Estimating the Long-Term Clinical Impact of Cervical Cancer Vaccination in Taiwan

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Abstract: The high burden of human papillomavirus (HPV) infection and subsequent cervical cancer in the presence of screening in Taiwan suggests the need for further prevention strategies. Epidemiology and screening practices vary considerably between countries, and specific analyses are required to estimate the impact of HPV vaccination. This study adapted a computer-based health economic model to Taiwan to project the clinical impact of the introduction of a prophylactic vaccine against persistent HPV 16/18 infection on cervical disease. A Markov model based on the natural history of HPV and cervical cancer was developed to simulate transitions between health states (normal, HPV, cervical intraepithelial neoplasia [CIN] stages I to III, cervical cancer stages I to IV, and death) in the presence of screening. The model was calibrated to Taiwan epidemiological end points including age-specific HPV prevalence, prevalence of CIN lesions, and predicted cervical cancer incidence and mortality. Taiwanese screening and treatment practices were modeled, and published clinical trial data were used to estimate vaccine efficacy. With 100% vaccine coverage in a 13-year-old cohort of females, there is estimated to be a 71% reduction in cervical cancer cases and deaths due to all HPV types and substantial reductions in the prevalence of precancerous lesions and screening outcomes. Removing the risk of HPV infection of a large proportion of Taiwanese females, with a high underlying cervical cancer incidence rate, would be expected to have dramatic effects on the health care system and mortality in Taiwan.

Key Words: Cervical cancer, Human papillomavirus, Vaccination, Mathematical model

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Human papillomavirus (HPV) has been implicated as a causal factor in cervical cancer with HPV DNA detected in up to 99.7% of all cervical cancers.[1] Human papillomavirus commonly infects the genital mucosa of sexually active women leading to the development of cervical neoplasia as a complication of the infection.[2] Invasive cervical cancer (ICC) is the second most common cancer and third leading cause of cancer deaths in women worldwide.[3]

In Western countries, rates of ICC have been on the decline, whereas in developing countries, it is still one of the most common forms of cancer in females.[4] These high rates compared with other countries may be explained by the observed differences in country-specific sexual practices and screening programs. Among Taiwanese women, ICC is the most common malignancy with an age-standardized incidence rate of 18.6 per 100,000 with approximately 2431 new cases and 939 deaths annually despite the existence of a national screening program.[5] The annual cervical screening program using the Papanicolaou test was launched for women in 1995 in Taiwan, and given these recent improvements to screening practices, country-specific epidemiology is anticipated to be dynamic.[4] Chou et al[6] have found that ICC incidence in women aged 30 and older has decreased by 30% since 1979, which corresponds with the increase in screening rates. There has already been an observed decline in the incidence of ICC, which corresponds to the increase in screening rates. By 2001, 61% of women had at least one Papanicolaou test, a dramatic increase from before the introduction of the screening program. Despite the improvements, ICC remains high for a country with a nationally implemented screening program, and there is uncertainty as to what extent these rates will decrease in the future.

Globally, infection with HPV 16 and 18 accounts for approximately 70% of ICC cases, comparable to Taiwan-specific studies.[7–13] Two vaccines that prevent HPV infection are now being tested in clinical trials with results indicating close to 100% efficacy against persistent infection with HPV 16 and 18 (Gall SA, Teixeira J, Wheeler C, et al., unpublished data).[14–22] One of these vaccines has also indicated evidence of cross-protection against other oncogenic HPV types.[14] The long-term impact of vaccination has not yet been observed, and therefore, mathematical models are needed to simulate the consequences of vaccination. In the United Kingdom, modeling analyses have shown that vaccination of a cohort of girls with an HPV 16/18 vaccine, including cross-protection against other oncogenic types, was predicted to result in a 66% reduction in the prevalence of high-grade precancerous lesions and a 76% reduction in cervical cancer cases.[23] There have been no published analyses evaluating the long-term impact of HPV vaccination in Taiwan, where cervical disease and screening markedly differs from that in the United Kingdom. Differences in the impact of vaccination would be expected in Asia compared with the rest of the world owing to a known difference in cervical cancer incidence and geographical HPV-type distribution.[7–13,24]

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The objective of the study was to develop a decision-analytic model to assess the impact of a prophylactic cervical cancer vaccine on key clinical and screening outcomes and to adopt the model to represent the natural history of disease and epidemiology for Taiwan. Even with a national screening program, the incidence and mortality rates in Taiwan remain high, which, in the presence of the national health insurance system, necessitates an analysis of the potential impact of vaccination as screening seems to be inadequate. Also of importance was to project the long-term public health impact of introducing the HPV vaccine in Taiwan when considering (1) current observed epidemiology and (2) predicted changes to future epidemiology given dynamic screening practices.

