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The Estimated Lifetime Probability of Acquiring Human Papillomavirus in the United States

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Abstract

Background: Estimates of the lifetime probability of acquiring human papillomavirus (HPV) can help to quantify HPV incidence, illustrate how common HPV infection is, and highlight the importance of HPV vaccination.

Methods: We developed a simple model, based primarily on the distribution of lifetime numbers of sex partners across the population and the per-partnership probability of acquiring HPV, to estimate the lifetime probability of acquiring HPV in the United States in the time frame before HPV vaccine availability.

Results: We estimated the average lifetime probability of acquiring HPV among those with at least 1 opposite sex partner to be 84.6% (range, 53.6%–95.0%) for women and 91.3% (range, 69.5–97.7%) for men. Under base case assumptions, more than 80% of women and men acquire HPV by age 45 years.

Conclusions: Our results are consistent with estimates in the existing literature suggesting a high lifetime probability of HPV acquisition and are supported by cohort studies showing high cumulative HPV incidence over a relatively short period, such as 3 to 5 years.

Estimates of the lifetime probability of acquiring human papillomavirus (HPV) can help to quantify HPV incidence, illustrate how common HPV infection is, and highlight the importance of HPV vaccination. Because no study has ever followed a birth cohort for an entire lifetime to estimate cumulative incidence of HPV infection, the lifetime probability of acquiring HPV can only be estimated based on available evidence. We sought to provide an estimate of the average lifetime probability of acquiring HPV in the United States in the prevaccine era, using a model based primarily on the lifetime number of opposite sex partners and the per-partnership probability of HPV acquisition.

MATERIALS AND METHODS

To estimate the lifetime probability of acquiring HPV, we estimated the probability of acquiring HPV over 2 phases of the lifetime: from sexual debut through age 44 years and

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from age 45 years through age 70 years. The probability of HPV acquisition in the first phase (from the onset of the first sex partnership through age 44 years) was calculated based on the lifetime number of sex partners (for vaginal, oral, or anal sex) through age 44 years and the per-partnership probability of HPV acquisition. The probability of HPV acquisition in the second phase was calculated using estimates of the annual probability of HPV acquisition. We used these 2 phases because age 44 years is the oldest age at which nationally representative data on lifetime number of sex partners are available from the National Survey of Family Growth (NSFG).[1] Those with no opposite-sex partners through age 44 years (approximately 1% of the population) were excluded from the analysis.

HPV Acquisition Through Age 44 Years

We estimated the probability of acquiring HPV through age 44 years for each of 5 lifetime partner groups (Table 1), using data from men and women aged 40 to 44 years in the 2006–2008 NSFG.[1] To account for heterogeneity in the length of partnerships, we classified partnerships as either primary or secondary (Table 1). The per-partnership HPV acquisition probability for a primary partnership (49.1%; range, 35.8%–64.2%) was based on cumulative 3-year HPV incidence observed among young women with 1 male partner for vaginal sex.[2] The per-partnership HPV acquisition probability for a secondary partnership (28.5%; range, 20.6%–38.6%) was based on cumulative 1-year HPV incidence observed among young women with 1 male partner for vaginal sex.[2] We assumed that the per-partnership HPV acquisition probabilities were the same for men as for women. Those with 1 lifetime sex partner through age 44 years were assumed to have 1 primary partner and no secondary partners. Those with at least 2 lifetime sex partners through age 44 years were assumed to have exactly 2 primary partners; all other partners (if any) were considered secondary.

