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Prevalence and Predictors of Human Papillomavirus (HPV) Vaccination among Young Women Surviving Childhood Cancer

James L. Klosky, PhD¹, Brianne Favaro, B.A.², Kelly R. Peck, M.A.^{1,5}, Jessica L. Simmons, M.S.¹, Kathryn M. Russell, Ph.D.¹, Daniel M. Green, M.D.^{3,4}, and Melissa M. Hudson, M.D.^{3,4}

¹Department of Psychology, St. Jude Children's Research Hospital, 262 Danny Thomas Place, Memphis, TN 38105-2794

²Department of Psychology, Winona State University, 175 W Mark St, Winona, MN 55987

³Department of Oncology, St. Jude Children's Research Hospital, 262 Danny Thomas Place, Memphis, TN 38105-2794

⁴Department of Epidemiology & Cancer Control, St. Jude Children's Research Hospital, 262 Danny Thomas Place, Memphis, TN 38105-2794

⁵Department of Psychology, University of Mississippi, 205 Peabody, University, MS 38677

Abstract

Purpose—Human papillomavirus (HPV) is a sexually transmitted infection and the cause of cervical and other cancers. Vaccination is available to protect against genital HPV and is recommended for individuals aged 9-26 years. This study aimed to estimate the prevalence of HPV vaccination among childhood cancer survivors and to identify factors associated with vaccine outcomes.

Methods—Young adult females with ($n = 114$; M age = 21.18 years, $SD = 2.48$) and without ($n = 98$; M age = 20.65 years, $SD = 2.29$) a childhood cancer history completed surveys querying HPV vaccination initiation/completion, as well as sociodemographic, medical, and health belief factors. Multivariable logistic regression was used to calculate odds ratios (OR) and 95% confidence intervals (CI) for vaccine outcomes.

Results—Among survivors, 38.6% (44/114) and 26.3% (30/114) initiated or completed vaccination compared to 44.9% (44/98) and 28.6% (28/98) among controls, respectively. In the combined survivor/control group, physician recommendation (OR = 11.24, 95% CI, 3.15 – 40.14), and familial HPV communication (OR = 7.28, 95% CI, 1.89 – 28.05) associated with vaccine initiation. Perceptions of vaccine benefit associated with vaccine completion (OR = 10.55, 95% CI, 1.59 – 69.92), whereas perceptions of HPV-related severity associated with non-completion (OR = 0.14, 95% CI, 0.03 – 0.71).

Conclusion—Despite their increased risk for HPV-related complication, a minority of childhood cancer survivors have initiated or completed HPV vaccination. Modifiable factors associating with vaccine outcomes were identified.

Implications—HPV vaccination is a useful tool for cancer prevention in survivorship, and interventions to increase vaccine uptake are warranted.

Keywords

Oncology; Young Adults; Human Papillomavirus; Vaccination

INTRODUCTION

Genital human papillomavirus (HPV) is the most common sexually transmitted infection (STI) in the United States. Almost 80 million Americans are currently infected with HPV, with an estimated 14 million becoming newly infected annually [1]. Whereas persistent high-risk HPV plays a causal role in over 90% of cervical and anal cancers, it is also responsible for 63-75% of oropharyngeal, vaginal, vulvar, and penile cancers [2-4]. Approximately 75% of new HPV diagnoses are made between the ages of 15 and 24 years [5], with women being at highest risk for contracting HPV between 17 and 26 years [6]. Nearly 80% of sexually-active women contract HPV during their lifetime with those younger at sexual debut or having an increased number of lifetime partners being at highest risk for infection [7, 8]. Genital HPV is prevalent due to the ease of transmission; skin to skin contact via oral, anal, or vaginal sex, or even digital-genital contact with someone HPV + [9]. As a result, HPV vaccination is indicated as a preventive effort prior to sexual debut.

Relative to those without a history of childhood cancer, female survivors have an overall 40% increased risk of developing a late HPV-associated cancer [10]. This risk increases among those previously treated with radiation therapy; the standardized incidence ratio for developing a late vaginal cancer in this group, for example, is 11.0 (95% confidence interval, 3.5 - 27.0). One potential mechanism explaining this increased risk in survivors is immunocompromise secondary to cancer therapy. Fortunately, HPV vaccination was first approved for use in females in 2006 and is now recommended for both immunocompetent and compromised survivors [11-13].

