Published in final edited form as:

Vaccine. 2013 June 24; 31(29): 3019–3024. doi:10.1016/j.vaccine.2013.04.051.

Modeling the impact of quadrivalent HPV vaccination on the incidence of Pap test abnormalities in the United States

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Abstract

Background—We present data on Pap test results and HPV prevalence from the HPV Sentinel Surveillance project, a multiyear surveillance project enrolling women from a diverse set of 26 clinics throughout the US from 2003 to 2005. We use mathematical modeling to illustrate the potential timing and magnitude of decreases in Pap test abnormalities in sexually transmitted disease (STD), family planning, and primary care clinics in the US as a result of HPV vaccination.

Methods—The probability of an abnormal Pap result was based on three factors: (1) infection with HPV 16/18, or both; (2) infection with high-risk HPV types other than HPV 16/18; and (3) infection with HPV 6/11, or both. We estimated the relative reduction in the probability of an abnormal Pap result over the first 25 years of a female-only, quadrivalent HPV vaccination program, compared to a scenario of no HPV vaccination in which the probability of abnormal Pap results was assumed constant.

Results—The probability of an abnormal Pap result ranged from 7.0% for the lowest risk group (those without any high-risk HPV types and without HPV 6/11) to 45.2% for the highest risk group (those with HPV 16/18 and at least one other high-risk HPV type). Estimated reductions in abnormal Pap results among women in the 21- to 29-year age group were 0.8%, 10.2%, and 11.3%

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Conflicts of interest statement: Consultancies: M. Hagensee (Merck); Grants received: L. Koutsky (Merck).

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.vaccine.2013.04.051>.

in years 5, 15, and 25 of the vaccine program respectively, in the lower vaccine coverage scenario, and 7.4%, 21.4%, and 22.2%, respectively, in the higher coverage scenario.

Conclusions—Our results suggest that HPV vaccination will have a discernable impact on the probability of Pap abnormalities, but the timing and magnitude of the reduction will depend substantially on vaccine coverage and the degree of cross-protection against high risk HPV types other than HPV 16/18.

Keywords

HPV; HPV vaccine; Papanicolaou test; Vaccination effects

1. Background

HPV vaccination can reduce the substantial health and economic burden of HPV-associated health outcomes. Accordingly, numerous modeling studies have suggested that vaccinating 12-year-old girls in the United States is a cost-effective use of public health resources [1-8]. These and other modeling studies have quantified the potential reduction in HPV-associated health outcomes such as cervical intraepithelial neoplasia (CIN), cervical and other cancers, genital warts, and recurrent respiratory papillomatosis that can be achieved through HPV vaccination [1-3,5-7,9]. In contrast to these health outcomes, however, relatively few estimates are available regarding the impact of HPV vaccination on the incidence of abnormal Papanicolaou (Pap) test results in the United States. Abnormal Pap results impose a substantial health and psychosocial burden [10], and the follow-up costs of abnormal Pap results can exceed \$1 billion each year in the United States [11,12].

Mathematical modeling using baseline data on HPV prevalence and Pap test abnormalities among cervical screening populations can help to estimate the potential timing and magnitude of decreases in Pap test abnormalities as a result of HPV vaccination. In this study, we present data on Pap test results and HPV prevalence from the HPV Sentinel Surveillance (HSS) project [13]. Using the HSS data on the probability of abnormal Pap results based on HPV infection status, we created a simple model of the potential impact of quadrivalent HPV vaccination on the probability of Pap test abnormalities among attendees of STD clinics, family planning clinics, and primary care clinics in six US locations.