MATERIALS AND METHODS

Model Overview

A Markov model has been developed reflecting the natural history of type-specific HPV infection and subsequent progression to cervical lesions and cancer. The model is based on a set of mutually exclusive health states corresponding to HPV infection, cervical intraepithelial neoplasias (CIN), and ICC, among which women transition according to age-specific transition probabilities (Fig. 1). The model is composed of 3 modules. Further detail on model structure is provided in an article published by Kohli et al.[23] The natural history module reflects the epidemiology of HPV infection and its progression to cervical cancer in the absence of intervention using a Markov process with transitions in 6-month cycles. Health states are stratified by HPV type, namely, 16, 18, 31, 45, and 52, other oncogenic type, and low risk. The screening module simulates disease progression in the presence of country-specific screening practices. The model is based on a decision tree representing options after varying diagnoses and test results, where probabilities associated with each procedure capture the variability in test and treatment pathways. These include repeat cytology test, colposcopy, biopsy, treatment, and cytologic follow-up. Observed compliance to screening is reflected through data on the percentage of women never screened, age-specific coverage rates, and screening practices.[25,26] Finally, the vaccine module incorporates efficacy by decreasing the probability of acquiring HPV infection in the different HPV types. The model can accommodate any pattern of vaccine waning and inclusion of booster shots. With a booster shot, it is assumed that vaccine efficacy is restored to original levels.

Calibration Methods

Estimates for disease progression rates are produced by varying transition probabilities within established ranges, so that modeled predictions of key end points for unvaccinated girls match the currently available epidemiological data. Although there may be some uncertainty concerning such estimates, they provide a credible starting point for analysis. A comprehensive review of the literature was completed to determine plausible transition probability ranges for calibration as reported by Kohli et al.[23] The model was calibrated to recently published Taiwan-specific data for various end points: age-specific HPV prevalence[27]; HPV-type distribution with a focus on cervical cancer[8–13]; overall CIN 1, 2, and 3 prevalence[27]; age-specific cervical cancer incidence[5]; and mortality.[28]

In Taiwan, the percentage of females undergoing screening has significantly increased during the last decade.[4] These dynamic screening practices suggest that cervical cancer incidence rates observed today may be much different from those in the future. Considering this, 2 different calibration scenarios need to be considered:

Model Predicts Currently Observed Cancer Incidence (Scenario 1)

In this scenario, the model is calibrated to current Taiwan data for cervical cancer incidence and mortality, assuming current screening practices. Transition probabilities for progression to cancer are manipulated beyond established ranges to force the model to output high incidence rates in the presence of current screening practices. This calibration allows the model to simulate the impact of HPV vaccination if future cohorts showed similar incidence patterns as observed today.

Model Predicts Lower than Currently Observed Cancer Incidence (Scenario 2)

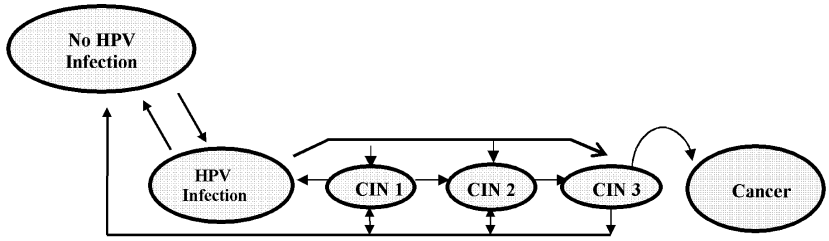
In this scenario, currently observed screening practices are incorporated, and transition probabilities for progression to cancer remain within established ranges (comparable to other countries).[23] This calibration results in lower-than-observed cancer rates with the model inputs reflecting current understanding of the data and allows the model to simulate the impact of HPV vaccination for a cohort of girls screened at currently observed rates that may have lower-than-observed cancer rates in the future.