HPV Acquisition From Ages 45 to 70 Years

The annual probabilities of acquiring HPV were calculated as follows. First, we assumed that the average annual probability of acquiring HPV across all 5 lifetime partner groups was 2.2% (range, 1.0%–3.3%) for ages 45 to 49 years and 1.4% (range, 0.5%–2.2%) for ages 50 years and beyond, based on the values applied in 2 cervical cancer screening models.[3,4] Second, to account for heterogeneity in lifetime risk behavior, we assumed that the annual probability of HPV acquisition among those in groups 4 and 5 would be 5.1 times that of those in groups 1, 2, and 3. This 5.1 ratio is the annual HPV incidence rate ratio reported among women with 5 or more lifetime partners (vs. those with fewer than 5 lifetime partners) in a recent study of sexual behavior and HPV incidence in older women.[5]

Under these assumptions, the annual probability of acquiring HPV for ages 45 to 49 years was 1.1% for groups 1, 2, and 3 and 5.4% for groups 4 and 5. These values (1.1% and 5.4%) yield an average annual probability of 2.2% [(73.9% × 1.1%) + (26.1% 5.4%) = 2.2%, where 73.9% is the percent of women in groups 1, 2, and 3 and 26.1% is the percent of women in groups 4 and 5] and a rate ratio of approximately 5.1 [(5.4/ 1.1) = 4.9, which differs from 5.1 because of rounding of the annual probabilities]. The values for the annual probability of acquiring HPV for ages 50 to 70 years (0.7% and 3.5%) were calculated in an analogous manner, such that they yielded an average annual probability of 1.4% and a rate

ratio of approximately 5.1. As with the per-partnership probabilities we applied, we assumed that the annual probabilities of acquiring HPV were the same for men as for women.

Calculation of Lifetime Probability of Acquiring HPV Through Age 70 Years

The probability of acquiring HPV through age 70 years was calculated as 1 minus the probability of not acquiring HPV. For each lifetime partner group, we calculated the probability of not acquiring HPV through age 70 years as the product of the probability of not acquiring HPV over the lifetime of sex partners through age 44 years (using the per-partnership probabilities of HPV acquisition) and the probability of not acquiring HPV from ages 45 to 70 years (using the annual probabilities of HPV acquisition). For example, for group 1, the cumulative probability of acquiring HPV was calculated as $1 – (1 – 0.49)\ (1 – 0.011)^{[5]}(1 – 0.007)^{[21]}$, where 0.49 is the probability of acquiring HPV from their 1 sex partner through age 44 years, 0.011 is the annual probability of acquiring HPV over the 5-year period from ages 45 to 49 years, and 0.007 is the annual probability of acquiring HPV over the 21-year period from ages 50 to 70 years (Table 1). The cumulative probability of acquiring HPV for Groups 2 to 5 was calculated in an analogous manner.

In June 2006, quadrivalent HPV vaccine was licensed for use among females aged 9 to 26 years,[6] and the studies that inform our assumptions include data obtained in the time frame before HPV vaccine availability. Thus, our lifetime probability estimates can be thought of as the approximate cumulative lifetime probability of acquiring HPV in the United States before the onset of HPV vaccination.

Sensitivity Analyses (1-Way and Multiway)

We first performed 1-way sensitivity analyses in which each of the following parameter groups was varied one at a time to their lower and upper bound values, holding all other parameter values at their base case value: the per-partnership probability of HPV acquisition, the annual probability of HPV acquisition, the distribution of the population across the 5 lifetime partner groups, the number of lifetime partners, and the number of lifetime partners classified as primary partnerships.

In the base case, the per-partnership HPV acquisition probabilities we applied did not vary across the 5 lifetime partner groups. We performed an additional 1-way sensitivity analysis in which the per-partnership probabilities of HPV acquisition for groups 1 and 2 were reduced by 50% to account for possibility that HPV prevalence in the partner pool of those in groups 1 and 2 might be lower than HPV prevalence in the partner pool of those in groups 3 to 5.

We performed another 1-way sensitivity analysis in which we allowed for the possibility of HPV acquisition from mechanisms other than sexual intercourse. Transmission by other types of genital contact other than intercourse occurs but is less common.[7–9] To account for this possibility, we examined a ‘‘nonintercourse acquisition’’ scenario in which an additional lifetime risk of non-intercourse acquisition of HPV of 8.0% was applied for everyone regardless of lifetime partner group.[8,9]

We also conducted multiway sensitivity analyses, in which all of the parameter values that we varied in the 1-way sensitivity analyses were varied simultaneously. Specifically, we found the minimum and maximum values of the lifetime probability of acquiring HPV that could be obtained when all parameters were set to their lower or upper bound values.

