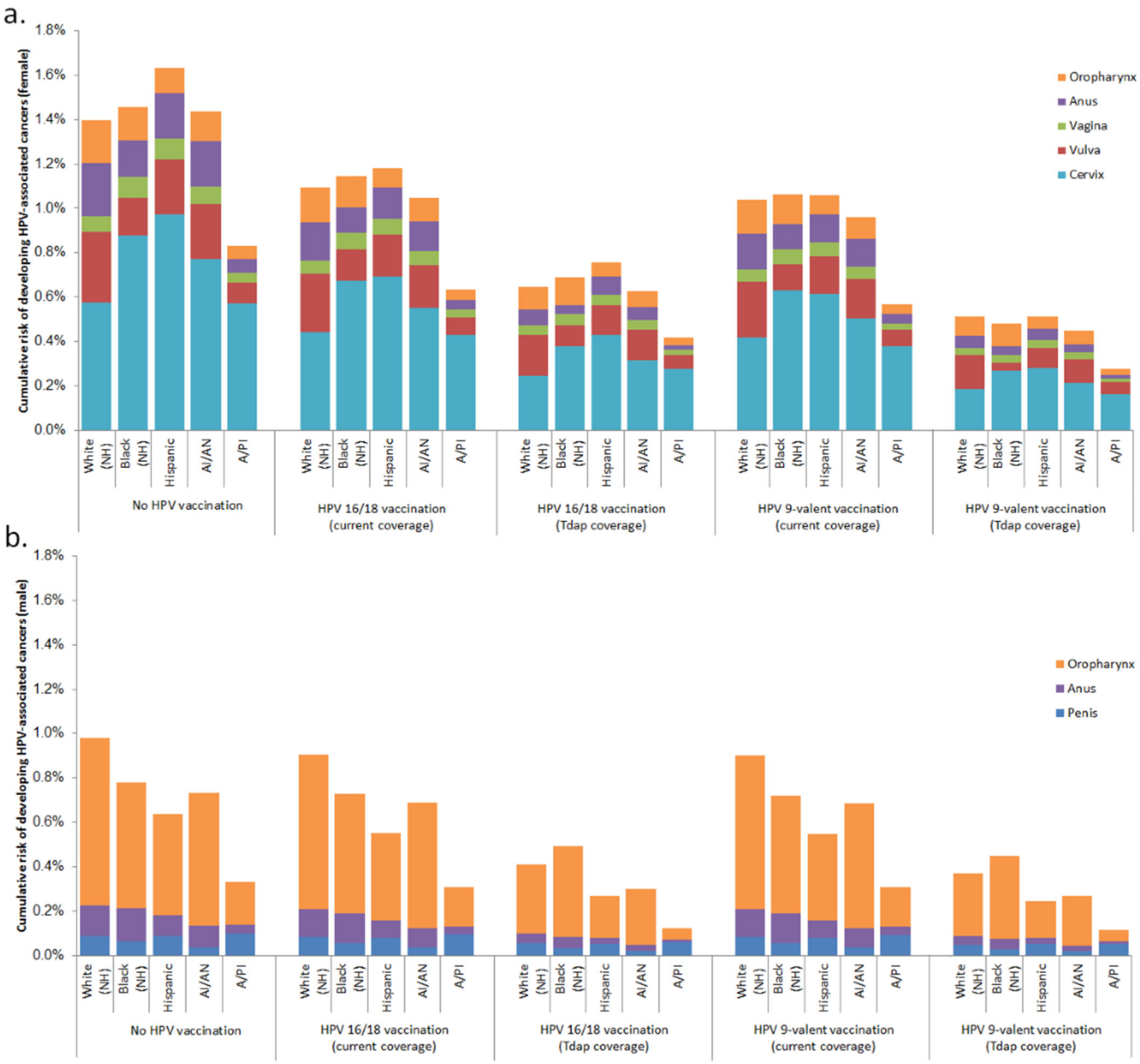


**Figure 1.**

Cumulative lifetime risk of developing a human papillomavirus (HPV)-associated cancer by HPV vaccination scenario for a) females, and b) males. AI/AN: American Indian, Alaska Native; API: Asian, Pacific Islander; NH: Non-Hispanic; Tdap: Tetanus, diphtheria & acellular pertussis