Model Inputs and Assumptions

Table 1 provides inputs and assumptions used for each of the proposed calibration scenarios.

Analyses

We conducted analyses to estimate the clinical effects of HPV 16/18 vaccination of a cohort of old females in the presence of



Model simulates the natural history of human papillomavirus (HPV) infection and cervical carcinogenesis while incorporating the underlying type-specific HPV distribution within each stage of cervical disease, by use of a sequence of 6-month transitions among mutually exclusive health states. Health states are defined by use of eight general categories of HPV infection (normal/no HPV, HPV16, HPV18, HPV31, HPV45, HPV52, other high-risk HPV types, low-risk HPV types), three general categories of cervical disease (CIN 1, CIN 2, and CIN 3), and four categories of invasive cervical cancer (Stage I, Stage II, Stage III and Stage IV). The probabilities governing each of these transitions are conditional on the type of HPV infection and age. Transitions to death due to natural causes can occur from any health state in the model at any time during the simulation.

FIGURE 1. Simplified structure of the HPV and cervical cancer natural history model.[23]

TABLE 1. Comparison of model inputs and assumptions for the plausible calibration scenarios

	Currently observed cancer incidence (Scenario 1)	Predicted lower cancer incidence (Scenario 2)
Screening[25,26]		
Start and stop age, y	30–100	No change
% Screened every 3 y	~24	
% never screened in a lifetime	31	
Test characteristics[30]		
Cytology—sensitivity (specificity)	0.41–0.67 (0.966)	No change
Screening practices[25]		
ASCUS to triage cytology (colposcopy), %	50 (50)	No change
LSIL to triage cytology (colposcopy), %	0 (100)	
HSIL to colposcopy, %	100	
Negative triage cytology to regular screening (repeat test), %	0 (100)	
Positive triage cytology to colposcopy, %	100	
Negative colposcopy/biopsy to regular screening, %	50	
Negative colposcopy/biopsy to increased screening, %	50	
CIN 1 diagnosis to increased screening (treatment), %	100 (0)	
CIN 2 or 3 diagnosis to treatment, %	100	
Lesion progression and regression (oncogenic HPV)[31–38]		
Normal to HPV		
<35 y	0.04–0.08	No change
≥35 y	0.03–0.04	
HPV to CIN 1		
<35 y	0.01–0.02	
≥35 y	0.02–0.03	
CIN 1 to CIN 2		
<35 y	0.03–0.14	
≥35 y	0.07–0.31	
CIN 2 to CIN 3		
<35 y	0.10–0.15	
≥35 y	0.15–0.20	
HPV clearance		
<35 y	0.43	
≥35 y	0.43	
CIN 1 regression		
<35 y	0.34–0.54	
≥35 y	0.31–0.41	
CIN 2/3 regression		
<35 y	0.052–0.053	
≥35 y	0.01–0.05	
Progression to invasive cancer[39,40]		
CIN 3 to cancer	0.001–0.12	0.002–0.05
Stage I progression to stage II	0.11	0.11
Stage II progression to stage III	0.12	0.12
Stage III progression to stage IV	0.12	0.12
Stage I-IV mortality	0.005–0.15	0.005–0.12
Cancer probability of symptoms	0.08–0.45	0.08–0.45

Transition probabilities are for 6-month cycles.

The model includes probability of abnormal cytology according to lesion type (ie, CIN 1–3), and therefore, a range of values is provided. Transition probability ranges are reported owing to probability variation in age and HPV type. References that support the resulting transition probability values are provided. The CIN 1 lesions can regress to HPV infection or normal; CIN 2/3 lesions can regress to HPV infection or normal. Details of the point estimates from the calibrated models are available from the authors on request.

