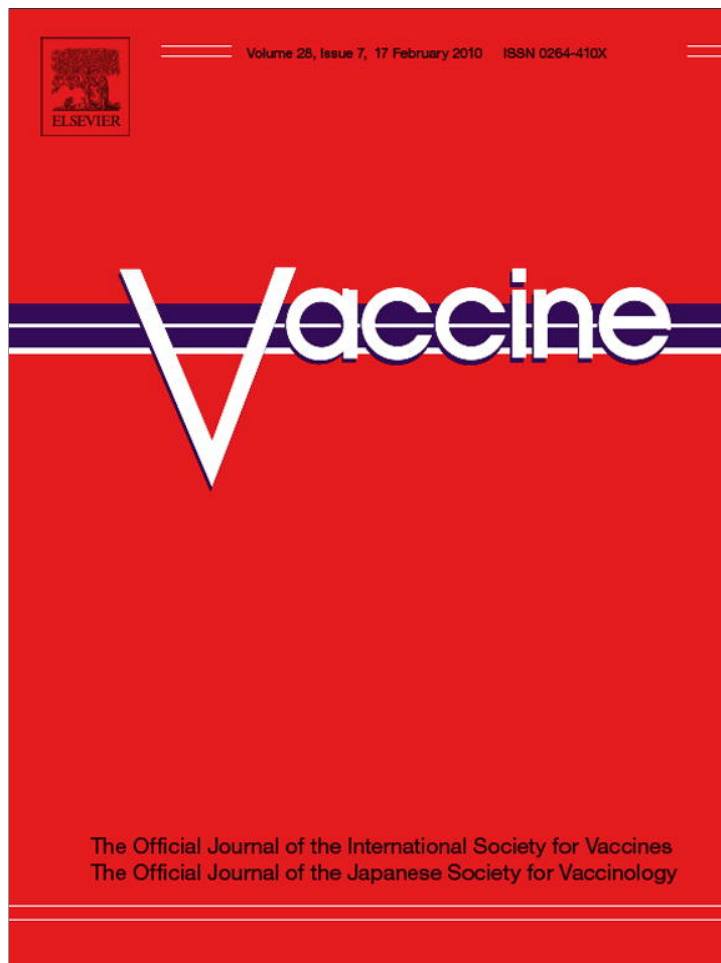


Provided for non-commercial research and education use.  
Not for reproduction, distribution or commercial use.



This article appeared in a journal published by Elsevier. The attached copy is furnished to the author for internal non-commercial research and education use, including for instruction at the authors institution and sharing with colleagues.

Other uses, including reproduction and distribution, or selling or licensing copies, or posting to personal, institutional or third party websites are prohibited.

In most cases authors are permitted to post their version of the article (e.g. in Word or Tex form) to their personal website or institutional repository. Authors requiring further information regarding Elsevier's archiving and manuscript policies are encouraged to visit:

<http://www.elsevier.com/copyright>



Contents lists available at ScienceDirect

Vaccine

journal homepage: [www.elsevier.com/locate/vaccine](http://www.elsevier.com/locate/vaccine)

## Mothers' preferences and willingness to pay for vaccinating daughters against human papillomavirus

Derek S. Brown<sup>a,\*</sup>, F. Reed Johnson<sup>a</sup>, Christine Poulos<sup>a</sup>, Mark L. Messonnier<sup>b</sup>

<sup>a</sup> RTI International, 3040 Cornwallis Road, P.O. Box 12194, Research Triangle Park, NC 27709-2194, United States

<sup>b</sup> Centers for Disease Control and Prevention, Immunization Services Division, National Center for Immunization and Respiratory Diseases, Atlanta 30329, GA, United States

### ARTICLE INFO

#### Article history:

Received 11 September 2009

Received in revised form

12 December 2009

Accepted 14 December 2009

Available online 29 December 2009

#### Keywords:

Conjoint analysis

Human papillomavirus vaccine

Cost-benefit analysis

Preferences

Demand

Mothers

Adolescent girls

Discrete choice experiment

### ABSTRACT

A choice-format, conjoint-analysis survey was developed and fielded to estimate how features of human papillomavirus (HPV) vaccines affect mothers' perceived benefit and stated vaccine uptake for daughters. Data were collected from a national sample of 307 U.S. mothers of girls aged 13–17 years who had not yet received an HPV vaccine. Preferences for four features of HPV vaccines were evaluated: protection against cervical cancer, protection against genital warts, duration of protection, and cost. We estimate that mean maximum willingness-to-pay (WTP)—an economic measure of the total benefits to consumers—for current HPV vaccine technology ranges between \$560 and \$660. All vaccine features were statistically significant determinants of WTP and uptake. Mothers were willing to pay \$238 more for a vaccine that provides 90% protection for genital warts relative to a vaccine that provides no protection against warts. WTP for lifetime protection vs. 10 years protection was \$245. Mothers strongly valued greater cervical cancer efficacy, with 100% protection against cervical cancers the most desired feature overall. Adding a second HPV vaccine choice to U.S. consumers' alternatives is predicted to increase stated uptake by 16%. Several features were significantly associated with stated choices and uptake: age of mother, race/ethnicity, household income, and concern about HPV risks. These findings provide new data on how HPV vaccines are viewed and valued by mothers, and how uptake may change in the context of evolving vaccine technology and as new data are reported on duration and efficacy.

© 2009 Elsevier Ltd. All rights reserved.

### 1. Introduction

Genital human papillomavirus (HPV) is the most prevalent sexually transmitted infection in the United States, affecting more than 25% of U.S. women aged 14–59 years in 2003–2004 [1]. Prevalence of HPV is highest among younger age groups and approaches 50% among sexually active 20 to 24-year-old women [1]. The more than 40 types of genital HPV are classified as either low-risk or high-risk types, depending on whether or not they are associated with cervical cancer [2]. High-risk HPV types cause virtually all cases of cervical cancer, and also may lead to anal, penile, vaginal, vulvar, oropharyngeal, and mouth cancers [3]. Low-risk HPV types may cause genital warts or recurrent respiratory papillomatosis.

