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The Estimated Impact of Human Papillomavirus Vaccine Coverage on the Lifetime Cervical Cancer Burden Among Girls Currently Aged 12 Years and Younger in the United States

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Abstract

Using a previously published dynamic model, we illustrate the potential benefits of human papillomavirus vaccination among girls currently 12 years or younger in the United States. Increasing vaccine coverage of young girls to 80% would avert 53,300 lifetime cervical cancer cases versus 30% coverage and 28,800 cases versus 50% coverage.

One of the Healthy People 2020 objectives is to increase 3-dose human papillomavirus (HPV) vaccine coverage among girls aged 13 to 15 years, with a target of 80%.[1] In 2012, however, coverage in this age group is approximately 30% for all 3 doses and 50% for at least 1 dose.[2] In this report, we illustrate the potential benefits of increasing HPV vaccine coverage among young girls to 80% in terms of cervical cancer prevention. Specifically, we estimate the potential reduction in the lifetime number of cervical cancer cases and deaths among 13 consecutive female birth cohorts (i.e., girls currently 12 years and younger) in the United States.

The deterministic, dynamic, population-based HPV model we used has been described in detail elsewhere.[3] Previous applications of this model have yielded cost-effectiveness results that are generally consistent with other published models. For example, our estimates of the cost per quality-adjusted life year gained by male vaccination[3] were generally in between those of Elbasha et al.[4] and Kim et al.[5] Briefly, our model takes into account the incidence of cervical cancer in the absence of HPV vaccination (but in the context of historical and current cervical cancer prevention activities), using data from population-based cancer registries that participate in the Centers for Disease Control and Prevention's National Program of Cancer Registries and the National Cancer Institute's Surveillance,

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Epidemiology, and End Results Program.[6,7] Then, reductions in the incidence of cervical cancer are estimated based on vaccine coverage, vaccine efficacy, and the percentage of cervical cancer cases attributable to HPV 16 and HPV 18. We assumed that vaccination would provide no cross-protection against other high-risk HPV types. To estimate vaccine impact on cervical cancer deaths, we assumed that 32.1% of cervical cancer cases would result in death, based on the overall 5-year relative survival probability of 67.9% reported in Surveillance, Epidemiology, and End Results.[8]

We calculated lifetime cervical cancer incidence among girls currently 12 years old and younger in the United States under different HPV vaccine coverage scenarios. We examined the benefits of increasing HPV vaccine coverage at age 12 years to 80% from 2 different baseline coverage rates: 30% and 50%. We chose these 2 baseline coverage rates because they reflect approximate 2012 coverage rates among young girls. Specifically, among 13- to 15-year-old girls in 2012, approximately 30% had received all 3 doses of the vaccine and approximately 50% had received at least 1 dose of the vaccine.[2]

The 4 specific coverage scenarios we examined when comparing 80% coverage to 30% coverage were as follows: (1) no HPV vaccination, (2) vaccination at age 12 years with 30% coverage of all cohorts currently aged 12 years and younger, (3) vaccination at age 12 years with 80% coverage of all cohorts currently aged 12 years and younger, and (4) vaccination at age 12 years with 30% coverage of the first cohort (year 1) and 80% coverage of all other cohorts in subsequent years (those currently aged 0Y11 years). When comparing 80% coverage to 50% coverage, we used 4 analogous coverage scenarios.

The model simulates the US population and includes males and females ages 8 to 99 years over a 100-year time frame. However, for this exercise, we assessed the benefits of vaccination of 13 consecutive female birth cohorts (i.e., girls currently aged 12 years and younger) in the United States and assessed the reduction in cervical cancer among these 13 birth cohorts. For simplicity, we did not include vaccination of females at ages other than 12 years, thus assuming the “status quo” coverage rates in our analysis (30% and 50%), and the target coverage rate (80%) would be achieved at age 12 years. We did not include male vaccination at any age. We did not consider vaccination of future birth cohorts (those not yet born). Selected model assumptions are summarized in Table 1; a complete description of the model is available elsewhere.[3] Assumptions regarding vaccine efficacy and the percentage of cervical cancers attributable to HPV 16 and HPV 18 were varied in sensitivity analyses according to the ranges shown in Table 1.