Cytology sensitivity, probability of abnormal cytology given true state is CIN 1+; Cytology specificity, probability of normal cytology given true state is negative for lesions; HSIL, high-grade squamous intraepithelial lesion; LSIL, low-grade squamous intraepithelial lesion.

current screening in Taiwan. For vaccinated and unvaccinated females, clinical events (HPV infections, CIN lesions, cervical cancer cases, and deaths) were derived from the model for one birth cohort of girls from age of vaccination (13 years old) for a lifetime time horizon. Rates of screening events (abnormal cytology tests, biopsies, colposcopies, and CIN treatments) were also estimated.

All analyses were conducted using the model calibrated to scenario 2 (future predicted lower cancer incidence). It was determined that this calibration scenario would conservatively simulate the future cancer incidence for a cohort of females in Taiwan, given the recent changes to screening practices. Analyses were conducted based on the conservative assumption that current screening practice does not change because the extent to which the introduction of the vaccine will affect screening is difficult to predict.

Base Case Assumptions

In the base case analysis, a cohort of 151,550 13-year-old adolescent girls in Taiwan with 100% vaccine coverage in the presence of screening was compared with the same cohort with screening alone.[41] Vaccine efficacy is modeled by assuming that vaccination reduces the probability of transitioning from the normal

to the persistent HPV 16, 18, 31, and 45 infection health states. We assumed 95% efficacy against persistent HPV 16 and 18 infections based on previous modeling studies,[42] which reflect values reported in vaccine clinical trials (Gall SA, Teixeira J, Wheeler C, et al., unpublished data).[14–22] We further assumed 53% and 88% efficacy against HPV 31 and HPV 45, respectively (Gall SA, Teixeira J, Wheeler C, et al., unpublished data). It was also assumed that adolescents would receive 3 doses of the vaccine and be fully immunized after 1 year and that vaccine efficacy does not wane over time. The study conducted by Harper et al[15] showed absence of waning up to 4.5 years after vaccination, and this was assumed to remain true over a lifetime. In the longer term, such waning could in principle, be countered by a booster. As no long-term data are available, the impact of waning and a booster shot was assessed using sensitivity analyses.

Sensitivity Analyses Assumptions

Sensitivity analyses were used to explore alternate assumptions about vaccine efficacy and waning, vaccine coverage rate, and vaccination age. Vaccine efficacy for HPV types 16 and 18 was varied from 90% to 100%. Because cross-protection against types 31 and 45 has as yet only been demonstrated for incident infection, alternative scenarios where cross-protection was absent or waned were also analyzed. Waning of immunity against 31 and 45 was assumed to occur in a linear manner to 0% of initial efficacy after 10 years and was analyzed with and without a booster at 10 years after initial vaccination. Waning of all types was examined starting 15 years after initial vaccination to 0% efficacy for 5 years. The impact of vaccinating older and younger girls was also analyzed (10, 18, and 30 years). Also, because 100% vaccination coverage is likely not achievable in practice in the near term, an alternative vaccination coverage rate of 80% was explored.

RESULTS

Model Calibration

Table 1 provides the transition probabilities that resulted from calibration for the base case analysis (scenario 2 [calibration to predicted lower cancer incidence] and scenario 1 [calibration to currently observed cancer incidence]). Calibration results for age-specific cervical cancer incidence and mortality for both scenarios are provided in Figures 2A and B. Because scenario 2 was chosen as the base case, only calibration results from this model are reported further. Age-specific HPV prevalence was well matched to the Taiwan data, with overall model-predicted prevalence at 20.7% and