The health and economic burden of HPV in the U.S. is substantial and is largely borne by women. In 2005, 11,999 U.S. women were diagnosed with cervical cancer and nearly 3924 deaths were caused by it [4]. Treatment of precancerous lesions, follow-up exams, and false-positive Pap tests incur significant financial and quality-of-life costs [5]. Prior to the use of HPV vaccines, direct medical costs

from prevention and treatment of HPV-related genital warts and HPV-related cervical disease were estimated to be at least \$4 billion per year [6,7]. Worldwide impacts of HPV include over 274,000 cancer deaths per year [8]. Given the prevalence and burden of HPV, the public health benefits of HPV vaccines appear quite large. Yet, for the U.S. and other western countries, cost-effectiveness results are mixed. Routine HPV vaccination of pre-teen girls generally meets accepted thresholds for value, such as \$50,000 or £30,000 per quality-adjusted life-year (QALY) [9,10]. Catch-up vaccination of older girls is less cost-effective than routine vaccination of pre-teens [9,11], and cost-effectiveness results are sensitive to duration of protection, vaccine coverage, and the types of HPV protected against.

Two prophylactic vaccines against HPV currently are in production, a quadrivalent vaccine (Gardasil<sup>®</sup>, Merck & Co., Inc., Whitehouse Station, NJ, USA) and a bivalent vaccine (Cervarix<sup>™</sup>, GlaxoSmithKline Biologicals, Rixensart, Belgium). Both protect against high-risk HPV types 16 and 18, responsible for an estimated 70% of cervical cancers [12]. The quadrivalent vaccine also protects against low-risk HPV types 6 and 11, responsible for an estimated 90% of genital warts [13]. Both vaccines provide nearly 100% efficacy against pre-cancerous lesions associated with types 16/18 and may provide cross-protection against additional HPV types [14].

\* Corresponding author. Tel.: +1 919 316 3514; fax: +1 919 541 6683.

E-mail address: [dsbrown@rti.org](mailto:dsbrown@rti.org) (D.S. Brown).

The duration of protection from both vaccines exceeds 5 years and continues to be assessed [15]. Additional vaccines, possibly with broader protection or other features, are in development [16,17]. The bivalent vaccine does not protect against low-risk HPV types 6 and 11 but it has other features that may be important to consumers. It uses a new adjuvant [18], which is reported to generate a strong and sustained immune response [19], and it may have cross-protection against different high-risk types than the quadrivalent vaccine [14].

Both HPV vaccines are approved by the U.S. Food and Drug Administration (FDA), the quadrivalent in June 2006 and the bivalent in October 2009. Further, both are also recommended for routine vaccination in females aged 11–12 years (and for catch-up immunization for those aged 13–26 years) [2] by the Advisory Committee on Immunization Practices (ACIP). ACIP also approved resolutions to add both to the Vaccines for Children Program (VFC). Many private health insurance plans follow the same coverage. Recently released U.S. data for 2008 indicate that about 37% of girls aged 13–17 years had begun the HPV series [20].

Although cost-effectiveness studies of HPV vaccination can be an important tool for policymakers, cost-effectiveness studies do not account for consumer preferences [21]. Preferences of consumers do not necessarily align with those of policymakers or providers, who may have difference objectives. Cost-effectiveness studies also do not include the value of non-medical consumer benefits, such as “peace of mind,” risk aversion, and parent–child altruism, which may be important factors in vaccine uptake and acceptability [22]. To address these important factors, we developed a conjoint-analysis (CA) survey to provide new data on preferences of mothers for HPV vaccines for their daughters.

Our study addresses three research questions. First, we hypothesized that consumers would have clear preferences over several features of HPV vaccines, favoring cervical cancer protection over all other features. To test and quantify this, we developed a CA survey and estimated the relative importance of difference vaccine features. Given related findings in the literature [22–32], we also assumed that these preferences would differ by some individual characteristics and assessed this through extensions of the main preference model. Second, we postulate that the estimated value of consumer benefits would exceed the current retail prices of HPV vaccines given the positive and increasing demand for HPV vaccines [20]. This was tested by using the CA results to estimate the average maximum “willingness-to-pay” (WTP) among our survey sample. WTP is the value that individuals place on the vaccine and may be used as a measure of private economic benefits in cost-benefit analyses of vaccine programs. Finally, we hypothesized that total uptake of HPV vaccines would increase when a second vaccine was added to the U.S., although only one was available at the time of our survey. We tested this by using the main survey data and model to predict uptake under a variety of different scenarios.

## 2. Methods

### 2.1. Survey sampling

We developed and collected a national sample of 307 U.S. mothers in June 2008 with at least one daughter aged 13–17 years who had not received an HPV vaccine. An online survey was administered by Knowledge Networks (KN), a survey research firm that maintains a probability-based national online panel that is representative of the U.S. population and built on random-digit dialing and address-based sampling, not voluntary opt-in [33]. For this study, KN randomly sampled 1485 mothers who had a female child in the household and invited them to complete a short screener for eligibility. 825 mothers (56%) responded and completed the

screener. 433 of the 825 (52%) were eligible for this study, reporting that at least one daughter aged 13–17 years living in the household had not yet received an HPV vaccine. No restrictions were placed on the number of other daughters, if any, or if the mother or any other daughters had been vaccinated against HPV. Mothers with more than one eligible daughter were told to answer the remaining survey questions thinking about the daughter whose birthday came next and who had not yet received any doses of an HPV vaccine. Finally, 307 of the 433 (71%) provided informed consent according to procedures approved by our institutional review boards (IRBs), and completed the full questionnaire.<sup>1</sup>

### 2.2. Conjoint analysis

Although we included several questions on aspects of health, HPV, cervical cancer, genital warts, vaccine experiences, and sociodemographics, the survey was primarily designed to elicit CA data. Choice-format CA is a stated-preference survey method that simulates choice behavior by eliciting tradeoffs among attributes of hypothetical goods, programs, or policies [34,35]. Also known as “stated choice” or “discrete choice experiments,” CA has been used widely in health and pharmacoeconomics, and recently, in public health applications [36,37], including vaccines. CA is particularly well-suited to evaluate preferences for HPV vaccines since only one HPV vaccine was available at the time of the survey; thus, there were no data on actual choices between alternative vaccines.