2. Methods

2.1. Overview of the model

We estimated the relative reduction in the probability of an abnormal Pap result over the first 25 years of a female-only, quadrivalent (Gardasil®, Merck & Co., Inc.) HPV vaccination program, compared to a scenario of no HPV vaccination in which we assumed the probability of an abnormal Pap result would remain constant. We estimated only the direct effects of vaccination among those vaccinated; indirect effects (herd immunity) were not addressed in our model. We examined changes in the probability of an abnormal Pap result for two age groups (21–29 years and 30–39 years). In each year, a new cohort of 12-year-olds would enter the model and a cohort of 40-year-olds would exit the model. Thus,

the composition of the 21- to 29-year age group and the 30- to 39-year age group changed over time as well.

The probability of an abnormal Pap result was based on three factors: (1) infection with HPV 16 and/or 18; (2) infection with a high-risk HPV type other than 16/18 (e.g., 31 or 45); and (3) infection with HPV 6 and/or 11. Eight risk groups were defined based on the possible combinations of these three factors, and a probability of an abnormal Pap test was assigned to each group (Fig. 1). We did not explicitly model the impact of low-risk HPV types other than HPV 6 and 11. To do so would have required us to double the number of HPV risk groups in our model from 8 to 16, and our sample size precluded us from obtaining reliable estimates of the probability of an abnormal Pap result for 16 HPV risk groups. Instead, the influence of low-risk HPV types other than HPV 6 and 11 is reflected in the probability of an abnormal Pap test we assigned to each group.

We estimated how HPV vaccination might change the population distribution across these eight risk groups, by reducing the percentage of women infected with HPV 16/18, HPV 6/11, and, in the scenario of cross-protection, other high-risk HPV types. That is, the impact of HPV vaccination on the probability of an abnormal Pap result was calculated based on the probability of an abnormal Pap result for each of the eight groups and the changing distribution of the population across the eight risk groups as a result of vaccination.

2.2. Pap test and HPV prevalence data

The probability of an abnormal Pap result was based on data on prevalence of HPV types and Pap test abnormalities among participants of the HSS study, 2003–2005 (Table 1). The HSS study has been described in more detail elsewhere [13,14]. Briefly, the HSS study enrolled 10,208 women aged 14–65 years from 26 venues in 6 US sites from January 2003 to December 2005. The six sites were Boston and other locations in Massachusetts; Baltimore, Maryland; New Orleans, Louisiana; Denver, Colorado; Seattle, Washington; and Los Angeles, California. The venues from which women were recruited included STD clinics, family planning clinics, and primary care clinics. Women were invited to enroll if they were eligible for a routine cervical cancer screening test. The HSS study protocol was reviewed and approved by human subjects committees at local institutions and at the Centers for Disease Control and Prevention (CDC). Written informed consent was provided by all women prior to participation in the HSS study.

In this analysis, we used data from 8815 specimens in the HSS study from women aged 14 to 49 years and for which information was available regarding Pap test results and type-specific, cervical HPV prevalence (which was assessed using samples obtained at the same visit as the Pap test). HSS had a total of 10,208 records from women aged 14 to 65 years from STD, family planning and primary care clinics. Per protocol, and to ensure that each Pap test was part of routine screening, no records were from women presenting for follow-up Pap tests and all repeat visits were at least 1 year apart; most women (96.0%) with repeat visits had only 2 visits. Of the total 10,208 HSS records, 9624 were from women aged 14 to 49 years; of these, 9126 (94.8%) records had valid cervical HPV PCR results and 8815 (91.6%) also had a valid, non-missing Pap test result. Of the 8815 records with valid cervical HPV PCR and valid Pap test results, 6.4% were from women with repeat visits.

Abnormal Pap results were defined as any of the following outcomes: atypical squamous cells of undetermined significance (ASC-US); atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesion (ASC-H); low-grade squamous intraepithelial lesion (LSIL); high-grade squamous intraepithelial lesion (HSIL); atypical glandular cells (AGC); and adenocarcinoma in situ (AIS). For each of the eight HPV groups, we calculated the probability of an abnormal Pap result as the number of abnormal Pap results in each HPV group divided by the number of total Pap tests in each HPV group. When doing so, we combined groups 1 and 2 and we combined groups 3 and 4, owing to the small sample size in group 1 and group 3 (Table 1).