**Figure 2.**

Cumulative lifetime risk of dying from a human papillomavirus (HPV)-associated cancer by HPV vaccination scenario for a) females, and b) males. AI/AN: American Indian, Alaska Native; API: Asian, Pacific Islander; NH: Non-Hispanic; Tdap: Tetanus, diphtheria & acellular pertussis

**Table 1**

Selected model input parameters

| HPV-related cancers[a] | Non-Hispanic White | Non-Hispanic Black | Hispanic | American Indian/Alaska Native | Asian/Pacific Islander |
|---|---|---|---|---|---|
| **Anus, female** | | | | | |
| Incidence rate per 100,000[b] | 2.2 | 1.6 | 1.5 | 1.4 | 0.5 |
| Stage of detection: Local, Regional, Distant[b] | 53%, 34%, 13% | 49%, 36%, 15% | 52%, 35%, 13% | 48%, 32%, 20% | 43%, 36%, 21% |
| 5-year survival: Local, Regional, Distant[c] | 84%, 66%, 38% | 77%, 61%, 32% | 84%, 68%, 47% | 62%, 82%, 38% | 70%, 79%, 27% |
| Attributable to HPV-16/18 (other 5 HR types[d]) | 82% (9%) | 91% (0%) | 69% (15%) | 80% (11%) | 80% (11%) |
| **Anus, male** | | | | | |
| Incidence rate per 100,000[b] | 1.4 | 1.9 | 1.0 | 1.1 | 0.4 |
| Stage of detection: Local, Regional, Distant[b] | 55%, 34%, 11% | 49%, 40%, 11% | 53%, 33%, 13% | 44%, 42%, 14% | 47%, 40%, 14% |
| 5-year survival: Local, Regional, Distant[c] | 77%, 55%, 19% | 69%, 45%, 17% | 80%, 54%, 30% | 56%, 53%, 20% | 92%, 45%, 13% |
| Attributable to HPV-16/18 (other 5 HR types[d]) | 77% (3%) | 79% (4%) | 79% (4%) | 79% (4%) | 79% (4%) |
| **Cervix** | | | | | |
| Incidence rate per 100,000[b] | 6.9 | 9.8 | 10.2 | 8.7 | 6.3 |
| Stage of detection: Local, Regional, Distant[b] | 48%, 37%, 14% | 39%, 44%, 17% | 51%, 38%, 11% | 46%, 40%, 14% | 47%, 40%, 13% |
| 5-year survival: Local, Regional, Distant[c] | 92%, 56%, 16% | 85%, 51%,12% | 92%, 64%, 23% | 89%, 43%, 19% | 93%, 62%, 19% |
| Attributable to HPV-16/18 (other 5 HR types[d]) | 67% (12%) | 68% (15%) | 64% (18%) | 66%* (15%)* | 61% (23%)* |
| **Oropharynx, female** | | | | | |
| Incidence rate per 100,000[b] | 1.7 | 1.5 | 0.9 | 1.1 | 0.6 |
| Stage of detection: Local, Regional, Distant[b] | 22, 61%, 17% | 16%, 55%, 29% | 19%, 62%, 19% | 25%, 58%, 17% | 29%, 55%, 16% |
| 5-year survival: Local, Regional, Distant[c] | 69%, 62%, 36% | 56%, 38%, 22% | 84%, 64%, 32% | 69%, 53%, 33% | 79%, 74%, 39% |
| Attributable to HPV-16/18 (other 5 HR types[d]) | 54% (9%) | 21% (18%) | 51% (10%) | 51% (10%) | 51% (10%) |
| **Oropharynx, male** | | | | | |
| Incidence rate per 100,000[b] | 7.9 | 6.5 | 4.1 | 5.2 | 2.0 |
| Stage of detection: Local, Regional, Distant[b] | 12%, 69%, 18% | 11%, 60%, 29% | 13%, 65%, 22% | 11%, 64%, 25% | 14%, 63%, 23% |