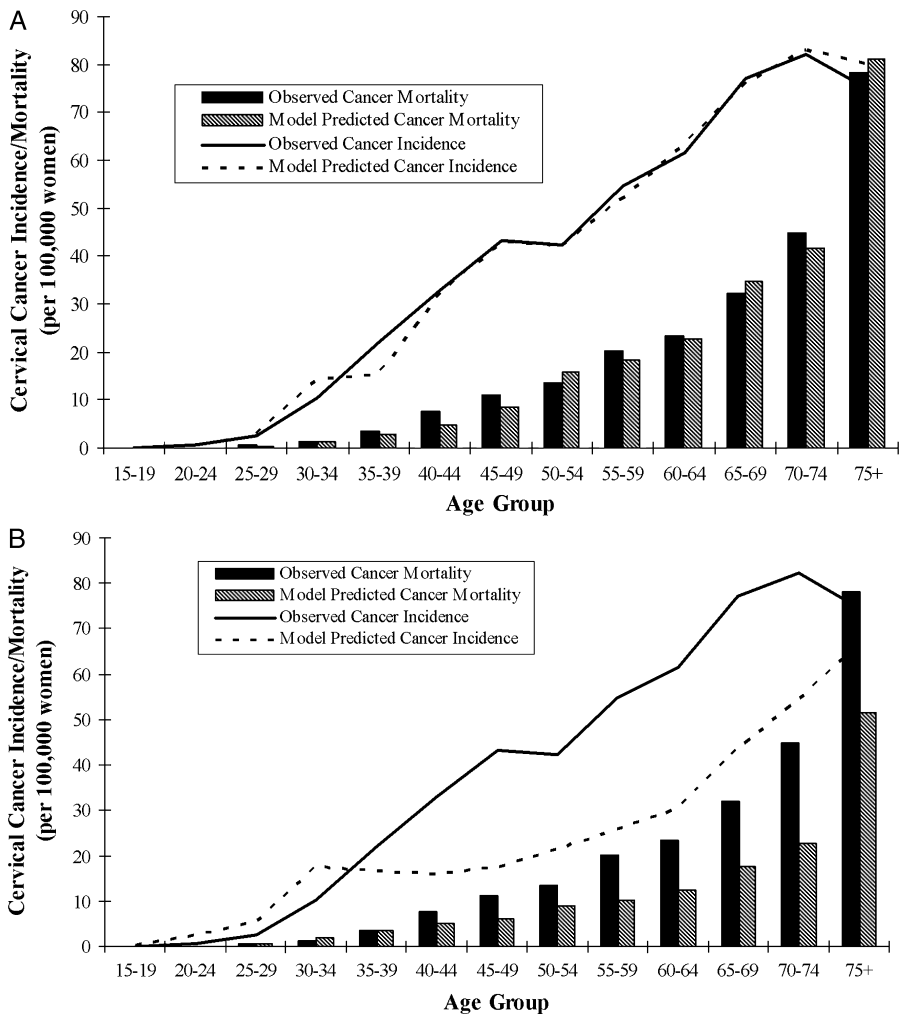


FIGURE 2. A, Taiwan calibration results for Scenario 1 (currently observed cancer incidence). B, Taiwan calibration results for Scenario 2 (predicted lower cancer incidence).

TABLE 2. Key nondiscounted health outcomes for Scenario 2 for a cohort of 151,550 13-year-old adolescent girls due to All HPV types and to Oncogenic HPV types

		All HPV	Oncogenic HPV
Abnormal cytology test	Vaccination	135,155	40,346
	No vaccination	158,430	62,270
	% reduction	14.7%	35.2%
Colposcopy	Vaccination	107,468	32,277
	No vaccination	126,373	50,115
	% reduction	15.0%	35.6%
Biopsy	Vaccination	60,670	20,729
	No vaccination	73,559	33,072
	% reduction	17.5%	37.%
Treated CIN lesions	Vaccination	13,853	6291
	No vaccination	18,305	10,657
	% reduction	24.3%	41.0%
Cancer cases	Vaccination	670	620
	No vaccination	2290	2242
	% reduction	70.7%	72.3%
Cancer deaths	Vaccination	308	284
	No vaccination	1058	1035
	% reduction	70.9%	72.5%

an observed prevalence of 21.2%.[27] Model-predicted CIN prevalence (CIN 1, 0.6%; CIN 2/3, 1.1%) was comparable to observed data (CIN 1, 0.6%; CIN 2/3, 0.7%).[28] The model closely reproduced HPV-type distribution within cervical cancer, where values generally remained within the range observed from studies across Taiwan (model-predicted value of 71% of cervical cancers due to HPV 16/18).[8–13]

Given that we are reporting results for scenario 2, cancer incidence rates are predicted by the model to be lower than currently observed rates. The model predicted an average cervical cancer incidence rate of 24.4 per 100,000 compared with the reported rate[5] of 38.8 per 100,000. This reduction in incidence is likely for future cohorts given recent improvements to screening coverage. Cervical cancer mortality was predicted to be 10.9 per 100,000 compared with 18.2 per 100,000 in the literature.[29]