RESULTS

Under base case assumptions, the average lifetime probability of acquiring HPV was 84.6% for women and 91.3% for men (Table 2). This probability ranged from 58.4% for those in lifetime partner group 1 (1 partner through age 44 years) to 100% (when rounded to nearest 0.1%) for those in lifetime partner group 5 (15 or more partners through age 44 years). For each lifetime partner group, most of the lifetime probability of acquiring HPV was attributable to acquisition of HPV through age 44 years. Under base case assumptions, more than 80% of women and men acquire HPV by age 45 years.

In sensitivity analyses, the average lifetime probability of acquiring HPV ranged from 76.5% to 91.0% for women and 85.9% to 95.2% for men when varying one assumption at a time (Table 3). The most influential assumptions were those regarding the probability of HPV acquisition per partnership (up to age 44 years), the annual probability of HPV acquisition (ages 45–70 years), and allowing for lower per-partnership HPV acquisition probabilities among groups 1 and 2 (the ‘‘low-risk group adjustment’’ scenario). When varying all assumptions simultaneously, the average lifetime probability of HPV acquisition ranged from 53.6% to 95.0% for women and 69.5% to 97.7% for men (Table 3). These values for women and men reflect the weighted average across the 5 lifetime partner groups. When varying all assumptions simultaneously, the lifetime probability of acquiring HPV ranged from 23.2% to 75.9% for group 1 (1 partner through age 44 years) and from 98.3% to 100% for group 5 (Q15 partners through age 44 years).

DISCUSSION

Our estimates of the lifetime probability of acquiring HPV are consistent with those in the existing literature, which typically range from at least 50% to almost 100%.[10–13] Our lower bound estimates (53.6% for women and 69.5% for men) support the more conservative estimate that at least half of sexually active adults will acquire HPV in their lifetime, and our upper bound estimates (95.0% for women and 97.7% for men) are consistent with the claim that nearly all sexually active adults will acquire HPV at some point in their lifetimes. Our results are also consistent with seroprevalence data from the National Health and Nutrition Examination Survey 2003–2004, in which seroprevalence of the quadrivalent HPV vaccine types (6, 11, 16, 18) was 42% among women aged 30 to 39 years.[14] Because an estimated 60% of women develop antibodies after infection,[15] seroprevalence of 42% reflects cumulative exposure as high as 70%.[14] The estimate of 70% cumulative acquisition of HPV types 6/11/16/18 among women through age 40 years based on the National Health and Nutrition Examination Survey data supports our model-based estimate of 81% cumulative incidence of any HPV type among women through age 44 years.

Commonly cited sources for estimates of the lifetime probability of acquiring HPV are cohort analyses showing a high cumulative incidence of HPV over a relatively brief period of time, such as studies reviewed by Baseman and Koutsky,[16] showing 60% cumulative 5-year incidence among young women in the United Kingdom[17] and cumulative 3-year incidence rates in excess of 40% among college women in the United States.[7,18] Another method to estimate lifetime HPV acquisition has been to calculate the cumulative incidence over time based on the annual probability of HPVacquisition. For example, Myers et al.[4] provide age-specific annual probabilities of acquiring HPV, which when extrapolated yield a high cumulative lifetime incidence of HPV among sexually active men and women,[19] such as 80% through age 50 years.[12] A strength of using annual, age-specific probabilities of acquiring HPV to estimate the lifetime probability of acquiring HPV is that these probabilities can be obtained from models of cervical cancer screening[3,4] which have been calibrated to match relevant epidemiological data. A weakness of this approach is that it applies the same annual, age-specific probabilities of acquiring HPV to everyone, thereby ignoring the substantial heterogeneity in sexual behavior across the population. A main contribution of our study was to account for heterogeneity in sexual behavior by stratifying according to the lifetime number of sex partners and using per-partnership HPV acquisition probabilities.