| HPV-related cancers[a] | Non-Hispanic White | Non-Hispanic Black | Hispanic | American Indian/Alaska Native | Asian/Pacific Islander |
|---|---|---|---|---|---|
| 5-year survival: Local, Regional, Distant[c] | 77%, 73%, 44% | 62%, 42%, 26% | 75%, 66%, 34% | 63%, 65%, 35% | 90%, 66%, 49% |
| Attributable to HPV-16/18 (other 5 HR types[d]) | 69% (4%) | 33% (8%) | 68% (6%) | 65% (5%) | 85% (0%) |
| **Penis** | | | | | |
| Incidence rate per 100,000[b] | 0.8 | 0.6 | 0.6 | 0.7 | 0.9 |
| Stage of detection: Local, Regional, Distant[b] | 42%, 33%, 25% | 28%, 36%, 36% | 30%, 37%, 33% | 37%, 30%, 33% | 42%, 25%, 33% |
| 5-year survival: Local, Regional, Distant[c] | 78%, 49%, 27% | 80%, 41%, 24% | 87%, 51%, 46% | 90%, 48%, 30% | 70%, 47%, 38% |
| Attributable to HPV-16/18 (other 5 HR types[d]) | 45% (12%) | 58% (6%) | 46% (0%) | 48% (9%) | 48% (9%) |
| **Vagina** | | | | | |
| Incidence rate per 100,000[b] | 0.6 | 0.8 | 0.6 | 0.6 | 0.4 |
| Stage of detection: Local, Regional, Distant[b] | 40%, 41%, 19% | 35%, 46%, 19% | 41%, 41%, 18% | 24%, 52%, 24% | 45%, 36%, 18% |
| 5-year survival: Local, Regional, Distant[c] | 72%, 57%, 20% | 67%, 53%, 11% | 77%, 48%, 16% | 72%, 54%, 18% | 78%, 50%, 33% |
| Attributable to HPV-16/18 (other 5 HR types[d]) | 49% (18%) | 55% (18%) | 55% (18%) | 55% (18%) | 55% (18%) |
| **Vulva** | | | | | |
| Incidence rate per 100,000[b] | 2.6 | 1.7 | 1.6 | 1.5 | 0.8 |
| Stage of detection: Local, Regional, Distant[b] | 63%, 33%, 4% | 59%, 36%, 6% | 62%, 33%, 5% | 61%, 31%, 7% | 65%, 27%, 8% |
| 5-year survival: Local, Regional, Distant[c] | 88%, 55%, 17% | 84%, 64%, 22% | 90%, 54%, 23% | 78%, 42%, 19% | 93%, 53%, 15% |
| Attributable to HPV-16/18 (other 5 HR types[d]) | 48% (12%) | 53% (40%) | 55% (18%) | 49% (14%) | 36% (14%) |
| **Vaccine[e]** | | | | | |
| **HPV vaccine coverage, ages 13–17 (3-dose)** | | | | | |
| Females | 34.9% | 34.2% | 44.8% | 43.2% | 40.4% |
| Males | 11.1% | 15.7% | 20.3% | 20.3%[f] | 9.1% |
| **Tdap vaccine coverage (≥ 1 dose)** | 85.9% | 84.1% | 87.1% | 85.3% | 89.7% |

HPV: Human papillomavirus; HR: high-risk; Tdap: Tetanus, diphtheria & acellular pertussis

[a]Include both Centers for Disease Control and Prevention's (CDC) National Program of Cancer Registries (NPCR) and the National Cancer Institute's (NCI) Surveillance, Epidemiology, and End Results Program (SEER) registries for 2007–2011 and include all states except Nevada (they do not meet USCS publication criteria). Included registries cover 99.1% of the U.S. population. Missing or suppressed values assumed to be "all race" value unless otherwise specified. Percentage values rounded and may not sum to 1. Oropharyngeal cancers include: Base of tongue, tonsils, and oropharynx;

[b] Overall incidence rates provided for illustrative purposes; age-specific values were used as model inputs. The following histologies were excluded as they were excluded from the HPV typing study[11] 8720–8790, 8800–8991, 9050–9055, 9140, 9590–9989;

[c] SEER registries only, 2000–2011. Individual life tables are not available in SEER*Stat for Hispanics, Asian/Pacific Islander, and American Indian/Alaska Natives; therefore, relative survival estimates may be biased for these groups;

[d] Other five high-risk HPV genotypes include HPV-31, -33, -45, -52, -58. HPV type estimates are based on proportional weighting attribution when multiple infections were present. Suppressed HPV distribution estimates for subgroups with N<10;

[e] HPV vaccination coverage rates reported in the 2013 National Immunization Survey-Teen (NIS-Teen);

[f] 3-dose HPV vaccination coverage not available; rate was assumed to be that of Hispanics, due to the similarity in coverage among females, as well as the 2-dose male coverage.