Despite the potential health benefits associated with HPV vaccination, as of 2012, only 33-35% of population 19-26 year old females have initiated the HPV vaccine [9, 14]. However, even with low vaccination rates, HPV infections have dropped by 56% in the U.S. since vaccine introduction [11]. Commonly reported barriers to initiating vaccination include perceptions that vaccination is unnecessary, insufficient vaccine knowledge, safety concerns, lack of physician recommendation, not being sexually active, being in a monogamous relationship, and falling outside of the vaccine age indication [14-16]. In order to achieve maximum vaccine benefit, rates of initiation and completion must increase.

To assist in vaccine promotion, factors associated with vaccination initiation and completion must be identified. Among population young adults, race, sexual behavior, and social history appear to have a particular influence on vaccine uptake [12, 15, 17, 18, 19, 20]. Although

young women are old enough to independently consent to HPV vaccination, parental attitudes regarding vaccination also appear to play a key role in the formation of such perceptions [16]. For example, maternal approval of HPV vaccination and mother-daughter communication about sex were predictive of vaccine completion among undergraduates between the ages 18-25 [21], whereas parental concerns about vaccine safety remain a significant barrier to vaccine initiation [22]. Physician recommendation may be particularly influential in overcoming barriers to vaccination; strong physician recommendation for HPV-vaccination, for example, has consistently been associated with vaccine initiation among young women [16, 18, 20, 23]. When non-vaccinated 18-22 year olds were asked if they would initiate HPV vaccination secondary to a physician recommendation delivered with conviction, 90% reported they would likely initiate. However, intention does not always translate to action, as only half of individuals who intended to initiate the vaccine actually initiated [17]. Despite these findings, more research is needed to make conclusive statements regarding predictors of vaccine initiation and completion among young women surviving childhood cancer.

Survivors of pediatric cancer are at an increased risk for HPV-related cancers and complication, and later associated malignancies [10, 24]. Despite this increased susceptibility, rates of HPV vaccination initiation and completion for adolescent survivors of childhood cancer are slightly lower when compared to controls [25]. Moreover, there is a paucity of research examining factors associated with vaccine uptake and completion among young adult cancer survivors. Therefore, the purpose of this study is to estimate the prevalence of HPV vaccination among young women surviving childhood cancer, while identifying factors associated with HPV vaccination initiation and completion in those with and without a childhood cancer history.

METHODS

Participants

Young women surviving childhood cancer were recruited from the After Completion of Therapy (ACT) Clinic at St. Jude Children's Research Hospital. The ACT Clinic is a long-term follow-up clinic for childhood cancer survivors who are greater than 5 years post diagnosis and two years disease free. Eligibility criteria for study participants included: 1) 18 – 26 years of age, 2) proficiency in reading and writing English, and 3) cognitively able to understand and complete the study questionnaire. Over an 18-month interval, a total of 114 women with a history of childhood cancer (“cancer survivors,” mean age = 21.18 years, SD = 2.48) and 98 women without cancer (“controls,” mean age = 20.65 years, SD = 2.29) were enrolled in the study and completed questionnaires. See Figure 1 for participation rates among survivors, and Table 1 for participant characteristics.

Survivors were recruited during regularly scheduled ACT Clinic visits. A trained member of the research team explained the purpose of the study and obtained verbal informed consent as approved by the Institutional Review Board (IRB). After consent was obtained, participants took approximately 15-30 minutes to complete study questionnaires. Each participant was then asked to provide contact information for up to 5 acquaintances. This was done in efforts to obtain a control sample demographically similar to the cancer group.

Potential control participants were contacted via telephone. Those who verbally consented were provided the option of completing the study questionnaire online or via a mailed paper survey (n=28). The control sample was supplemented by college students taking Introductory Psychology (n = 70) at the University of Memphis (study IRB approved at both institutions). Questionnaires were identical for all groups. Both acquaintance controls and college control groups were combined into one larger control group (n=98). After completing questionnaires, all participants were provided with an information sheet on HPV and HPV vaccination.

Outcome Variables

HPV vaccine initiation was defined as a binary outcome variable such that participants who reported receiving one or more HPV vaccine doses were categorized as “initiated,” whereas those reporting zero doses were categorized as “non-initiated.” HPV vaccine completion was also defined as a binary outcome variable such that participants who reported receiving all three vaccine doses were categorized as “completers,” whereas those who reported receiving at least one vaccine dose (but less than three doses) were categorized as “non-completers.” HPV vaccination completion was only examined as an outcome variable among those participants having reported initiation of the vaccine.