Our analysis is subject to limitations. Our calculations are illustrative in nature and intended to supplement existing estimates of the lifetime probability of acquiring HPV.[10–13] Estimating the probability of acquiring HPV from sexual debut through age 70 years required the use of cross-sectional data, drawn across various ages, birth cohorts, and time frames. Owing to data limitations, we were unable to perform separate analyses for low-risk HPV types (e.g., 6 and 11) and high-risk HPV types (e.g., 16 and 18). There is uncertainty in the assumptions we applied. For example, the per-partnership probability of acquiring HPV depends on the HPV status of the partner as well as the duration of the partnership,[20] which can influence the number of sex acts and type(s) of sex acts within the partnership. We note, however, that the 28.5% base case value we applied for the HPV acquisition probability per secondary partnership is consistent with the 25.5% probability that results when multiplying a recent estimate of HPV prevalence among females aged 14 to 59 years (42.5%)[21] by estimates of the per-partnership probability of HPV transmission (60%).[22,23] We did not explicitly model the mixing of sex partners. If lower-risk women are more likely to have partnerships with lower-risk men than would be expected if mixing were random (i.e., ‘‘assortative mixing’’),[24] we may have overestimated the lifetime probability of HPV acquisition among the lower-risk groups (e.g., groups 1 and 2). We addressed this limitation by applying lower per-partnership HPV acquisition probabilities for groups 1 and 2 in the sensitivity analyses. We assumed that males and females had the same HPV acquisition probabilities (per-partnership and annual), although the probabilities we applied were based on studies of HPV acquisition among females.[2–5] This simplifying assumption is supported by a recent study that reported HPV incidence rates in men to be comparable with incidence rates reported for women,[25] although there is also evidence to suggest that HPV transmission probabilities might vary by sex.[26] To account for this uncertainty, the sensitivity analyses we performed were stratified by sex to illustrate how the lifetime probability of HPV acquisition might change for women and men when assuming lower or

higher sex-specific probabilities of HPV acquisition. The lifetime number of sex partners we applied was based on NSFG reports of number of partners for vaginal, oral, or anal sex, whereas the per-partnership probabilities we applied for HPV acquisition were based on studies of women with vaginal sex partners. We did not include those who reported no lifetime opposite sex partners through age 44 years. We interpret our results as being most applicable to heterosexual men and women, although we were unable to limit the analyses to those who were exclusively heterosexual. We did not attempt to estimate the lifetime probability of HPV acquisition specifically for men who have sex with men or women who have sex with women, owing to data limitations. However, HPV is common in both of these groups, particularly in men who have sex with men who bear a disproportionate share of the burden of HPV-associated diseases in men.[27–30]

Our study provides insights into the lifetime probability of acquiring HPV. Our results are consistent with published estimates in which 50% to 100% of sexually active men and women will acquire HPV in their lifetime and are supported by cohort studies showing high cumulative HPV incidence after relatively short follow-up intervals.[7,16–18,31] Our results also highlight the importance of HPV vaccination as a tool to reduce the potential burden of HPV. In fact, the high probability of HPV acquisition within several years of sexual debut was cited by the Advisory Committee on Immunization Practices as part of the rationale for the recommendation for routine HPV vaccination at ages 11 to 12 years in the United States.[6] As HPV vaccine coverage increases in the population over time, the lifetime probability of acquiring HPV vaccine types should decrease due to direct effects among those vaccinated as well as indirect effects (‘‘herd effects’’) due to decreased prevalence of HPV in the population.[32,33]

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TABLE 1.