Base Case Analysis

Table 2 displays key nondiscounted health outcomes for the base case analysis of a cohort of 13-year-old adolescent girls. Without vaccination, the model predicts 2290 cervical cancer cases during the lifetime of the cohort, which is reduced to 670 cases in the presence of vaccination (71% reduction), assuming that screening practices remain constant. The model also predicts 1058 deaths from cervical cancer during the lifetime of the cohort without vaccination and as low as 308 cases for those who are vaccinated (71% reduction). With the projected reductions in cervical disease owing to vaccination, additional clinical benefit was anticipated in the reduction in screening tests and treatments. Vaccination was predicted to produce benefits in relation to HPV prevalence, screening tests, and treatment of CIN lesions, although to a lesser extent than the observed cervical cancer benefits. As seen in Table 2, vaccination could result in a 15% reduction in both the number of abnormal cytology tests and colposcopies and in an 18% reduction in biopsies. Additionally, the model predicted a 24% reduction in the number of treated CIN lesions. If only screening tests owing to oncogenic HPV

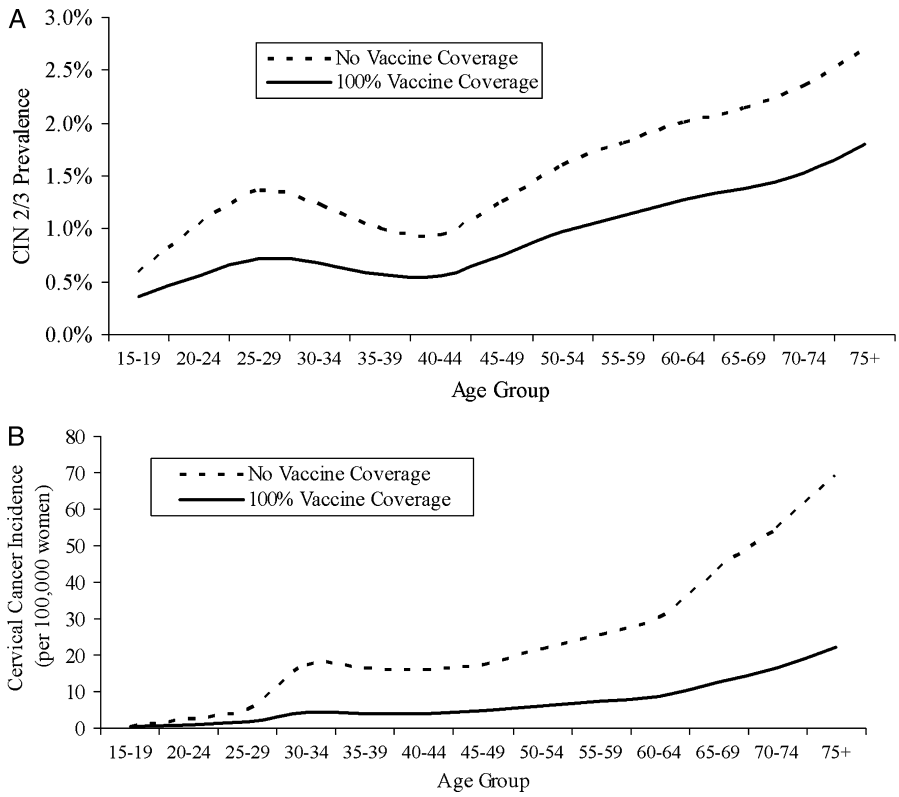


FIGURE 3. Impact of 100% vaccination coverage on CIN 2/3 prevalence (A) and cervical cancer incidence (B) compared with no vaccine for Scenario 2, nondiscounted.