The survey contained eight main CA choice questions, which are described by vaccine “attributes,” or features, each taking on one of several levels. Fig. 1 shows an example CA choice question. Each CA question described two alternative vaccines in terms of four attributes: protection against cervical cancer (50%, 70%, 90% or 100% (full protection)), protection against genital warts (0% (no protection) or 90%), duration of protection, and out-of-pocket cost (\$0, \$100, \$300, or \$700). Subjects were then asked, “If you were actually offered the two vaccines above, which would you buy?” At the start of the CA questions, we specified that all vaccines compared would be equivalent in the number of doses (3), boosters (full series needed to restore protection after the duration shown), risk of possible side effects (rare), mode of delivery (injection), and time frame for the decision shown (within the next year). Further details on the selection of attributes and levels, survey development, and the statistical properties of CA are provided in the technical appendix.

## 3. Results

Descriptive statistics of the sample are shown in Table 1. The average age of mothers is 44 years, and the average age of daughters is 15 years. 82% of the sample is white, 60% has less than a college degree, and half has a household income between \$50,000 and \$100,000. Awareness of HPV vaccines is high: 95% of subjects report that they had heard of an HPV vaccine before, although only 57% report being somewhat or very familiar (on a 4-point Likert scale) with risk factors for HPV infection. Reported history of HPV and related conditions are 7% for HPV, 8% genital warts, 1% cervical cancer, and 5% other cancers, in the range of epidemiologic estimates [1,2,4]. One-third of mothers also report a past abnormal Pap test result.

A mother’s level of concern for her daughter about HPV, genital warts, and cervical cancer may impact perceived benefit from HPV vaccines [22]. 15% are somewhat or very concerned about cervical cancer; 13% report the same for warts and 9% for HPV. Nearly half of

<sup>1</sup> Daughter preferences were measured in a survey completed separately by the daughters that were the focus of the mothers’ survey questions. The results of the daughter survey will be reported elsewhere.

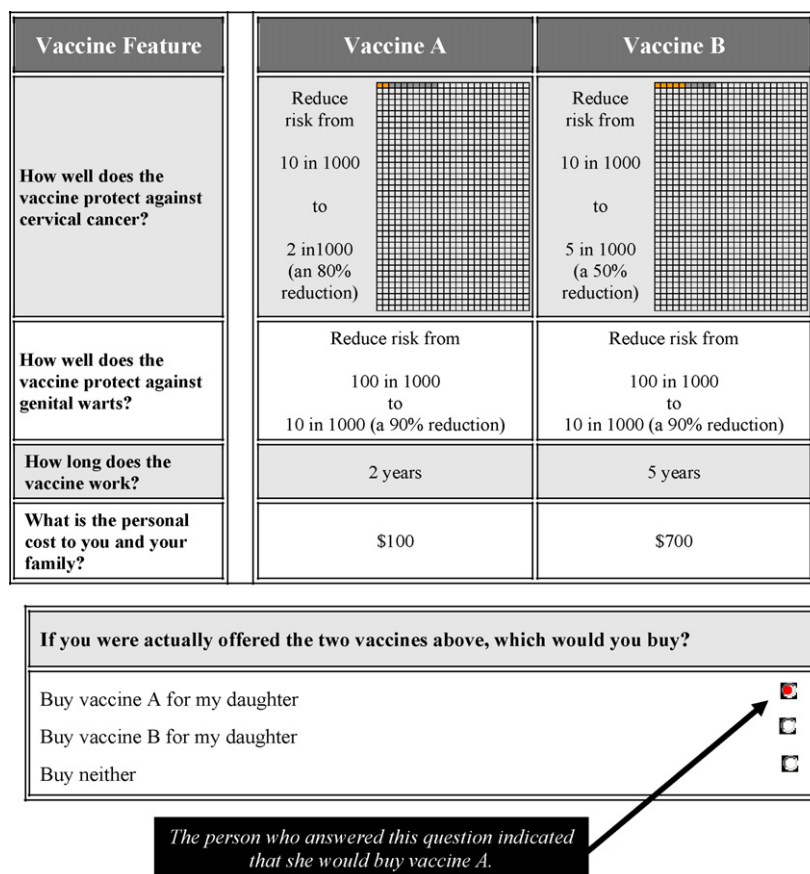


Fig. 1. Example conjoint analysis choice question.

Table 1  
Characteristics of survey respondents.

Characteristic	Mean	Standard deviation
Age of mother	44.0	5.9
Age of daughter	15.1	1.3
Black	.081	.273
Hispanic (any race)	.065	.247
Other or multiple races	.036	.189
High school degree or less	.179	.384
College graduate	.397	.490
Household income < \$50,000	.254	.436
Household income \$100,000+	.254	.436
Heard of HPV vaccines before this survey	.947	.222
Somewhat or very familiar with HPV (n = 306) <sup>a</sup>	.573	.495
Somewhat or very familiar with genital warts	.619	.486
Somewhat or very familiar with cervical cancer	.717	.451
Knows a minor who's had HPV vaccine (n = 291) <sup>b</sup>	.247	.432
Has had HPV (n = 305) <sup>a</sup>	.072	.259
Has had genital warts (n = 305) <sup>a</sup>	.075	.264
Has had cervical cancer	.013	.113
Has had other cancer	.052	.222
Has had abnormal Pap	.338	.474
Daughter has had Pap test	.111	.314
Somewhat or much more concerned about daughter's risk of HPV (n = 306) <sup>a</sup>	.092	.289
Somewhat or much more concerned about daughter's risk of genital warts	.133	.341
Somewhat or much more concerned about daughter's risk of cervical cancer	.153	.360
Believes daughter not at risk for HPV because not sexually active (n = 291) <sup>b</sup>	.481	.501
Refused a vaccine for daughter before	.212	.409
Believe vaccines are somewhat/very unsafe	.098	.297
Believes either no sex education or abstinence only should be taught in schools (n = 306) <sup>a</sup>	.216	.412

Notes: Sample size n = 307, except as noted.