Independent Variables

All participants completed questionnaires regarding their HPV vaccination history, in addition to sociodemographic, medical and sexual history information. Cancer-specific data was abstracted from survivors’ medical records.

Sociodemographic, Medical, and Sexual History Variables—Participants provided demographic information, including age, race/ethnicity, marital status, education level, and annual household income, as well as gynecological, relationship, and sexual behavior history (i.e., history of pap smears, safe sex practices, and number of partners, etc.). Items were adapted from previously published HPV research studies [23, 26-31]. Medical and treatment history, including cancer type, time since diagnosis, and age at diagnosis were obtained from the participants’ institutional medical records.

HPV Vaccine Health Beliefs and HPV Communication—The HPV Vaccine Health Beliefs Questionnaire was designed to assess perceptions of vulnerability to HPV, severity of HPV, barriers to initiating vaccine, and benefits and efficacy of the vaccine [32]. This instrument has shown high internal reliability and acceptable predictive validity [32]. An additional scale measuring vaccine-related self-efficacy was also included, adapted from a previously validated survey [33, 34]. Familial communication regarding the messages and purpose of HPV vaccination was assessed via a 4-item scale adapted from Brabin and colleagues [26].

Statistical Analysis

Univariate analyses were conducted to examine differences between groups (cancer and control) regarding HPV vaccination initiation and completion. Univariate comparisons with *p*-values less than .10 were included in the multivariable models (vaccine initiation and

completion). Differences for continuous variables (age, health beliefs, communication, and HPV knowledge) were assessed using univariate oneway analysis of variance (ANOVA). All other variables were categorical and assessed using Chi Square tests or Fisher's Exact test. Multivariable logistic regression models were used to calculate odds ratios (OR) and 95% confidence intervals for vaccine outcomes.

Given that no significant differences emerged between groups on vaccination outcomes, the cancer survivor and control groups were combined for subsequent analyses, including the presented multivariate models. Despite the equivalency in vaccine status across groups, participant medical status (cancer vs. control) was retained in the presented models.

RESULTS

Prevalence

Among cancer survivors, 38.6% (44/114) initiated the HPV vaccine compared to 44.9% (44/98) of the control group. Furthermore, 68.2% (30/44) of the survivors and 63.6% (28/44) of the controls who initiated the vaccine subsequently completed the vaccine series. No significant differences were identified with regards to rate of vaccine initiation or completion between survivors and healthy controls.

Univariate Cancer/Control Comparisons

Univariate differences emerged between cancer and control groups on race/ethnicity ($p < .001$; See Table 1). Specifically, a greater proportion of the cancer participants were white relative to control participants. Due to this significant group difference, race/ethnicity was included in both the vaccine initiation and completion models. No other significant cancer/control differences were identified.

HPV Vaccine Initiation

In the combined sample group of 212 participants, 41.5% (n=88) had initiated the HPV vaccination series. Univariate analyses revealed significant differences between those who have/have not initiated the HPV vaccine (Tables 2 and 3). On the basis of univariate findings, the multivariable model for HPV vaccination initiation included: group (cancer/control), race, education, current dating status, current sexual activity status, history of gynecologic care, history of annual Pap test, history of STI, lifetime number of opposite sex partners, birth control use at last intercourse, doctor recommendation for vaccine, HPV communication, health beliefs of HPV severity, barriers to vaccination, benefits to vaccination, and self-efficacy regarding HPV vaccination. The final multivariable logistic regression model predicting binary vaccine initiation outcome indicated that physician recommendation for vaccine (OR = 11.24, 95% CI 3.15 - 40.14, $p < .001$), and familial HPV communication (OR = 7.28, 95% CI 1.89 - 28.05, $p = .01$) were associated with an increased likelihood of initiating the HPV vaccination (Table 4).

HPV Vaccine Completion

In the combined sample group of 88 vaccine initiated participants, 65.9% (n=58) had completed the HPV vaccine series. Univariate analyses for participants who had initiated the

vaccine revealed significant differences between those who have/have not completed the HPV vaccine (Tables 2 and 3). On the basis of univariate findings, the multivariable model for HPV vaccination completion included: group (cancer/control), race, education, health beliefs of HPV severity, barriers to vaccination, and benefits of vaccination (Table 5). The final multivariable logistic regression model predicting binary vaccine completion outcome (among those who had initiated the vaccine series) indicated that young women with high perceptions of vaccine benefit were more likely to have completed the vaccine series (OR = 10.55, 95% CI 1.59 – 69.92, $p = .02$; See Table 5). Additionally, young adults expressing increased perceptions of HPV-related severity were less likely to have completed the vaccine series (OR = 0.14, 95% CI 0.03 – 0.71, $p = .02$).