To examine the reasonableness of our dynamic modeling results, we performed an alternate set of calculations of the potential benefits of HPV vaccination. These alternate calculations approximate the direct benefits of vaccination (without regard to “herd effects”) using relatively few parameters: the number of girls aged 12 years and younger, vaccine coverage, vaccine efficacy, the percentage of cervical cancer attributable to HPV 16 and HPV 18, and the lifetime risk of cervical cancer morbidity and mortality in the absence of vaccination. Specifically, the number of cervical cancer cases in the absence of vaccination was calculated by multiplying the approximate population of girls currently aged 12 years and younger (26 million) by the estimated lifetime risk of cervical cancer (0.68%[8]). The number

of cervical cancer cases averted by vaccination in the 30% coverage scenario was calculated by multiplying the number of cervical cancer cases in the absence of vaccination by 30% × 95% × 70%, where 30% reflects vaccine coverage, 95% is our assumed vaccine efficacy against HPV 16 and HPV 18, and 70% is our assumed percentage of cervical cancers attributable to HPV 16 and HPV 18. The number of cervical cancer cases averted in the 50% and 80% coverage scenarios was calculated in an analogous manner.

The dynamic modeling results suggest that vaccination will have substantial population-level impacts on the lifetime number of cervical cancer cases among girls currently 12 years and younger (Table 2). In the absence of vaccination, there would be an estimated 168,400 lifetime cases of cervical cancer among these 13 birth cohorts, including 54,100 cervical cancer deaths. At 30% coverage, there would be 122,900 lifetime cases of cancer, including 39,500 cervical cancer deaths, for a reduction of 45,500 cases and 14,600 deaths compared with no vaccination. Vaccination at 80% coverage would avert an additional 53,300 lifetime cervical cancer cases (17,100 deaths) compared with 30% coverage, where the 53,300 averted cases reflect the number of cases at 30% coverage (122,900) minus the number of cases at 80% coverage (69,600).

Although the results in the final 3 scenarios in Table 1 are similar, these 3 scenarios show the benefits of increasing vaccine coverage for a single birth cohort. For example, for each female birth cohort that vaccine coverage remains at 30% instead of the target of 80%, there is a missed opportunity to prevent 4400 lifetime cervical cancer cases (1400 deaths). This 4400 estimate reflects the number of cases in the scenario of 30% coverage for 1 year, 80% thereafter (74,000) minus the number of cases in the scenario of 80% coverage (69,600).

Increasing vaccine coverage to 80% yielded substantial benefits even when using 50% as the baseline coverage rate instead of 30% (Table 2). The dynamic modeling results found that vaccination at 80% coverage would avert an additional 28,800 lifetime cervical cancer cases (9200 deaths) compared with 50% coverage. For each birth cohort that vaccine coverage remains at 50% instead of the target of 80% there is a missed opportunity to prevent 2600 lifetime cervical cancer cases (800 deaths). Results of the alternate calculations (Table 2) are generally consistent with the dynamic model results.

The estimated impact of HPV vaccination varied in the sensitivity analyses when we simultaneously modified the assumptions regarding vaccine efficacy and the percentage of cervical cancer attributable to HPV types 16 and 18. For example, in the dynamic model, the reduction in cervical cancer (compared with the scenario of no vaccination) ranged from 20.7% to 32.5% for 30% coverage, from 32.3% to 49.7% for 50% coverage, and from 46.3% to 69.6% for 80% coverage (Table 2).