<sup>a</sup> Sample size as noted because of respondent skips.

<sup>b</sup> Question asked only if mother reported having heard of an HPV vaccine before this survey.

**Table 2**  
Coefficients from mixed logit vaccine preference model.

Variable	Estimated coefficient (rescaled coefficient)	Standard error	Estimated coefficient	Standard error
50% cancer protection	-0.780*** (0.00)		-0.762***	0.155
70% cancer protection	-0.346*** (2.46)	0.086	-0.334***	0.088
80% cancer protection	0.142*** (5.23)	0.086	0.129***	0.087
100% cancer protection (omitted)	0.984*** (10.00)	0.156	0.967***	0.165
No genital warts protection	-0.414*** (2.07)	0.059	-0.394***	0.061
90% genital warts protection (omitted)	0.414*** (6.77)	0.059	0.394***	0.061
Vaccine duration 2 years	-0.748*** (0.18)	0.090	-0.742***	0.093
Vaccine duration 5 years	-0.116 (3.76)	0.087	-0.121	0.091
Vaccine duration 10 years	0.064*** (4.78)	0.077	0.056***	0.079
Vaccine duration lifetime (omitted)	0.801*** (8.96)	0.094	0.807***	0.094
Out-of-pocket cost	-0.003***	0.0002	-0.003***	0.0003
Neither vaccine (opt-out)	-2.109***	0.121	-3.692***	1.250
Neither* age of mother	-	-	-0.039**	0.018
Neither* age of daughter	-	-	0.178**	0.073
Neither* Black	-	-	-2.155***	0.635
Neither* Hispanic (any race)	-	-	-0.091	0.401
Neither* other or multiple races	-	-	0.709	0.512
Neither* high school degree or less	-	-	0.111	0.278
Neither* college graduate	-	-	0.413*	0.233
Neither* household income <\$50,000	-	-	-0.165	0.246
Neither* household income \$100,000+	-	-	-0.472*	0.243
Neither* has had HPV, genital warts, or cervical cancer	-	-	0.838***	0.273
Neither* somewhat or much more concerned about daughter's risk of HPV, genital warts, or cervical cancer	-	-	-1.394***	0.299
Neither* believes daughter not at risk for HPV because not sexually active	-	-	0.864***	0.199
Neither* refused a vaccine for daughter before or believes vaccines are somewhat/very unsafe	-	-	1.207***	0.212

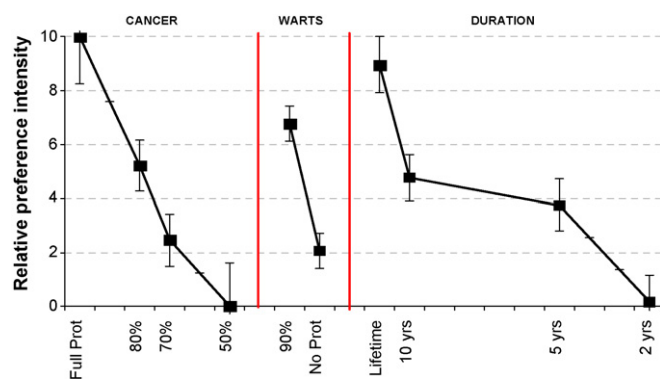
Notes: (1) Effects coded variables used for cancer protection, genital warts protection, and duration. (2) Standard errors on omitted coefficients were estimated by Krinsky–Robb parametric bootstraps. (3) Estimated standard deviations of random coefficients are reported in the technical appendix. (4) Binary indicators for dominant preferences, as described in the text, were included where significant but are not shown here as they are not key parameters of interest. (5) \*\*\* denotes  $p < .01$ , \*\* $p < .05$ , \* $p < .10$  for statistical significance relative to adjacent categories (for vaccine features) or relative to 0 for interacted terms; in both models above, the difference between 2 and 5 years duration is significant at  $p < .01$  but the difference between 5 and 10 years is not significant at conventional levels. (6) 0–10 rescaled coefficients depicted in Fig. 2 are shown in parentheses.

mothers say their daughter is not currently at risk for HPV because she is not sexually active. 11% of mothers report that their daughter has had a prior Pap test, possibly indicating that these daughters are sexually active and thus at greater risk for HPV. 22% of the sample report that sex education should be excluded from school or should be abstinence-only, a proxy for conservative values. 21% say they have previously refused a vaccine for their daughter at some point in the past, although only 10% of the sample believes that vaccines were somewhat or very unsafe.

For the first research question, Table 2 (columns 2–3) shows the statistical model of preferences. Larger numbers indicate more preferred vaccine features than smaller ones. All estimates pass basic face validity checks, with greater levels of protection, longer duration, and lower out-of-pocket costs preferred. Fig. 2 provides a visual depiction of the same data, with coefficients rescaled so that 10 is the most preferred feature, 0 is least preferred, and bars indicate 95% confidence intervals. Confirming our hypothesis, the most important attribute (over the levels shown) is cervical cancer protection, followed by duration of effectiveness. At specific attribute levels, mothers had the strongest preference for full cervical cancer protection followed by lifetime protection. The difference between these two is not statistically significantly ( $p < .05$ ), but both are significant relative to all other features and levels at  $p < .01$ . Next most important is protection against genital warts, which is not significantly greater statistically than the preference for 80% cervical cancer protection.