2.3. Vaccine coverage assumptions

We examined three vaccine coverage scenarios: lower, intermediate, and higher. The probability of initiating the vaccine series in the lower, intermediate, and higher coverage scenarios, respectively, was: 0.20, 0.28, and 0.70 (age 12 years), 0.10, 0.17, and 0.60 (ages 13–18 years), and 0.01, 0.02, and 0.35 (ages 19–26 years). These annual probabilities for the lower and intermediate scenarios were selected so that vaccine coverage in our model would be consistent with estimates of HPV vaccine coverage in the US from the National Immunization Survey-Teen [15]. Specifically, using the annual probabilities of vaccination described above, coverage of 13- to 17-year olds in year 5 of the vaccine program would be about 35% in the lower coverage scenario, which is consistent with estimated 3-dose coverage of 32% among 13- to 17-year old females in the US through 2010 [15]. Similarly, coverage of 13- to 17-year olds in year 5 of the vaccine program would be about 50% in the intermediate scenario, which is consistent with the estimate that 49% of 13- to 17-year old females in the US had initiated the HPV vaccine through 2010 [15]. The annual probabilities of receiving vaccination in the higher coverage scenario are arbitrary and were selected to illustrate the potential impact of vaccination if the US were able to exceed 70% coverage in the targeted age groups.

2.4. Vaccine efficacy assumptions

We assumed that vaccine protection would not wane over time. For those vaccinated prior to HPV exposure to the vaccine types, we assumed vaccine efficacy of 96% (range: 75–100%). This efficacy assumption was based on reported quadrivalent vaccine efficacy of 95.9% (range: 75.1–99.9%) in reducing the incidence of any abnormal Pap test associated with HPV 6, 11, 16 and 18 among those aged 24–34 years [16].

To account for potential cross-protection, we assumed that vaccination prior to HPV exposure would provide 15% protection (range: 0–30%) against abnormal Pap results attributable to high-risk HPV types other than HPV 16 and 18. This 15% estimate was based on reported quadrivalent vaccine efficacy against CIN 1–3 or adenocarcinoma in situ due to 10 high risk HPV types (31, 33, 35, 39, 45, 51, 52, 56, 58, or 59) of 23.4% [17], which we multiplied by 0.64, the approximate contribution of these 10 types to the overall prevalence of high risk HPV types (other than 16 and 18) in the HSS study [14].

We assumed that all 12-year-olds were naïve to all HPV types. To account for HPV acquisition prior to HPV vaccination for those vaccinated between ages 13 and 26 years, we

adjusted the efficacy of vaccination using age-specific efficacy-adjustment factors (see supplemental appendix). These age-specific adjustment factors took into account cumulative HPV exposure by the age at vaccination as well as cumulative HPV exposure through age 30 years. For example, vaccine efficacy against HPV 6/11 was reduced by about 30% for females vaccinated at age 17 years, because about 30% of the women who would have eventually been infected with HPV 6/11 by age 30 years were already infected with HPV 6/11 at age 17 years. Our approach of adjusting vaccine efficacy by age at vaccination to account for previous exposure is comparable to that of Cuzick et al. [18].

2.5. Reductions in Pap test abnormalities in three venues

Potential reductions in Pap test abnormalities were calculated separately for attendees of STD clinics, family planning clinics, and primary care clinics. To do so, we applied venue-specific estimates of the percentage of attendees in each HPV group to account for differences in HPV prevalence across the venues (Table 1). These distributions were obtained from the HSS study and reflect the actual distributions of study participants across the eight HPV groups, stratified by age group and by the type of venue attended.