**Table 2**

Absolute, relative and index of disparity (ID) associated with developing and dying from a human papillomavirus (HPV)-associated cancer under current[a] and expanded[b] coverage rates for the first- (HPV-16/18) and second-generation (9-valent) HPV vaccines

| | Female | | | | Male | | | |
|---|---|---|---|---|---|---|---|---|
| | Average lifetime risk[c] | Absolute Disparity[d] | Relative Disparity[e] | ID[f] | Average lifetime risk[c] | Absolute Disparity[d] | Relative Disparity[e] | ID[f] |
| **Cumulative lifetime risk of developing cancer** | | | | | | | | |
| No HPV vaccination | 1.41% | 0.80% | 2.0 | 12.5 | 0.91% | 0.65% | 3.0 | 26.9 |
| HPV-16, -18 vaccination (current coverage) | 1.08% | 0.55% | 1.9 | 12.1 | 0.83% | 0.60% | 2.9 | 26.8 |
| HPV-16, -18 vaccination (Tdap coverage) | 0.66% | 0.34% | 1.8 | 12.7 | 0.40% | 0.37% | 4.0 | 30.6 |
| 9-valent HPV vaccination (current coverage) | 1.01% | 0.49% | 1.9 | 12.2 | 0.82% | 0.59% | 2.9 | 26.9 |
| 9-valent HPV vaccination (Tdap coverage) | 0.49% | 0.24% | 1.9 | 12.7 | 0.36% | 0.33% | 3.9 | 30.7 |
| **Cumulative lifetime risk of dying from cancer** | | | | | | | | |
| No HPV vaccination | 0.24% | 0.19% | 2.4 | 20.2 | 0.20% | 0.17% | 3.1 | 21.8 |
| HPV-16, -18 vaccination (current coverage) | 0.18% | 0.15% | 2.5 | 20.9 | 0.18% | 0.16% | 3.1 | 23.8 |
| HPV-16, -18 vaccination (Tdap coverage) | 0.11% | 0.09% | 2.4 | 20.4 | 0.09% | 0.13% | 5.1 | 37.5 |
| 9-valent HPV vaccination (current coverage) | 0.17% | 0.15% | 2.6 | 21.6 | 0.18% | 0.16% | 3.1 | 23.8 |
| 9-valent HPV vaccination (Tdap coverage) | 0.08% | 0.07% | 2.7 | 21.0 | 0.08% | 0.12% | 5.1 | 37.8 |

ID: Index of Disparity; Tdap: Tetanus, diphtheria & acellular pertussis.

[a]"Current coverage" reflects the current level of any HPV vaccine uptake[5];

[b]"Tdap coverage" reflects the current level of the 1-dose Tdap vaccine uptake[5];

[c]Average cumulative lifetime risk of developing an HPV-associated cancer for the total population;

[d]Absolute disparity = (maximum cumulative lifetime risk-minimum cumulative lifetime risk);

[e] Relative disparity = (maximum cumulative lifetime risk/minimum cumulative lifetime risk);

[f] $IID = (\sum_{j=1}^{j=N} \frac{|r_j - R|}{N}) / R \times 100$, where r is the group cumulative lifetime risk and R is the total population cumulative lifetime risk.

**Table 3**

Impact of human papillomavirus (HPV)-positive status and background mortality on the absolute disparity[a], relative disparity[b] and Index of Disparity[c] metrics for females and males under current[d] and expanded[e] coverage rates for the first- (HPV-16/18) and second-generation (9-valent) HPV vaccines