To assess our assumption that preferences would vary among individuals, columns 4–5 of Table 2 show the mixed logit model with individual characteristics interacted with the “neither vaccine” indicator. For the interacted terms, positive values are associated with decreased stated uptake and negative values are

associated with an increased stated uptake. Older mothers, Blacks, those from high income households (\$100,000+), and those who said they were somewhat or much more concerned about daughter's risk of HPV, cervical cancer, or genital warts were more likely to choose a vaccine than to choose “neither vaccine.” Conversely, mothers of older daughters, college graduates, those with a past diagnosis of HPV, genital warts, or cancer, those who believe their daughter is not at risk for HPV because she is not sexually active, and mother who have refused a vaccine in the past or who believe that vaccines are unsafe were less likely to choose a vaccine and selected “neither vaccine” more often.



**Fig. 2.** Relative preferences for features of HPV vaccines. Notes: figure reflects estimated coefficients from the mixed logit model without interaction terms. Estimated coefficients from the non-interacted model in Table 2 are rescaled from 0.0 (least preferred) to 10.0 (most preferred). Upper and lower bars indicate 95% confidence intervals.



**Table 3**  
Mean willingness-to-pay (WTP) for features of HPV vaccines.

Scenario/feature	Estimated WTP	95% confidence interval
"A": 70% cervical cancer protection, 90% genital warts protection, 10 year duration (relative to "neither vaccine")	\$663	[\$544, \$802]
"B": 80% cervical cancer protection, 0% genital warts protection, 10 year duration (relative to "neither vaccine")	\$560	[\$451, \$685]
WTP for 90% genital warts protection in vaccine "A" (WTP "A"–WTP "A" without warts protection)	\$238	[\$184, \$294]
WTP for increasing cervical cancer protection from 70% to 100% (WTP "A" with 100%–WTP "A" with 70%)	\$457	[\$348, \$567]
WTP for lifetime duration (WTP "A" with lifetime–WTP "A" with 10 yr. duration)	\$245	[\$175, \$319]
WTP for ideal technology (WTP for vaccine with 100% cancer protection, 0% warts protection, and lifetime duration relative to "neither vaccine")	\$1086	[\$159, \$264]

Notes: WTP calculations are mean estimates derived from the mixed logit model without interactions in Table 2. (Results from interactions model are comparable when evaluated at the mean of the interacted terms.)

Table 3 shows the estimated mean WTP for features of HPV vaccines, used to address the second research question. The mean value of vaccines with the features of current bivalent and quadrivalent HPV vaccines is \$560–\$660. Both estimates are significantly different from \$0 at  $p < .01$  and statistically different from each other at  $p < .05$ . Mean WTP for 90% genital warts protection is \$238 ( $p < .01$ ). WTP for protection that would last a lifetime instead of 10 years is \$245 ( $p < .01$ ). Cervical cancer protection is highly valued, consistent with the strong preference for vaccine efficacy indicated in Fig. 2. An increase from 70% to 100% protection is estimated to be valued at \$457 ( $p < .01$ ). WTP for an ideal technology with the best of all features shown is \$1086 ( $p < .01$ ).

For the third research question, Table 4 provides estimates of predicted uptake for similar scenarios as with WTP. The baseline scenario is a vaccine costing \$300 out-of-pocket and similar to the currently approved quadrivalent vaccine (70% cervical cancer protection, 90% genital warts protection, 10 years assumed duration). Predicted demand for this vaccine is 67% [61–73%]. Factors beyond those in our survey influence actual decisions, so we emphasize relative changes from the baseline. Eliminating out-of-pocket costs would increase uptake almost 22% [16–29%]. Our hypothesis about total uptake increasing when a second HPV vaccine is added to the U.S. environment is supported by a simulation. Given two alternatives, our data and model predict that 78% [73%, 81%] would choose an HPV vaccine, a 16% [11%, 21%] increase from the baseline level of only one vaccine. This reflects predicted substitution away from the quadrivalent-like vaccine; with two choices, 33% [27%, 38%] choose the bivalent-like vaccine and 45% [40%, 51%] the quadrivalent-like vaccine (vs. 67% at baseline).

Finally, we note that 19% of the sample always chose "neither vaccine" for all the scenarios that they were shown. Such subjects are not in the market for any HPV vaccine, at least over the range of features shown in the experimental design. Some of these subjects may be willing to choose a vaccine under different scenarios than they were shown (e.g., improved technology, additional protection, long-term safety data), while others may not choose a vaccine under any conditions because of religious considerations or opposition to vaccines in general. However, we

have no data to identify motives for those who rejected all scenarios.

#### 4. Discussion

This study provides new data on mothers' preferences for vaccinating daughters aged 13–17 years against HPV. To date, no published research has quantified preferences of mothers for HPV vaccines for economic evaluation. Although there is a large literature on cost-effectiveness and general acceptability of HPV vaccines, there is a gap in our understanding of how parents value HPV vaccines and vaccine features. Understanding the determinants of HPV vaccine demand is particularly important for designing more effective vaccine-promotion programs and for reassessing public health recommendations and guidelines as new vaccines are made available. To achieve this, we developed a CA survey and used an economic model of decision-making to estimate the value of private benefits for cervical cancer risk reduction. The results pass fundamental face validity checks: greater levels of protection for cancer or warts are preferred to less, longer duration of protection is preferred to shorter duration, and lower out-of-pocket cost is preferred. Mothers had the strongest preference for full cervical cancer protection followed by lifetime protection.

In our sample and analysis, the estimated mean private benefits (WTP) of current bivalent and quadrivalent HPV vaccines are approximately \$560–\$660. A different sample or survey design may produce different values, possibly within the estimated 95% confidence interval. Our estimates are significantly different from \$0 at  $p < .01$ , so a simple cost-benefit assessment, they may be compared to the average U.S. retail price of \$375 for the quadrivalent vaccine [39]. Since estimated benefits exceed retail costs, mothers would, on average, realize net private benefits from vaccinating their daughters against HPV infection, confirming our postulate about net positive benefits at current costs.