2.6. Sensitivity analyses

We performed a range of sensitivity analyses to examine how the results changed when we varied key assumptions in the model. First, we conducted “one-way” sensitivity analyses in which we examined the reduction in abnormal Pap results under the intermediate coverage scenario when varying one of the following parameters at a time: vaccine efficacy against HPV vaccine types (75–100%), cross-protection efficacy (0–30%), the HPV group-specific probabilities of an abnormal Pap test (Table 1), the percentage of clinic attendees in each HPV group (Table 1), and the efficacy-adjustment factors to account for HPV exposure prior to vaccination (see supplement). Second, we conducted “multi-way” sensitivity analyses in which we simultaneously varied all of the parameters described above for the one-way sensitivity analyses for both the lower and higher coverage scenarios.

3. Results

In the intermediate coverage scenario, HPV vaccination reduced the probability of abnormal Pap results across all clinic types by 15.4% and 7.5% for ages 21–29 years and for ages 30–39 years, respectively, 25 years after introduction of HPV vaccination (Table 2, and Figs. 2 and 3). These results reflect the estimated reduction in the probability of an abnormal Pap result per Pap test conducted, assuming cervical screening practices remain constant over time. These reductions were 14.2% and 1.1% for ages 21–29 years and ages 30–39 years, respectively, after 15 years of vaccination, and 1.5% and 0.0%, respectively, after 5 years of vaccination.

In the sensitivity analyses, when varying one parameter at a time, cross protection efficacy was the most influential parameter (Table 3). When varying all parameters simultaneously (including coverage), estimated reductions in abnormal Pap results in year 25 of the vaccine program ranged from 4.4% to 32.8% for ages 21–29 years and from 1.3% to 21.0% for ages 30–39 years.

4. Discussion

Abnormal Pap results impose substantial psychosocial and economic costs and represent an important component of the overall health and economic burden of HPV in the US [10-12,19,20]. Our model suggests that HPV vaccination will have a discernable impact on the incidence of abnormal Pap results, but the timing and magnitude of the reduction will depend substantially on vaccine coverage. Further, the reduction in abnormal Pap results will be more pronounced among women aged 21–29 years than among women aged 30–39 years. Our results were not overly sensitive to any particular parameter value except for vaccine coverage and the degree of cross-protection. However, because vaccine coverage is an important factor, vaccine efficacy among those with 1 dose will also be an important determinant of the timing and magnitude of the impact of vaccination on abnormal Pap results. Because our lower coverage scenario is consistent with current three-dose coverage in the US through 2010 [15], the lower coverage scenario would be the most applicable coverage scenario if all three vaccine doses are needed to achieve high efficacy and long duration of protection. In contrast, our intermediate coverage scenario is consistent with coverage of 1 dose in the US through 2010 [15] and might be the most applicable coverage scenario if high vaccine efficacy can be obtained with less than three doses [21,22].

Cuzick et al. [18] predicted long-term reductions in abnormal Pap results of 21–34% in women aged 21–29 years in the UK under the assumption of 80% coverage [18]. In our higher coverage scenario (the most comparable of our coverage scenarios to the 80% coverage applied by Cuzick et al.), we estimated long-term reductions in abnormal Pap results among women aged 21–29 years of 22.2%. Bogaards et al. predicted long-term reductions in the abnormal cytology rate among women aged 30–60 years of about 20% at 50% vaccine coverage and about 33% at 90% vaccine coverage [23]. Although these predicted decreases are more pronounced than those of our model, the model of Bogaards et al. includes indirect effects (herd immunity) and our model does not. Our results are also consistent with the estimates of Schiffman, who predicted reductions in abnormal Pap results of 20% if HPV types 16 and 18 were eliminated from the population [24]. Although cervical cancer screening will still be of critical importance after onset of HPV vaccination, secondary screening strategies can potentially be modified over time to become more effective and cost-effective in vaccinated populations [18,23,24].