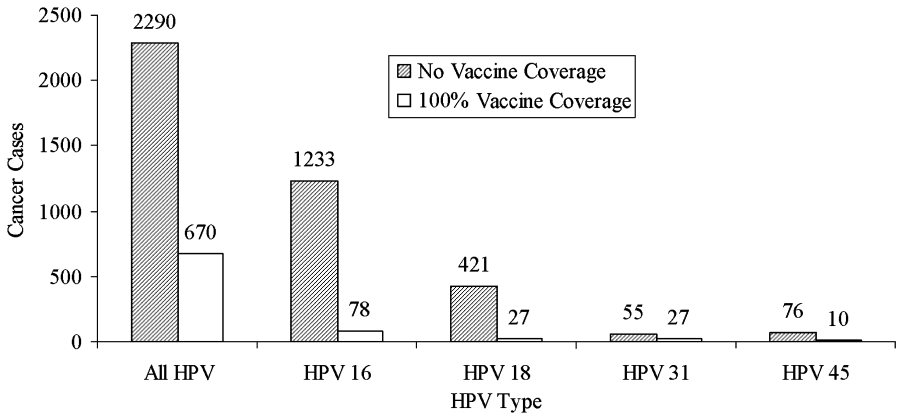


FIGURE 4. Human papillomavirus type–specific cervical cancer cases, with and without vaccination, for Scenario 2, nondiscounted.

were considered, reductions would be as high as 35% for abnormal cytology tests, 36% for colposcopies, 37% for biopsies, and 41% for treated CIN lesions. These reductions in the number of screening tests would have some implications for reducing health care costs.

When considering only oncogenic HPV, vaccination was estimated to lead to a 29% reduction in HPV prevalence and to a 41% reduction in high-grade lesions (CIN 2/3). Figure 3 displays the projected impact of vaccination on the observed distribution of CIN prevalence and cervical cancer incidence across ages. There is a greater impact of vaccination on ICC incidence and mortality when the cohort of girls gets older because vaccination is a long-term strategy to benefit cervical disease. When only considering cancers due to HPV types 16 and 18, vaccination was estimated to produce a 94% reduction in cervical cancer cases and a 93% reduction in mortality. The type-specific reductions in cervical cancer cases owing to vaccination are presented in Figure 4.

Sensitivity Analyses

Through sensitivity analyses, we investigated the impact of varying assumptions concerning vaccine efficacy and waning,

TABLE 3. Impact of alternative assumptions for vaccine efficacy, waning, and vaccination age on selected cervical cancer outcomes in Taiwan for Scenario 2

		CIN 2 and CIN 3 prevalence	Cervical cancer cases, n	Cervical cancer deaths, n
No vaccine		1.79%	2290	1058
Base case	Vaccination	1.13%	670	308
	% reduction	36.8%	70.7%	70.9%
Low efficacy (HPV 16/18)	Vaccination	1.17%	754	347
	% reduction	34.9%	67.1%	67.2%
High efficacy	Vaccination	1.10%	585	269
	% reduction	38.7%	74.4%	74.6%
No cross-protection	Vaccination	1.18%	766	352
	% reduction	34.1%	66.5%	66.7%
Vaccination coverage (80%)	Vaccination	1.13%	994	458
	% reduction	36.8%	56.6%	56.7%
Lower age at 2vaccination (10 y)	Vaccination	1.11%	665	302
	% reduction	38.0%	71.0%	71.5%
Higher age at vaccination (18 y)	Vaccination	1.22%	715	344
	% reduction	31.9%	68.8%	67.5%
Higher age at vaccination (30 y)	Vaccination	1.33%	1026	561
	% reduction	26.0%	55.2%	47.0%
Vaccine waning (HPV types 31 and 45)	Vaccination	1.18%	763	350
	% reduction	34.2%	66.7%	66.9%
Vaccine waning (HPV types 31 and 45) + booster at 10 y	Vaccination	1.18%	758	347
	% reduction	34.3%	66.9%	67.2%
Vaccine waning (HPV types 16, 18, 31, and 45)	Vaccination	1.68%	2017	886
	% reduction	6.4%	11.9%	16.2%

vaccination coverage, and age at vaccination. The consequences of these assumptions on CIN 2 and 3 cases, cervical cancer cases, and cervical cancer deaths are presented in Table 3. Despite the range of sensitivity analyses conducted, model predictions consistently identified vaccination as effective in reducing the effects of cervical disease. Waning of efficacy for all HPV types had the most impact on these effects, with results also sensitive to age at vaccination and the vaccination coverage rate.