Our findings may be compared to several previous findings in the existing literature on the economics and acceptability of HPV vaccines. In Jit et al.'s [10] cost-effectiveness study, they find that

**Table 4**  
Changes in predicted uptake for alternative policy scenarios.

Feature/scenario	Uptake level or relative change	95% confidence interval
One vaccine only available, "A" (70% cervical cancer protection, 90% genital warts protection, 10 year duration, \$300 out-of-pocket cost)	67.3%	[61.4, 72.9]
Decrease price of "A" to \$0	+21.7%	[15.8, 28.6]
Two vaccines available, "A" and "B." Vaccine "B" has 80% cervical cancer protection, 0% genital warts protection, 10 year duration, \$300 out-of-pocket cost	77.9% increase +15.9% relative to A only	[73.6, 81.9] [relative increase: +11.4, +21.4]
Predicted share choosing vaccine "A"	45.4%	[40.0, 50.8]
Predicted share choosing vaccine "B"	32.5%	[27.5, 37.8]

Notes: Estimates are from the mixed logit model without interactions from Table 2. (Results from interactions model are comparable when evaluated at the mean of the interacted terms.)

the cost-effectiveness of the bivalent vaccine in routine vaccination would be comparable to that of the quadrivalent vaccine if the bivalent vaccine were 13–23 GBP (\$20–35 USD) less expensive per dose, or 39–69 GBP (\$60–105 USD) per series, than the quadrivalent vaccine (depending on the target age group). Similarly, Brisson et al. [40] estimated that the bivalent vaccine would have to be \$105 (range 53–165) CAN dollars (\$97 USD, range 49–152) cheaper than the quadrivalent to equate their cost-effectiveness ratios. Our benefit analysis finds that the quadrivalent vaccine provides a statistically significant larger (\$237) economic benefit to mothers than the bivalent vaccine. However, if the bivalent vaccine provides greater cancer protection [18,19], the difference in consumer benefit narrows to \$103 (\$663 quadrivalent, \$560 bivalent) and is no longer statistically significant. Regardless, a cost-benefit analysis using these results may lead to somewhat different conclusions than decisions based on the cost-effectiveness analyses of Jit et al. [10] or Brisson et al. [40].

Our predicted uptake results may be compared to Centers for Disease Control and Prevention (CDC) estimates of coverage for HPV vaccines in the U.S. from the National Immunization Survey (NIS) [20]. In 2008, 37% of girls 13–17 were estimated to have begun the quadrivalent HPV series, a substantial increase over 2007. Our base case scenario in Table 4, which may approximate the U.S. environment in June 2008, was about 67%. This is significantly higher than the NIS estimates, but may indicate longer-term uptake observable a few years from now. However, many factors besides those in our survey may influence actual decisions, such as physician recommendations [22] and the use of active offer [28] or reminder programs [41]. Recent reports [42,43] show that providers are increasingly offering and recommending HPV vaccines, with a few exceptions [44]. We recommend focusing on our estimates of relative changes in uptake rather than absolute levels, since the relative changes are predicted by factors within our data. Nonetheless, CA has been shown to predict actual decisions well in the limited contexts in which stated and actual choices are compared (e.g., [45]; and comparing [36] and [46]).

Our estimates compare favorably to previous results on stated vaccine acceptability. Our results are close to a 70% level for received or intend to vaccinate among a study of females 13–26 [26] but somewhat higher than a 48% level for received or intend to vaccinate among girls 11–17 [27]. Longer-term surveillance will be needed to evaluate our estimates against observed trends. One explanation for our higher estimates of uptake is that we report higher levels of HPV vaccine awareness than many other studies [22,23], which were mainly based on data from before, or just after, the approval of the quadrivalent vaccine in the U.S. in June 2006. Since direct consumer advertising started after that, it is not surprising that we found that 95% of an audience presumably targeted by marketers (mothers of eligible teenage girls) had heard of a vaccine for HPV by June 2008. Finally, many of our findings, although not all, from the interacted model in Table 2 match well with other studies [22,27].

Although we believe that this study makes a major contribution by addressing an area previously unstudied in the literature, our analysis has some limitations. First, the data are from a national sample but are not nationally representative since sampling weights do not apply to the statistical model (see Appendix A). Data were obtained from mothers with a daughter aged 13–17 who had not yet received an HPV vaccine. We excluded mothers if all eligible daughters aged 13–17 years had previously received an HPV vaccine because we felt it would be difficult for them to evaluate hypothetical vaccine scenarios that were not actually available to them. As a result, our estimates about uptake do not reflect the entire population. Second, CA, like all stated preference methods including traditional WTP or CV, has been critiqued for its cognitive burden and design matters such as information bias or framing

[47], hypothetical bias or realism [48], and interpretation of the “neither vaccine,” or “opt-out,” parameter [49]. While results are specific to this model and sample, they are robust to the levels of accepted statistical confidence intervals. Third, because our focus was on vaccine features, we did not present information about the travel or time cost associated with having to get three injections about 2 months apart for each. These aspects are part of consumer costs, whether paid directly out-of-pocket or not, and may reduce consumers’ net welfare, or the difference between their maximum WTP and the out-of-pocket cost paid. Although many studies do not formally include such costs, this may be one explanation for another limitation of our results, the relatively high predicted uptake rates, discussed above. Other factors beyond those in our survey affect individual decisions and may be responsible for some of the difference between our predicted rates and those from CDC’s survey data [20]. Finally, the 20% of the sample that did not choose a vaccine in any of the scenarios shown should be considered. This segment does not cause problems for estimating relative preferences (since no vaccine tradeoffs were observed for these), but it may influence the uptake estimates if not properly controlled for. We included dominance controls and an “opt-out” coefficient, as is standard in the conjoint literature [34,38]. Future research should explore this area through the use of a “revealed preference” follow-up survey in which stated and actual choices are combined.