The relative impact of HPV vaccination on abnormal Pap results is notably less than predicted for cervical cancer, for which reductions of 70% or greater have been estimated for high vaccine coverage scenarios (70% or higher) [2,3,5,18,25]. The reason for this difference in relative impact is that a high percentage of cervical cancer (about 70%) is attributable to HPV vaccine types 16 and 18, whereas these HPV vaccine types account for a much lower percentage of abnormal Pap results [18,24,26]. Of note, among the women included in this analysis, women without any of the HPV vaccine-preventable types 6, 11, 16 or 18 accounted for about 68% of the abnormal Pap results among women 21–29 years old and about 88% of the abnormal Pap results among women 30–39 years old.

Our study is subject to limitations. First, we estimated only the direct impact of vaccination. That is, we assessed only the effect conferred on women vaccinated, without considering the

potential benefits of “herd immunity.” Second, because data for our model came primarily from the HSS study, our results might not be generalizable to women in other settings. Third, the probabilities of abnormal Pap results we applied were based on screening practices at the time of the HSS study. We did not account for any changes over time in factors associated with cervical cancer screening [27]. Fourth, we were unable to obtain reliable estimates of the probability of an abnormal Pap result for HPV group 1 and HPV group 3 separately because of the limited number of women in these two groups. Similarly, sample size issues prevented us from assessing venue-specific probabilities of abnormal Paps (e.g., for STD clinics, family planning clinics, and primary care clinics). Fifth, we did not explicitly model the impact of low-risk HPV types other than HPV 6 and 11 on Pap abnormalities, although the influence of these other low-risk types was reflected in the probabilities we assigned to each of the HPV risk groups, as all eight groups included women with and without these other low-risk HPV types. Sixth, cross-protection efficacy was approximated using an average level of protection across all high risk HPV types other than HPV 16 and 18, rather than applying type-specific efficacy values. Finally, we assumed that the probability of an abnormal Pap test depends on HPV infection status at the time of the Pap test (i.e., HPV prevalence was based on a second sample obtained at the same time that cervical samples were collected for Pap testing).

An important strength of our study is that the probability of an abnormal Pap test we applied in our model was based on data on Pap test results and HPV prevalence from thousands of women in the HSS study. The type-specific HPV prevalence data allowed us to account not only for women with more than one HPV type but also for the potential benefits of cross-protection against high risk types other than HPV 16/18. Despite potential limitations, our model provides useful estimates of the timing and magnitude of potential decreases in abnormal Pap results in selected settings in the US. These estimates can help to inform efforts to monitor the impact of HPV vaccination [28].

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The authors thank Jim Braxton for assistance with analyzing the trial data. 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.

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Fig. 1.

Model summary: the population is divided into 8 groups, based on (1) infection with HPV types 16 or 18 or both; (2) infection with other (non 16/18) high risk HPV types; and (3) infection with HPV 6 or HPV 11 or both. The probability of an abnormal Pap result for each of the 8 groups and the distribution of the population across the 8 groups prior to onset of the vaccination program were based on data from the HPV Sentinel Surveillance (HSS) project. After onset of a quadrivalent HPV vaccination program, the distribution of the population across the 8 groups can change over time through reductions in HPV 6/11 and HPV 16/18 as described on the right of the chart. For simplicity, the potential benefits of cross-protection against high-risk HPV types other than HPV 16/18 are not illustrated.

Fig. 2.

Estimated percent reduction in abnormal Pap results among women aged 21-29 years over time after onset of a quadrivalent HPV vaccination program for three coverage scenarios (lower, intermediate, and higher) under base case assumptions, which include 96% vaccine efficacy against abnormal Pap results attributable to HPV 6, 11, 16, 18 and 15% efficacy against abnormal Pap results attributable to other high risk HPV types. Specifically, these results show the estimated percent reduction in the probability of an abnormal Pap result per Pap test conducted.

Fig. 3.

Estimated percent reduction in abnormal Pap results among women aged 30-39 years over time after onset of a quadrivalent HPV vaccination program for three coverage scenarios (lower, intermediate, and higher) under base case assumptions, which include 96% vaccine efficacy against abnormal Pap results attributable to HPV 6, 11, 16, 18 and 15% efficacy against abnormal Pap results attributable to other high risk HPV types. Specifically, these results show the estimated percent reduction in the probability of an abnormal Pap result per Pap test conducted.