DISCUSSION

Advances in the treatment of childhood cancer have resulted in a majority of patients living into adulthood [35]. Given the increased number of survivors, attention has been focused on preventing medical late effects and promoting quality of life in survivorship [36]. HPV vaccination is one tool used to reduce the HPV cancer burden in this population; however, low rates of vaccination initiation and completion in this group necessitate further examination of the determinants of vaccine uptake [12, 14, 37].

The results of our study found that 38.6% of cancer survivors have initiated the vaccine series, whereas 26.3% have completed it. Comparatively, 44.9% and 28.6% initiated and completed the series within the control group. Few differences in factors influencing vaccine uptake were identified among cancer survivor and control groups. Although survivors are at an increased risk for HPV-related complication, they were less likely to engage in vaccination relative to the control group. While this finding was not statistically significant, it is concerning based on the increased health vulnerability of childhood cancer survivors.

Within the combined survivor and control group, physician recommendation and familial HPV communication were associated with increased vaccine initiation. Our study aligns with previous research showing that physician recommendation for HPV immunization is a robust predictor of vaccine uptake [17]. However, it is interesting to note that survivors of childhood cancer were significantly less likely to report receiving a recommendation to vaccinate compared to controls ($\chi^2=4.08$, $p=.04$). Given survivors' frequent medical encounters and increased risk for HPV-related complication, physicians have ample opportunity to recommend HPV vaccination; yet, these data suggest that survivors are less likely to receive effective vaccine messaging [38]. These less than optimal vaccination rates among survivors may be explained by a lack of clarity regarding which provider (e.g. survivorship specialist, primary care provider, OB/GYN, etc.) is primarily responsible for discussing HPV vaccination with survivors. Physician communication is the most influential predictor of vaccine initiation; therefore, future guidelines should specify which physician in the survivor care constellation should be responsible not only for inquiring about and recommending the vaccine, but also for following-up regarding vaccine uptake. Alternatively, vaccine messaging from all medical providers interfacing with survivors (e.g. physicians, nurses, physician assistants, fellows, etc.) should also result in increased vaccine update in this group.

Once the vaccine has been initiated, the series must be completed to achieve maximum protection [12]. Physician communication regarding vaccine benefits and potential consequences of not completing the vaccine series should be prioritized in patient encounters, and may serve as mechanisms to promote vaccine completion post initiation. The present findings suggest that those who have completed the vaccine series are less concerned that exposure to HPV will have severe consequences. However, those who have initiated but not completed the series are aware of the risks (hence vaccine initiation) but are also aware that without having finished the series, they are not fully protected (and could experience more severe HPV-related complications post exposure). Given the opportunity, interventionists should consider targeting these and other relevant health belief factors as part of vaccine promotion efforts, particularly among those who have already initiated the vaccine series.

This is the first study to report the prevalence and correlates of HPV vaccination in young adults surviving childhood cancer; however, this work was limited by (i) inclusion of survivors from a single-site, (ii) consideration of survivors greater than 5 years post diagnosis only and (iii) utilization of self-report regarding vaccine history. Although the ideal method collecting HPV vaccination history is via medical record review or confirmation with participants' medical care team, the validity of self-reported HPV vaccination has been demonstrated among both healthy young adults, and those surviving childhood cancer [39, 40]. Furthermore, the present study is cross-sectional; therefore, even significant associations between the considered risk factors and vaccine outcomes should be interpreted as correlational rather than causal. The paucity of literature designed at understanding HPV-specific risk profiles among survivors of childhood cancer [41] necessitates additional research in this area which would then inform the content and design of future HPV vaccination interventions.

Future study directions should include the testing/implementation of communication interventions among oncologists/survivorship specialists to promote skills regarding the "when and how" to introduce discussion of HPV vaccination and sexual health. Askelson et al. (2011) reported that when engaging in HPV vaccination discussion with patients, 90% of physicians will concurrently discuss topics such as STIs, dating, contraceptive use, and abstinence [42]. Physicians and parents may use HPV vaccination as an opportunity to initiate discussions about sexual health and development with survivors at an earlier age [42, 43].