DISCUSSION

The high burden of HPV infection and subsequent cervical cancer in the presence of screening in Taiwan suggests the need for further prevention strategies. Clinical trials have established high efficacy for a vaccine against HPV 16 and 18 and other oncogenic types (Gall SA, Teixeira J, Wheeler C, et al., unpublished data).[14–22] To facilitate decisions regarding adoption of such vaccines, a detailed model of the natural history of HPV infection was developed and adapted to Taiwan. This study investigated the clinical impact of HPV vaccination in a cohort of 13-year-old Taiwanese adolescent girls.

Screening rates in Taiwan have increased dramatically in the last 10 years and recently reached a plateau. Even with these increased screening rates, ICC incidence rates remain high. Calibration of the model to Taiwan-specific epidemiology presented a novel challenge owing to the country-specific dynamic screening practices.[4] Typically, in countries with stable epidemiology and screening, model calibration can be completed to currently observed cross-sectional data and assumed that a future cohort will follow similar epidemiological trends. This has been the calibration strategy for several published HPV and cervical cancer mathematical models.[23,39,42,43] In Taiwan, currently observed cancer rates reflect a population of women with a screening history that is quite different from today's practices. If these women had been exposed to this increased screening, it is predicted that overall cervical cancer rates would be much lower. The base case analysis in this study reflected a population of women exposed to current screening practices, with disease progression rates comparable to other countries, resulting in overall lower cancer incidence than observed in Taiwan's cross-sectional data. The model was closely calibrated to country-specific HPV prevalence, type distribution, and CIN prevalence, under the assumption that these factors would not change as substantially as cancer incidence would with increased screening. This ensures that the predicted results can be translated as best as possible to a real cohort of today's Taiwanese females.

Reported cervical cancer incidence is much higher in Taiwan compared with other countries. The ICC incidence rate in Taiwan is almost double that observed in the United Kingdom,[5,44,45] for example, which has a rate of 10.6 per 100,000. Inadequate screening rates owing to poor compliance and a lack of program organization or possible higher progression rates to cancer may have also contributed to the level of disease observed today. Despite cervical cancer being the leading female cancer, women in Taiwan have received fewer screening examinations for this disease than populations in Western countries.[46] The high incidence of ICC in Taiwan results in a country with the potential for a significant impact on clinical outcomes after introduction of vaccination. The model predicted that 100% vaccine coverage of a cohort of 13-year-old adolescent girls would lead to a 71% reduction in cancers cases and mortality due to all HPV types. The model also predicted significant decreases in screening outcomes, exceeding more than one-third of tests and treatments being averted owing to oncogenic HPV types. These results are comparable to those predicted for the United Kingdom.[23] Sensitivity analyses indicated that waning of vaccine efficacy against all HPV types had the greatest impact on the effects of cervical disease, although in theory, the administration of a booster could negate that impact. Removing the risk of HPV infection for a large proportion of Taiwanese females, with such a high underlying ICC incidence rate, would be expected to have dramatic effects on the health care system, mortality, productivity, family, and society in Taiwan.

There are limitations to the clinical effects presented in this study. For example, it is difficult to adapt a model in a country with changing epidemiology. There are limited data available on disease progression rates for high-grade lesions to cervical cancer, and the assumption to use rates comparable to other countries provides some uncertainty around these model inputs. The model does not consider the natural history of multiple HPV infections, which is particularly important with low-grade lesions. However, we would not anticipate a significant change to results because most cancer cases are caused by one dominant HPV type. The model structure also has inherent limitations, as the benefits of herd immunity, and the potential impact of HPV vaccination on other sites, such as the vulva, vagina, anus, and penis, has not been explicitly modeled. The predicted effect of HPV vaccination may be conservative owing to these model characteristics. Although modeling the impact of HPV vaccination in Taiwan in the presence of dynamic screening practices required assumptions to be made, overall, there were large predicted reductions not only in ICC incidence and related mortality but also in the prevalence of precancerous lesions and screening outcomes. This study emphasizes the importance of vaccination in cervical cancer prevention.

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