Table 1

Description of eight HPV groups, number of women in each HPV group, and probability of abnormal Pap results by HPV group (HPV Sentinel Surveillance project data).

	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6	Group 7	Group 8
<i>Presence of HPV infection in group</i>								
HPV 16, 18, or both	Yes	Yes	Yes	Yes	No	No	No	No
Other high risk HPV types	Yes	Yes	No	No	Yes	Yes	No	No
HPV 6, 11, or both	Yes	No	Yes	No	Yes	No	Yes	No
Number of women in group	26	348	27	321	94	1533	116	6350
Number of women with abnormal Pap result	10	159	11	115	41	448	31	443
Percent of women with abnormal Pap result	38.5%	45.7%	40.7%	35.8%	43.6%	29.2%	26.7%	7.0%
<i>Probability of abnormal Pap applied in model^a</i>								
Base case	0.452 ^a	0.452 ^a	0.362 ^a	0.362 ^a	0.436	0.292	0.267	0.070
Lower bound value	0.402	0.402	0.312	0.312	0.336	0.269	0.186	0.064
Upper bound value	0.502	0.502	0.412	0.412	0.536	0.315	0.348	0.076
<i>Percentage of attendees in each HPV group, ages 21–29</i>								
All sites	0.4%	5.2%	0.3%	4.7%	1.2%	21.4%	1.6%	65.3%
STD clinics	0.2%	5.9%	0.7%	4.8%	1.1%	24.8%	2.4%	60.0%
Family planning clinics	0.5%	5.2%	0.1%	5.1%	1.2%	22.0%	1.0%	65.0%
Primary care clinics	0.3%	4.0%	0.3%	4.0%	1.1%	14.9%	1.6%	73.8%
<i>Percentage of attendees in each HPV group, ages 30–39</i>								
All sites	0.0%	0.8%	0.1%	2.0%	0.5%	10.7%	0.6%	85.4%
STD clinics	0.0%	1.4%	0.0%	1.6%	0.2%	15.3%	0.9%	80.7%
Family planning clinics	0.0%	0.3%	0.3%	2.2%	0.3%	11.2%	0.5%	85.2%
Primary care clinics	0.0%	0.6%	0.0%	2.1%	0.8%	7.0%	0.5%	89.0%

The population is divided into 8 groups, based on (1) infection with HPV types 16 or 18 or both; (2) infection with other (non 16/18) high risk HPV types; and (3) infection with HPV 6 or HPV 11 or both, as described in the top three rows. For example, Group 1 consists of those with HPV 16/18, other high risk HPV types, and HPV 6/11.

^aOwing to small sample sizes in group 1 and group 3, groups 1 and 2 were combined and groups 3 and 4 were combined for the purposes of calculating the probability of an abnormal Pap test. Lower and upper bound values for the probability of an abnormal Pap result applied in model represent approximate 95% confidence intervals. The category “other high risk HPV types” included the following HPV types: 26, 31, 33, 35, 39, 45, 51–53, 56, 58, 59, 66–70, 73, 82, and 85. The percentages of attendees in each HPV group for ages 21–29 years were obtained using data for ages 20–29 years.

Table 2

Base case results: percentage reduction in the probability of an abnormal Pap result, by age group and site and vaccine coverage scenario, in years 5, 15, and 25 of an HPV vaccination program.