Although physicians may be missing these opportunities, young adult women appear reluctant to initiate conversations of this nature. Approximately 94% of survivors reported a willingness to initiate health-related quality-of-life discussions with their doctor; however, 39% admitted they were unwilling to discuss sexual problems/concerns even upon physician initiation of discussion [41]. Despite this reluctance, there is a need for information regarding sexual health among survivors of childhood cancer, particularly as a lack of awareness regarding health vulnerabilities secondary to risky sexual behavior may exist [44].

In conclusion, survivors of childhood cancer are at increased risk for adverse late effects (including HPV-associated subsequent malignant neoplasms) of cancer and its treatment,

and as such, may experience a particular benefit from HPV vaccination. Findings of the current study not only estimate the prevalence of HPV vaccination among young women surviving childhood cancer, but identify factors influencing HPV vaccination. A minority of adolescents surviving childhood cancer have initiated or completed the HPV vaccine series despite their increased health vulnerabilities. Future interventions designed to increase vaccination among childhood cancer survivors may draw upon these findings to enhance immunization rates, while promoting quality of life through better health in this high risk population.

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Figure 1.
Participation Rates among Young Adult Females Surviving Childhood Cancer

Table 1 Demographic and Medical Characteristics of Young Adult Survivors and Control[‡]

	Cancer Survivors n = 114 <i>Freq (%)</i>	Controls n = 98 <i>Freq (%)</i>	Combined n = 212 <i>Freq (%)</i>
Race/Ethnicity			
White	85 (74.6)	42 (42.9)***	127 (59.9)
Non-White	29 (25.4)	56 (57.1)	85 (40.1)
Religious Orientation			
Christian	101 (91.0)	80 (87.0)	181 (89.2)
Non-Christian	10 (9.0)	12 (13.0)	22 (10.8)
Education Level			
Less than College Degree	98 (86.0)	85 (86.7)	183 (86.3)
College Degree or more	16 (14.0)	9 (9.2)	25 (11.8)
Household Income			
Less than \$20,000	29 (28.2)	34 (39.5)	63 (33.3)
\$20,000 to \$59,999	40 (38.8)	34 (39.5)	74 (39.2)
\$60,000 and above	34 (33.0)	18 (20.9)	52 (27.5)
Age (<i>in Years</i>)			
18-20	52 (45.6)	53 (56.4)	105 (50.5)
21-26	62 (54.4)	41 (43.6)	103 (49.5)
Cancer Diagnosis			
Leukemia/Lymphoma	53 (46.5)	--	--
Brain/CNS Tumors	25 (21.9)	--	--
Solid Tumors	36 (31.6)	--	--
Time from Diagnosis (<i>in Years</i>)			
5-9	74 (64.9)	--	--
10-14	25 (21.9)	--	--
15-19	15 (13.2)	--	--
Age at Diagnosis (<i>in Years</i>)			
0-4	16 (14.0)	--	--
5-9	16 (14.0)	--	--
10-14	54 (47.3)	--	--
15-19	28 (24.6)	--	--

* $p < .10$ ** $p < .05$ ***
 $p < .001$ [‡] All n's may not equal 114 (survivors), 98 (controls) or 212 (combined groups) due to missing data.

Table 2 Univariate Analysis for Sociodemographic and Medical Factors by HPV Vaccination Status[†]