Our study also has many strengths. We believe this is the first study to rigorously estimate mothers’ preferences for HPV vaccines for quantifying private economic benefit (WTP) and uptake analysis. We provide new information about consumer preferences and welfare from HPV vaccines, an approach that is increasingly recognized and valued [35,37] in other health care and public health applications. Our results provide not just a snapshot of current preferences and valuations, but a framework for conducting policy simulations about changes to vaccine technology, insurance coverage (through out-of-pocket cost), and the number of vaccines available to consumers.

## Acknowledgements

This study was supported by the Centers for Disease Control and Prevention (CDC) under contract # 200-2002-00776TO43 with RTI International. The findings and conclusions in the article are those of the authors and do not necessarily represent the views of CDC or RTI. The study was reviewed and approved by IRBs at RTI and CDC. Harrell Chesson and Lauri Markowitz of CDC provided valuable feedback several times. Juan Marcos Gonzalez, Thomas Hylands, Olga Khavjou, Ateasha Mohamed, Semra Özdemir, and Jui-Chen Yang of RTI all assisted in the study. Arne Rise Hole of the University of Sheffield generously shared Stata code. We also benefited from feedback by participants in seminars at CDC, RTI International, *Vaccine* 2nd Global Congress, the American Society of Health Economists 2008 Meeting, and the 2009 Conjoint Analysis in Health Conference.

## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.vaccine.2009.12.024.

## References

- [1] Dunne EF, Unger ER, Sternberg M, McQuillan G, Swan DC, Patel SS, et al. Prevalence of HPV infection among females in the United States. *JAMA* 2007;297:813–9.
- [2] Markowitz LE, Dunne EF, Saraiya M, Lawson HW, Chesson H, Unger ER. Quadrivalent human papillomavirus: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 2007;56:1–24.