	<u>Lower coverage scenario</u>			<u>Intermediate coverage scenario</u>			<u>Higher coverage scenario</u>		
	Year 5	Year 15	Year 25	Year 5	Year 15	Year 25	Year 5	Year 15	Year 25
<i>Ages 21–29 years</i>									
All sites	0.8%	10.2%	11.3%	1.5%	14.2%	15.4%	7.4%	21.4%	22.2%
STD clinics	0.9%	10.7%	11.9%	1.5%	14.9%	16.2%	7.8%	22.5%	23.3%
Family planning clinics	0.9%	10.3%	11.2%	1.6%	14.2%	15.2%	7.7%	21.2%	21.7%
Primary care clinics	0.6%	9.3%	10.7%	1.1%	13.0%	14.5%	6.2%	19.9%	20.8%
<i>Ages 30–39 years</i>									
All sites	0.0%	0.7%	5.4%	0.0%	1.1%	7.5%	0.0%	4.2%	11.3%
STD clinics	0.0%	0.6%	5.4%	0.0%	1.1%	7.5%	0.0%	4.1%	11.3%
Family planning clinics	0.0%	0.7%	5.5%	0.0%	1.2%	7.6%	0.1%	4.5%	11.4%
Primary care clinics	0.0%	0.6%	5.4%	0.0%	1.0%	7.4%	0.0%	4.1%	11.1%

These results show the estimated percent reduction in the probability of an abnormal Pap result per Pap test conducted. Year 5, year 15, and year 25 refer to the number of years after onset of the HPV vaccination program. Vaccine coverage scenarios are as described in the text.

Table 3

Sensitivity analyses: percentage reduction in the probability of an abnormal Pap result in years 5, 15 and 25, when varying model assumptions, all clinic sites.

Parameter(s) varied	Ages 21–29 years			Ages 30–39 years		
	Year 5	Year 15	Year 25	Year 5	Year 15	Year 25
None (base case)	1.5%	14.2%	15.4%	0.0%	1.1%	7.5%
Lower efficacy vs. HPV vaccine types (75%)	1.2%	11.7%	12.7%	0.0%	0.9%	6.3%
Higher efficacy vs. HPV vaccine types (100%)	1.5%	14.7%	16.0%	0.0%	1.1%	7.7%
Lower cross-protection efficacy (0%)	1.2%	11.0%	11.9%	0.0%	0.9%	5.4%
Higher cross-protection efficacy (30%)	1.7%	17.4%	19.0%	0.0%	1.3%	9.6%
Lower values of efficacy-adjustment factors (θ) ^a	0.7%	11.1%	12.5%	0.0%	0.6%	5.8%
Higher values of efficacy-adjustment factors (θ) ^a	2.2%	16.3%	17.2%	0.0%	1.7%	8.6%
Lower percent of people with no HPV ^b	1.6%	15.3%	16.6%	0.0%	1.4%	9.6%
Higher percent of people with no HPV ^b	1.3%	13.0%	14.1%	0.0%	0.8%	5.2%
Lower group-specific probabilities of abnormal Pap ^c	1.3%	13.2%	14.3%	0.0%	1.0%	6.9%
Higher group-specific probabilities of abnormal Pap ^c	1.6%	15.1%	16.4%	0.0%	1.2%	8.0%
All of the above and vaccine coverage: lowest impact scenario	0.3%	3.9%	4.4%	0.0%	0.1%	1.3%
All of the above and vaccine coverage: highest impact scenario	16.8%	32.6%	32.8%	0.3%	11.5%	21.0%

The intermediate coverage scenario was applied in all of the above calculations except the “lowest impact scenario” and the “highest impact scenario”, in which lower and higher coverage scenarios, respectively, were applied and other parameters (efficacy, efficacy-adjustment factors, percent of people with no HPV, and the probability of an abnormal Pap test) were also set to their extreme values.

^aThe efficacy adjustment factors adjust for the probability of acquiring HPV 16 or 18, HPV 6 or 11, or any high-risk HPV type other than 16/18 prior to vaccination.

^bRefers to the percent of people in the lowest risk group (group 8 – those without HPV 16/18, HPV 6/11, and other high-risk HPV types).

^cSee Table 1 for lower and upper-bound probabilities of abnormal Pap test results by group.