Although this analysis focuses on the potential health benefits of HPV vaccination and does not address cost issues, the potential medical costs averted by preventing cervical cancer can be substantial. For example, assuming a direct medical cost per case of cervical cancer of $38,800 in 2010 US dollars,[9–11] the prevention of 45,500 cervical cancer cases through 30% HPV vaccine coverage translates into approximately $1.8 billion in averted medical costs. However, because these averted costs would be realized decades into the future, these

averted costs would be notably less than $1.8 billion when expressed in terms of “present value” (e.g., if future costs are discounted at 3% annually).

This modeling exercise shows the potential benefits of HPV vaccination in terms of cervical cancer prevention over the lifetimes of all girls currently 12 years and younger in the United States. The model we applied is subject to several important limitations, which are discussed in more detail else-where.[3] Briefly, the model is relatively simple compared with other dynamic models of HPV vaccination.[4,5,12] A key simplifying assumption is that acquisition and clearance of HPV 16 (or HPV 18) infection provided lifelong, 100% type-specific natural immunity against reinfection, an assumption that reduces the estimated impact of vaccination.[13] Another simplifying feature of our model is that although it assumes that cervical cancer screening will continue, it does not explicitly include cervical cancer screening. Cervical cancer screening is instead incorporated indirectly in the model, as the observed rates of cervical cancer applied in the model are those that have occurred in the context of current and past cervical cancer screening practices in the United States. The baseline vaccine coverage levels we applied reflect approximate 2012 coverage rates for all 3 doses (30%) and for at least 1 dose (50%) among 13- to 15-year-old girls.[2] For the purposes of this analysis, a baseline coverage of 50% might be more applicable if there is high vaccine efficacy with less than 3 doses,[14] whereas a baseline coverage of 30% might be more applicable if all 3 doses are needed to sustain high vaccine efficacy over a long duration of time. For simplicity and ease of interpretation of results, we assessed benefits to girls who were aged 0 to 12 years in the first year of a hypothetical vaccine program, and we interpreted this assessment as an approximation of the potential benefits to girls currently aged 0 to 12 years in the United States. We did not consider vaccination of girls after age 12 years or male vaccination at any age, which could cause us to over-estimate the impact of increasing vaccine coverage of 12-year-old girls to 80%. Conversely, the impact of increasing vaccine coverage could be greater than we estimated in all coverage scenarios if there is vaccine protection against high-risk HPV types other than HPV 16 and HPV 18, such as through potential cross-protection of currently available HPV vaccines[15] or with an investigational 9-valent HPV vaccine that targets 5 additional high-risk HPV types.[16] In focusing on cervical cancer, we did not include other potential health benefits of increased HPV vaccine coverage, such as reductions in genital warts, recurrent respiratory papillo-matosis, and other HPV-associated cancers (i.e., vaginal, vulvar, anal, penile, and oropharyngeal).

Our model illustrates how increasing HPV vaccine coverage in the United States can prevent thousands of cervical cancer deaths over time. Furthermore, the results of the dynamic model were relatively consistent with the simple, static calculations we performed. The similarity in our findings across these 2 approaches is not unexpected. When considering HPV vaccination of adolescent girls under an assumption of high vaccine efficacy with lifelong duration, results are generally consistent regardless of model type (although the inclusion of “herd effects” produces a greater estimated impact of vaccination as one might expect).[17,18] Typically, however, complex dynamic models are needed for most other scenarios, such as examining HPV vaccination of males and older females, allowing for waning vaccine immunity, and accounting for changes in cervical cancer screening strategies.

Our modelling results suggest substantial reductions in the burden of cervical cancer over time at coverage levels of 30% and 50% for young girls, with even more marked reductions in cervical cancer if the Healthy People 2020 vaccination target of 80% HPV vaccine coverage is achieved. Although increasing HPV vaccine coverage in the United States has been challenging, several needed strategies have been identified, including the following: reducing the missed opportunities for HPV vaccination (such as health care encounters in which adolescents aged 11–12 years receive vaccines other than HPV but do not receive HPV vaccine); educating parents, providers, and patients on the importance of HPV vaccine; and increasing the strength and consistency in which providers recommend HPV vaccination in accordance with national vaccination recommendations.[19]

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TABLE 1.