- [3] Parkin DM, Bray F. The burden of HPV-related cancers. In: *Vaccine*, vol. 24; 2006. p. S11–25 [chapter 2].
- [4] U.S. Cancer Statistics Working Group. United states cancer statistics: 1999–2005 incidence and mortality web-based report. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute; 2009. Available at: [www.cdc.gov/uscs](http://www.cdc.gov/uscs) (accessed 31 August 2009).
- [5] Fleurence RL, Dixon JM, Milanova TF, Beusterien KM. Review of the economic and quality-of-life burden of cervical human papillomavirus disease. *Am J Obstet Gynecol* 2007;196:206–12.
- [6] Chesson HW, Blandford JM, Gift TL, Tao G, Irwin KL. The estimated direct medical cost of sexually transmitted diseases among American youth, 2000. *Perspect Sex Reprod Health* 2004;36:11–9.
- [7] Insinga RP, Dasbach EJ, Elbasha EH. Assessing the annual economic burden of preventing and treating anogenital human papillomavirus-related disease in the US: analytic framework and review of the literature. *Pharmacoeconomics* 2005;23:1107–22.
- [8] World Health Organization (WHO). Cervical cancer, human papillomavirus (HPV), and HPV vaccines: key points for policy-makers and health professionals. Geneva: WHO/RHR/08.14; 2007.
- [9] Kim JJ, Goldie SJ. Health and economic implications of HPV vaccination in the United States. *N Engl J Med* 2008;359:821–32.
- [10] Jit M, Choi YH, Edmunds WJ. Economic evaluation of human papillomavirus vaccination in the United Kingdom. *BMJ* 2008;377:a769.
- [11] Elbasha EH, Dasbach EJ, Insinga RP. Model for assessing human papillomavirus vaccination strategies. *Emerg Infect Dis* 2007;13(1):28–41.
- [12] Bosch FX, de Sanjose S, Goldie S, Castellsague X, de Sanjose S, Garnett G, et al. Assessment of causality. *J Natl Cancer Inst Monogr* 2003;31:3–13 [chapter 1].
- [13] Lacey CJ, Lowndes CM, Shah KV. Burden and management of non-cancerous HPV-related conditions: HPV-6/11 disease. *Vaccine* 2006;24:S35–41 [chapter 4].
- [14] Herrero R. Human papillomavirus (HPV) vaccines: limited cross-protection against additional HPV types. *J Infect Dis* 2008;199:919–22.
- [15] Cutts FT, Franceschi S, Goldie S, Castellsague X, de Sanjose S, Garnett G, et al. Human papillomavirus and HPV vaccines: a review. *Bull World Health Organ* 2007;85:719–26.
- [16] Alphs HH, Gambhira R, Karanam B, Roberts JN, Jagu S, Schiller JT, et al. Protection against heterologous human papillomavirus challenge by a synthetic lipopeptide vaccine containing a broadly cross-neutralizing epitope of L2. *PNAS* 2008;105:5850–5.
- [17] Roden RB, Ling M, Wu TC. Vaccination to prevent and treat cervical cancer. *Hum Pathol* 2004;35:971–82.
- [18] Schwarz TF, Spaczynski M, Schneider A, Wysocki J, Galaj A, Perona P, et al. Immunogenicity and tolerability of an HPV-16/18 AS04-adjuvanted prophylactic cervical cancer vaccine in women aged 15–55 years. *Vaccine* 2009;27:581–7.
- [19] Paavonen J, Naud P, Salmerón J, Wheeler CM, Chow S-N, Apter D, et al. Efficacy of human papillomavirus (HPV)-16/18 AS04-adjuvanted vaccine against cervical infection and precancer caused by oncogenic HPV types (PATRICIA): final analysis of a double-blind, randomised study in young women. *Lancet* 2009;374:310–4.
- [20] Centers for Disease Control and Prevention (CDC). National, state, and local area vaccination coverage among adolescents aged 13–17 years—United States, 2008. *MMWR Morb Mortal Wkly Rep* 2009;58:997–1001.
- [21] Ryan M, Farrar S. Using conjoint analysis to elicit preference for health care. *BMJ* 2000;320:1530–3.
- [22] Brewer NT, Fazekas KI. Predictors of HPV vaccine acceptability: a theory-informed, systematic review. *Prev Med* 2007;45:107–14.
- [23] Christian WJ, Christian A, Hopenhayn C. Acceptance of the HPV vaccine for adolescent girls: analysis of state-added questions from the BRFSS. *J Adolesc Health* 2009;44:437–45.
- [24] Zimet GD, Mays RM, Sturm LA, Ravert AA, Perkins SM, Juliar BE. Parental attitudes about sexually transmitted infection: vaccination for their adolescent children. *Arch Pediatr Adolesc Med* 2005;159:132–7.
- [25] Bair RM, Mays RM, Sturm LA, Perkins SM, Juliar BE, Zimet GD. Acceptability to Latino parents of sexually transmitted infection vaccination. *Ambul Pediatr* 2008;8:98–103.
- [26] Kahn JA, Rosenthal SL, Jin Y, Huang B, Namakydoust A, Zimet GD. Rates of human papillomavirus vaccination, attitudes about vaccination, and human papillomavirus prevalence in young women. *Obstet Gynecol* 2008;111:1103–10.
- [27] Rosenthal SL, Rupp R, Zimet GD, Meza HM, Loza ML, Short MB, et al. Uptake of HPV vaccine: demographics, sexual history and values, parenting style, and vaccine attitudes. *J Adolesc Health* 2008;43:239–45.
- [28] Tozzi AE, Rava L, Stata D, et al. Attitudes towards HPV immunization of Italian mothers of adolescent girls and potential role of health professionals in the immunization program. *Vaccine* 2009;27:2625–9.
- [29] Palanca-Tan R. The demand for a dengue vaccine: a contingent valuation survey in Metro Manila. *Vaccine* 2008;26(7):914–23.
- [30] Lucas ME, Jeuland M, Deen J, Lazaro N, MacMahon M, Nyamete A, et al. Private demand for cholera vaccines in Beira, Mozambique. *Vaccine* 2007;25:2599–609.
- [31] Hsu HC, Lin RS, Tung TH, Chen TH. Cost-benefit analysis of routine childhood vaccination against chickenpox in Taiwan: decision from different perspectives. *Vaccine* 2003;21:3982–7.
- [32] Whittington D, Matsui-Santana O, Freiburger J, Van Houtven J, Pattanayak GS. Private demand for a HIV/AIDS vaccine: evidence from Guadalajara, Mexico. *Vaccine* 2002;20:2585–91.
- [33] Dennis JM. Summary of KnowledgePanel® design. Online at <http://www.knowledgenetworks.com/ganp/docs/KnowledgePanel-Summary-Design-Description-041009.pdf> [accessed 31 August 2009].
- [34] Louviere J, Hensher D, Swait J. Stated choice methods: analysis and application. Cambridge: Cambridge University Press; 2000.
- [35] Johnson FR, Banzhaf MR, Desvousges WH. Willingness to pay for improved respiratory and cardiovascular health: a multiple-format, stated-preference approach. *Health Econ* 2000;9:295–317.
- [36] Brown DS, Finkelstein EA, Brown DR, Buchner DM, Johnson FR. Estimating older adults' preferences for walking programs via conjoint analysis. *Am J Prev Med* 2009;36:201–7.
- [37] Wordsworth S, Ryan M, Waugh N. Costs and benefits of cervical screening IV: valuation by women of the cervical screening programme. *Cytopathology* 2001;12(6):367–76. Dec.
- [38] Hensher DA, Rose JM, Greene WH. Applied choice analysis. Cambridge: Cambridge University Press; 2005.
- [39] Centers for disease control and prevention (CDC). HPV vaccine information for young women; <http://www.cdc.gov/std/hpv/STDFact-HPV-vaccine-young-women.htm> [accessed 12 May 2009].
- [40] Brisson M, Van de Velde N, De Wals P, Boily M-C. The potential cost-effectiveness of prophylactic human papillomavirus vaccines in Canada. *Vaccine* 2007;25(29):5399–408.
- [41] Daley MF, Curtis CR, Pyrzanowski J, et al. Adolescent immunization delivery in school-based health centers: a national survey. *J Adolesc Health* 2009;45:445–52.
- [42] Leddy MA, Anderson BL, Gall S, Schulkin J. Obstetrician-gynecologists and the HPV vaccine: practice patterns, beliefs, and knowledge. *J Pediatr Adolesc Gynecol* 2009;22:239–46.
- [43] Jensen ME, Hartenbach E, McElroy JA, et al. Brief report: Measuring the attitudes of health care professionals in Dane County toward adolescent immunization with HPV vaccine. *WMJ* 2009;108:203–5.
- [44] Kahn JA, Cooper HP, Vadaparampil ST, et al. Human papillomavirus vaccine recommendations and agreement with mandated human papillomavirus vaccination for 11-to-12-year-old girls: a statewide survey of Texas physicians. *Cancer Epidemiol Biomarkers Prev* 2009;18:2325–32.
- [45] Whitehead JC. Environmental risks and averting behavior: predictive validity of jointly estimated revealed and stated behavior data. *Env Resource Econ* 2005;32:301–16.
- [46] Finkelstein EA, Brown DS, Brown DR, Buchner DM. A randomized study of financial incentives to increase physical activity among sedentary older adults. *Prev Med* 2008;47:182–7.
- [47] San Miguel F, Ryan M, Amaya-Amaya M. 'Irrational' stated preferences: a quantitative and qualitative investigation. *Health Econ* 2005;14:307–22.
- [48] Viney R, Lanscar E, Louviere JJ. Discrete choice experiments to measure preferences for health and health care. *Expert Rev Pharmacoeconomics Outcomes Res* 2002;2:319–26.
- [49] Flynn TN, Louviere JJ, Peters TJ, Coast J. Best-worst scaling: what it can do for health care research and how to do it. *J Health Econ* 2007;26:171–89.