Key Model Assumptions: Distribution of Population Across 5 Lifetime Sex Partner Groups, Per-Partnership Probabilities of HPV Acquisition Through Age 44 Years, and Annual Probabilities of HPV Acquisition From Ages 45 to 70 Years

Model Assumption	Group 1: 1 partner	Group 2: 2 partners	Group 3: 3–6 partners	Group 4: 7–14 partners	Group 5: 15+ partners
Percent of women in each group[1]	22.5 (17.4–27.6)	10.8 (7.1–14.6)	40.6 (35.3–46.0)	18.1 (15.7–20.4)	8.0 (7.0–9.1)
Percent of men in each group[1]	10.4 (7.1–13.8)	7.3 (4.9–9.6)	30.1 (28.0–32.1)	21.9 (20.4–23.4)	30.4 (28.3–32.5)
Per-partnership probability (%) of HPV acquisition through age 44 y[2]			Groups 1–5		
Primary partnership(s)			49.1 (35.8–64.2)		
Secondary partnership(s)			28.5 (20.6–38.6)		
Annual probability (%) of HPV acquisition[3–5]		Groups 1–3		Groups 4–5	
Ages 45–49 y		1.1 (0.5–1.6)		5.4 (2.5–8.1)	
Ages 50–70 y		0.7 (0.2–1.1)		3.5 (1.2–5.4)	

All values are in percent. Base case values are shown first with ranges shown in parentheses. The 5 lifetime partner groups refer to the number of lifetime partners through age 44 years. We used the per-partnership probabilities to calculate the cumulative probability of acquiring HPV from sexual debut through age 44 years, and we used the annual probabilities of acquiring HPV to calculate the cumulative probability of acquiring HPV from ages 45 years through age 70 years. The lifetime partner data we used were reported for 6 categories: 0, 1, 2, 3–6, 7–14, and 15 or more opposite-sex partners (oral, anal, or vaginal sex).

[1]We excluded those who reported 0 lifetime sex partners, leaving 5 lifetime partner groups in our analysis. The base case number of partners in each group was 1 for group 1, 2 for group 2, 4.5 for group 3, 10.5 for group 4, and 20 for group 5. The ranges of the percent of the population in each lifetime partner group were based on approximate 95% confidence intervals for groups 1 and 2 and calculated for the other groups as follows. To ensure that these percentages summed to 1 in the sensitivity analyses, we calculated ranges for groups 3, 4, and 5 so that the percentages of the population across all 5 lifetime partner groups would sum to 1 when applying the lower bound values for groups 1 and 2 and the upper bound values for groups 3, 4 and 5 (and when applying the upper bound values for groups 1 and 2 and the lower bound values for groups 3, 4, and 5). As described in the text, the per-partnership probabilities of HPV acquisition were based on a study of HPV acquisition after onset of sexual activity with one male partner.

[2]The average annual probabilities of acquiring HPV were based on values applied in cervical cancer screening models,[3–4] adjusted to account for heterogeneity in lifetime risk behavior,[5] as described in the text.

TABLE 2.

Model Results: Estimates of the Probability (%) of Acquiring HPV From Sexual Debut Through Age 44 Years, From Age 45 Years Through Age 70 Years, and From Sexual Debut to Age 70 Years

Time Frame	Group 1: 1 partner	Group 2: 2 partners	Group 3: 3–6 partners	Group 4: 7–14 partners	Group 5: 15+ partners	Average (Women)*	Average (Men)*
Sexual debut to age 44 y	49.1	74.1	88.8	98.5	99.9	80.9	89.1
Ages 45 to 70 y†	18.4	18.4	18.4	64.1	64.1	30.3	42.3
Sexual debut to age 70 y	58.4	78.8	90.9	99.5	100	84.6	91.3

The 5 lifetime partner groups refer to the number of lifetime partners through age 44 years.

*The average lifetime probability of HPV acquisition differs for women and men because of different assumptions about the distribution of the male and female populations across the 5 lifetime partner groups (Table 1). All other assumptions (e.g., HPV acquisition probabilities per partnership) were the same for women and men.