Selected Assumptions in Dynamic Model

Assumption	Value Applied (Range)
Vaccine efficacy against HPV 16 and HPV 18	95% (85%−100%)
Vaccine duration of protection	Lifelong
Percent of cervical cancer attributable to HPV 16, HPV 18	70% (60%−80%)
Annual probability of acquiring HPV 16, HPV 18	Varied by age
Number of girls currently aged ≤12 y in the United States *	26 million

A complete description of the model, including a list of all parameter values and sources, is provided elsewhere.[3] Each of the 13 birth cohorts in the model (those aged 0–12 years) consisted of 2 million girls, for a total of 26 million. This overall population size is consistent with 2012 US Census Bureau estimate of 25.9 million girls aged 0 to 12 years.[20] The annual probability of acquiring HPV 16 and HPV 18 varied by age and was adjusted from year to year according to decreases in HPV 16 and HPV 18 in the population.

We assumed the vaccine would have no impact on the cervical cancers not attributable to HPV 16 or HPV 18, and thus, we made no assumptions about the percent of cervical cancers attributable to other HPV types.

* We estimated the number of cervical cancer cases (and deaths) expected to occur over the lifetimes of girls currently 12 years and younger in the United States, under various scenarios of HPV vaccine coverage.

TABLE 2.

Number of Lifetime Cervical Cancer Cases and Cervical Cancer Deaths Among the 26 Million Girls Currently 12 Years and Younger in the United States, and Percent Reduction in Cervical Cancer Cases Compared With No Vaccination, Under Various Coverage Scenarios for a Female-Only HPV Vaccination Program

	Dynamic Model Results			Alternate "Static" Calculations		
Vaccination Scenario	**No. Cervical Cancer Cases**	**No. Cervical Cancer Deaths**	**Percent Reduction in Cervical Cancer vs. no Vaccination (Range)**	**No. Cervical Cancer Cases**	**No. Cervical Cancer Deaths**	**Percent Reduction in Cervical Cancer vs. no Vaccination (Range)**
No vaccination	168,400	54,100	N/A	176,800	56,800	N/A
30% in all years	122,900	39,500	27.0 (20.7–32.5)	141,500	45,400	20.0 (15.3–24.0)
50% in all years	98,400	31,600	41.6 (32.3–9.7)	118,000	37,900	33.3 (25.5–40.0)
30% in year 1, then 80%	74,000	23,800	56.1 (44.2–66.5)	87,300	28,000	50.6 (38.8–60.9)
50% in year 1, then 80%	72,200	23,200	57.1 (45.0–67.8)	85,500	27,400	51.7 (39.6–62.2)
80% in all years	69,600	22,300	58.7 (46.3–69.6)	82,700	26,600	53.2 (40.8–64.0)

The number of cervical cancer cases and deaths are those estimated to occur among the lifetimes of 13 consecutive female birth cohorts (i.e., girls currently 12 years old and younger) in the United States. For simplicity, we focused on vaccination of 12-year-old girls only, thus assuming that coverage rates of 30%, 50%, and 80% could be achieved at age 12 years. We did not include vaccination of older females and males of any age. Cervical cancer screening is included in all vaccine coverage scenarios (including "no vaccination").

The alternate calculations use simple equations as described in the text to approximate the direct benefits of vaccination and do not include indirect or herd effects. The number of cervical cancer cases in the no-vaccination scenario in the alternate calculations differs from that of the dynamic model because the alternate calculations are based on estimates of the lifetime risk of cervical cancer, whereas the dynamic model applied age-specific annual rates of cervical cancer.

The range of values shown for the percent reduction in cervical cancer (vs. no vaccination) was obtained from the sensitivity analyses when we simultaneously modified our assumptions regarding vaccine efficacy and the percentage of cervical cancer attributable to HPV types 16 and 18, as described in Table 1.

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