| **Risk of developing HPV-associated cancers** | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | **Base case** | | | **HPV-positive cancers only** | | | **Standardized back mortality** | | |
| **HPV vaccination scenario (female)** | **Absolute Disparity** | **Relative Disparity** | **Index of Disparity** | **Absolute Disparity** | **Relative Disparity** | **Index of Disparity** | **Absolute Disparity** | **Relative Disparity** | **Index of Disparity** |
| No HPV vaccine | 0.80% | 2.0 | 12.5 | 0.70% | 2.0 | 15.8 | 0.67% | 1.7 | 11.5 |
| HPV-16, -18 vaccines (current coverage) | 0.55% | 1.9 | 12.1 | 0.47% | 1.9 | 15.3 | 0.54% | 1.8 | 11.8 |
| HPV-16, -18 vaccines (Tdap coverage) | 0.34% | 1.8 | 12.7 | 0.24% | 1.8 | 20.5 | 0.29% | 1.6 | 12.1 |
| 9-valent HPV vaccine (current coverage) | 0.49% | 1.9 | 12.2 | 0.45% | 2.0 | 14.8 | 0.52% | 1.9 | 12.9 |
| 9-valent HPV vaccine (Tdap coverage) | 0.24% | 1.9 | 12.7 | 0.16% | 2.0 | 21.1 | 0.22% | 1.7 | 12.5 |
| **HPV vaccination scenario (male)** | | | | | | | | | |
| No HPV vaccine | 0.65% | 3.0 | 26.9 | 0.49% | 2.9 | 30.6 | 0.63% | 2.8 | 26.6 |
| HPV-16, -18 vaccines (current coverage) | 0.60% | 2.9 | 26.8 | 0.44% | 2.8 | 31.0 | 0.58% | 2.8 | 26.4 |
| HPV-16, -18 vaccines (Tdap coverage) | 0.37% | 4.0 | 30.6 | 0.13% | 3.4 | 30.7 | 0.43% | 4.3 | 35.8 |
| 9-valent HPV vaccine (current coverage) | 0.59% | 2.9 | 26.9 | 0.44% | 2.8 | 31.0 | 0.57% | 2.8 | 26.5 |
| 9-valent HPV vaccine (Tdap coverage) | 0.33% | 3.9 | 30.7 | 0.09% | 2.9 | 27.1 | 0.39% | 4.2 | 35.9 |
| **Risk of dying from HPV-associated cancers** | | | | | | | | | |
| | **Base case** | | | **HPV-positive cancers only** | | | **Standardized back mortality** | | |
| **HPV vaccination scenario (female)** | **Absolute Disparity** | **Relative Disparity** | **Index of Disparity** | **Absolute Disparity** | **Relative Disparity** | **Index of Disparity** | **Absolute Disparity** | **Relative Disparity** | **Index of Disparity** |
| No HPV vaccine | 0.19% | 2.4 | 20.2 | 0.16% | 2.3 | 22.0 | 0.20% | 2.4 | 22.1 |
| HPV-16, -18 vaccines (current coverage) | 0.15% | 2.5 | 20.9 | 0.12% | 2.5 | 21.5 | 0.17% | 2.5 | 22.9 |
| HPV-16, -18 vaccines (Tdap coverage) | 0.09% | 2.4 | 20.4 | 0.06% | 2.3 | 26.2 | 0.10% | 2.4 | 22.3 |
| 9-valent HPV vaccine (current coverage) | 0.15% | 2.6 | 21.6 | 0.12% | 2.6 | 22.1 | 0.16% | 2.6 | 23.5 |
| 9-valent HPV vaccine (Tdap coverage) | 0.07% | 2.7 | 21.0 | 0.04% | 2.8 | 24.1 | 0.08% | 2.7 | 23.0 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **HPV vaccination scenario (male)** | | | | | | | | | |
| No HPV vaccine | 0.17% | 3.1 | 21.8 | 0.09% | 2.4 | 17.2 | 0.20% | 3.3 | 28.1 |
| HPV-16, -18 vaccines (current coverage) | 0.16% | 3.1 | 23.8 | 0.08% | 2.4 | 19.1 | 0.19% | 3.3 | 29.1 |
| HPV-16, -18 vaccines (Tdap coverage) | 0.13% | 5.1 | 37.5 | 0.05% | 4.4 | 34.3 | 0.16% | 5.5 | 45.7 |
| 9-valent HPV vaccine (current coverage) | 0.16% | 3.1 | 23.8 | 0.08% | 2.4 | 19.5 | 0.19% | 3.3 | 29.0 |
| 9-valent HPV vaccine (Tdap coverage) | 0.12% | 5.1 | 37.8 | 0.03% | 3.3 | 25.4 | 0.14% | 5.5 | 46.0 |

Tdap: Tetanus, diphtheria & acellular pertussis

[a] Absolute disparity = (maximum cumulative lifetime risk-minimum cumulative lifetime risk);

[b] Relative disparity = (maximum cumulative lifetime risk/minimum cumulative lifetime risk);

[c] $ID=(\sum_{j=1}^{j=N}\frac{|r_j-R|}{N})/R\times 100$, where r is the group cumulative lifetime risk and R is the total population cumulative lifetime risk;

[d] "Current coverage" reflects the current level of any HPV vaccine uptake[5];

[e] "Tdap coverage" reflects the current level of the 1-dose Tdap vaccine uptake[5].