†The probability of acquiring HPV from age 45 years through age 70 years applies to those who did not acquire HPV from sexual debut through age 44 years.

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TABLE 3.

Sensitivity Analyses: Cumulative Probability (%) of Acquiring HPV From Sexual Debut to Age 70 Years When Varying 1 or More Model Assumptions

Assumption Varied	Group 1: 1 partner	Group 2: 2 partners	Group 3: 3–6 partners	Group 4: 7–14 partners	Group 5: 15+ partners	Average (Women)	Average (Men)
None (base case)	58.4	78.8	90.9	99.5	100	84.6	91.3
No. lifetime partners	58.4–58.4	78.8–78.8	84.9–94.5	98.3–99.8	99.9–100	81.9–86.1	89.2–92.4
Per-partner HPV acquisition	47.6–70.8	66.3–89.5	81.1–96.9	97.9–99.9	99.8–100	76.5–91.0	85.9–95.2
Annual HPV acquisition	52.4–62.8	75.8–81.1	89.5–91.8	99.0–99.7	100–100	82.2–86.2	89.9–92.2
No. primary partnerships	58.4–58.4	70.3–78.8	87.2–95.4	99.2–99.7	100–100	82.1–86.4	89.5–92.7
Nonintercourse acquisition *	61.8	80.5	91.6	99.5	100	85.8	92.0
Low-risk group adjustment †	38.4	53.5	90.9	99.5	100	77.3	87.3
Multiple assumptions varied ‡	23.2–75.9	31.1–91.4	62.2–99.6	89.0–100	98.3–100	53.6–95.0	69.5–97.7

* In the nonintercourse acquisition scenario, an additional lifetime risk of acquisition of HPVof 8.0% was applied for everyone regardless of lifetime partner group to account for mechanisms of HPV acquisition other than sexual intercourse.

† In the low-risk group adjustment, the per-partnership probabilities of HPV acquisition were reduced by 50% for groups 1 and 2.

‡ The lowest values (53.6% for women and 69.5% for men) were obtained when applying the lower bound value for the following: the number of lifetime partners; the percent of the population in groups 3, 4, and 5; the probability of HPV acquisition per partnership (along with the additional low-risk group adjustment described above); the annual probability of HPV acquisition; and the number of primary partnerships per person. The highest values (95.0% for women and 97.7% for men) were obtained when applying the upper bound values for these assumptions and when assuming an additional lifetime risk of nonsexual acquisition of HPV of 8.0% for everyone.

The 5 lifetime partner groups refer to the number of lifetime partners through age 44 years. The number of lifetime partners was set at 1 for group 1 and 2 for group 2, and varied from 3 to 6 for group 3, from 7 to 14 for group 4, and from 15 to 30 for group 5. The per-partnership probability of acquiring HPV (used to estimate HPV acquisition through age 44 years) and the annual probability of HPV acquisition (used to estimate HPV acquisition from age 45 to age 70 years) were varied according to the ranges shown in Table 1. The number of primary partnerships per person was used to determine the maximum number of partnerships subject to the higher ‘‘primary partnership’’ probability and did not affect the lifetime number of partners. The maximum number of partnerships subject to the primary partnership probability was 2 in the base case and was varied from 1 to 4. For example, when the number of primary partnerships was set to 1, all groups had exactly 1 partnership subject to the primary partnership probability, and all other partnerships (if any) were subject to the secondary partnership probability. When the number of primary partnerships was set to 2, group 1 had 1 partnership subject to the primary partnership probability, all other groups had exactly 2 partnerships subject to the primary partnership probability, and all other partnerships (if any) were subject to the secondary partnership probability. When applying the lower (and upper) bound values for the percent of the population in groups 1 and 2 and the upper (and lower) bound values for the percent of the population in groups 3, 4, and 5, the lifetime probability of HPV acquisition ranged from 82.2% to 87.0% for women and from 89.6% to 92.9% for men (not shown).