	Not Initiated n = 124 <i>Freq (%)</i>	Initiated n = 88 <i>Freq (%)</i>	Incomplete n = 30 <i>Freq (%)</i>	Complete n = 58 <i>Freq (%)</i>
Health Status				
Healthy Control	54 (43.5)	44 (50.0)	16 (53.3)	28 (48.3)
Cancer Survivor	70 (56.5)	44 (49.0)	14 (46.7)	30 (51.7)
Race/Ethnicity				
White	76 (61.3)	51 (58.0)	14 (46.7)	37 (63.8)
Non-White	48 (38.7)	37 (42.0)	16 (53.3)	21 (36.2)
Currently Dating				
No	69 (55.6)	37 (43.5) *	11 (37.9)	22 (38.6)
Yes	55 (44.4)	48 (56.5)	18 (62.1)	35 (61.4)
Sexually Active, Current				
No	63 (53.4)	33 (39.3) **	10 (34.5)	23 (41.8)
Yes	55 (46.6)	51 (60.7)	19 (65.5)	32 (58.2)
Visit OB/GYN				
No	36 (30.3)	15 (17.4) **	4 (13.8)	11 (19.3)
Yes	83 (69.7)	71 (82.6)	25 (86.2)	46 (80.7)
Yearly Pap Test				
No	60 (50.4)	29 (33.7) **	10 (33.3)	19 (33.9)
Yes	59 (49.6)	57 (66.3)	20 (66.7)	37 (66.1)
Had an STI				
No	107 (89.2)	68 (80.0) *	23 (79.3)	45 (80.4)
Yes	13 (10.8)	17 (20.0)	6 (20.7)	11 (19.6)
Number of Opposite Sex Partners, Lifetime				
0-1	33 (41.8)	12 (20.7) ***	5 (31.2)	7 (16.7)
2+	46 (58.2)	46 (79.3)	11 (68.8)	35 (83.3)
Used Birth Control Last Intercourse				
No	64 (79.0)	60 (92.3) **	21 (95.4)	39 (90.7)
Yes	17 (21.0)	5 (7.7)	1 (4.6)	4 (9.3)
Doctor Recommended Vaccine				
No	80 (67.8)	12 (14.1) ***	4 (14.3)	8 (14.0)
Yes	38 (32.2)	73 (85.9)	24 (85.7)	49 (86.0)

[†]Percent based on number having received at least one dose of HPV vaccine.***
 $p < .01$ **
 $p < .05$

*
 $p < .10$.

*
All n's may not equal 124 (Not Initiated), 88 (Initiated), 30 (Incomplete), or 58 (Complete) due to missing data.

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Table 3 Univariate Analysis for Communication and Health Belief Factors by HPV Vaccination Status[‡]

	Not Initiated n = 124 Freq (%)	Initiated n = 88 Freq (%)	Incomplete n = 30 Freq (%)	Complete n = 58 Freq (%)
HPV Communication				
Low	73 (65.2)	19 (23.2)***	8 (28.6)	11 (20.4)
High	39 (34.8)	63 (76.8)	20 (71.4)	43 (79.6)
Health Belief Factor: Severity				
Low	61 (50.8)	30 (36.6)**	6 (20.7)	24 (45.3)**
High	59 (49.2)	52 (63.4)	23 (79.3)	29 (54.7)
Health Belief Factor: Barriers				
Low	43 (36.4)	58 (69.9)***	16 (55.2)	42 (77.8)**
High	75 (63.6)	25 (30.1)	13 (44.8)	12 (22.2)
Health Belief Factor: Benefits				
Low	72 (60.5)	21 (25.3)***	11 (39.3)	10 (18.2)**
High	47 (39.5)	62 (74.7)	17 (60.7)	45 (81.8)
Health Belief Factor: Self-Efficacy				
Low	78 (66.1)	35 (42.2)**	14 (51.9)	21 (37.5)
High	40 (33.9)	48 (57.8)	13 (48.1)	35 (62.5)

* $p < .10$.[†]Percent based on number having received at least one dose of HPV vaccine.***
 $p < .001$ **
 $p < .05$ [‡]All n's may not equal 124 (Not Initiated), 88 (Initiated), 30 (Incomplete), or 58 (Complete) due to missing data.

Table 4 Multivariate Logistic Regression for Factors Associating with HPV Vaccine Initiation[†]

Variable	OR	95% CI [*]	<i>p</i>
Health Status			
Control	1.00		
Cancer Survivor	1.01	0.23 to 4.36	.99
Doctor Recommended Vaccine			
No	1.00		
Yes	11.24	3.15 to 40.14	< .001
HPV Communication			
Low	1.00		
High	7.28	1.89 to 28.05	.01

^{*} CI = confidence interval for odds ratio (OR)

[†] Only statistically significant variables are presented, with the exception of the cancer/control group variable.

Table 5 Multivariate Logistic Regression for Factors Associating with HPV Vaccine Completion[†]

Variable	OR	95% CI [*]	<i>p</i>
Health Status			
Control	1.00		
Cancer Survivor	0.58	0.14 to 2.38	.45
Health Belief Factor: Severity			
Low	1.00		
High	0.14	0.03 to 0.71	.02
Health Belief Factor: Benefits			
Low	1.00		
High	10.55	1.59 to 69.92	.02

^{*} CI = confidence interval for odds ratio (OR)

[†] Only statistically significant variables are presented, with the exception of the cancer/control group variable.