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# Risk Factors for Non-Initiation of the Human Papillomavirus (HPV) Vaccine among Adolescent Survivors of Childhood Cancer

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## Abstract

Effective vaccination is now available to prevent human papillomavirus (HPV), the most common sexually transmitted infection and cause of cervical cancer. This study aimed to estimate the prevalence of HPV vaccination among childhood cancer survivors and identify factors associated with HPV vaccine initiation and completion. Mothers of daughters aged 9–17 years with/without a history of childhood cancer ($n$ = 235, $M_{age}$= 13.2 years, $SD$= 2.69; $n$ = 70, $M_{age}$= 13.3 years, $SD$=2.47, respectively) completed surveys querying HPV vaccination initiation and completion along with socio-demographic, medical, HPV knowledge and communication, and health belief factors, which may relate to vaccination outcomes. Multivariate logistic regression was utilized to identify factors which associate with HPV vaccination initiation and completion. Among cancer survivors, 32.6% initiated and 17.9% completed the 3-dose vaccine series, whereas 34.3% and 20.0% of controls initiated and completed, respectively. Univariate analyses indicated no differences between cancer/no cancer groups on considered risk factors. Among all participants, multivariate logistic regression analyses found vaccine initiation associated with older age of daughter and physician recommendation, while increased perceived barriers associated with a decreased likelihood of initiation (all $P$s < .05). Among those having initiated, risk factors for non-completion included being non-white, increased perceived severity of HPV, and increased perceived barriers to vaccination (all $P$s < .05). A minority of adolescents surviving childhood cancer have completed vaccination despite their increased risk for HPV-related complication. These results inform the prioritization of strategies to be included in vaccine promotion efforts.

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## INTRODUCTION

Genital human papillomavirus (HPV) is the most common sexually transmitted infection (1) and has a causal role in the expression of cervical and other cancers (2). Approximately 80% of sexually active women are exposed to HPV during their lifetime (3), and HPV is most prevalent among females aged 20–24 years (4). Rates rise sharply after the median age of sexual debut, 16.6 years for females in the US (5). Recent efforts to reduce cervical cancer have led to the development of vaccines to protect against HPV, which are currently available and have been demonstrated to be safe and effective (6–10). Quadrivalent HPV vaccination, approved in 2006 for females between 9–26 years of age (11) protects against HPV types 16 and 18 (which account for 70% of cervical cancers) and 6 and 11 (which account for 90% of genital warts) (12). In 2009, HPV vaccination was also approved for males (13).

Routine HPV vaccination is currently recommended by the Advisory Committee on Immunization Practices for adolescent girls aged 11 and 12 years, with catch-up vaccination for women up to age 26 (14). It is recommended that the vaccine be administered prior to sexual debut due to the mechanism of HPV transmission (11). With appropriate utilization of the vaccine, the American Cancer Society estimates a potential reduction of cervical cancer risk by over 70% over the next decade (15–16). HPV vaccine uptake is particularly important for females surviving childhood cancer, many of whom are at increased risk for HPV-related complications secondary to the direct and indirect effects of cancer treatment. Survivors at increased risk for HPV persistence and complications include those with a history of hematopoietic stem cell transplantation (17), Hodgkin lymphoma (18–19), treatment with pelvic irradiation (20–21), and those receiving other cancer treatments resulting in sustained immunosuppression (22–26). Survivors of childhood cancer appear to also be at increased risk for HPV infection/complication/escalation given the unique behavioral, cognitive, and educational consequences of treatment. Specifically, survivors of childhood cancer are less likely than their healthy siblings to have undergone a Papanicolaou (Pap) smear within the previous three years (27). Survivors are also more likely to experience neurocognitive deficits such as impulsivity and inattention resembling attention deficit hyperactivity disorder, which have been associated with increased risky and sexual behaviors (28–32). Additionally, survivors of childhood cancer are more likely to report unemployment, lower educational attainment, and lower annual incomes (33), factors independently associated with HPV infection. As such, the Children's Oncology Group's (COG) Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent and Young Adult Cancer Version 3.0, which is the template for screening late effects of cancer treatment, has recommended HPV vaccination for all eligible females surviving childhood cancer (34).

Over the last two years, the National Immunization Survey for Teens (utilizing clinic validated repots) found that initiation rates among adolescent females in the general population ranged from 48.7% to 53.0% whereas completion rates have ranged from 32.0% to 34.8% (35–36). Both rates of initiation and completion are significantly lower than the 80% target established by the Healthy People 2020 initiative (37). Because the HPV vaccine was only approved recently by the FDA (2006), little is known about the complexity of

vaccination uptake among those surviving cancer. To date, no rigorous examination of HPV vaccination among survivors of childhood cancer has been reported. The current study serves as the first prevalence estimation of HPV vaccination initiation and completion among a large cohort of childhood cancer survivors while also identifying factors which are most influential in HPV vaccination initiation and completion in this high-risk group.

## MATERIALS AND METHODS

### Participants

Maternal caregivers who have daughters with a history of childhood cancer were recruited from the After Completion of Therapy (ACT) Clinic at St. Jude Children's Research Hospital. ACT is a long-term follow-up clinic for childhood cancer survivors who are greater than 5 years post-diagnosis, and 2 years disease-free. Following completion of the study questionnaire, each mother was asked to provide contact information for up to 5 acquaintances in order to obtain a control sample demographically similar to the cancer group. This type of sampling allowed for the evaluation of HPV vaccination rates across cancer/no cancer groups while controlling for key demographic variables (daughter's age, socioeconomic status, maternal education, and region of the country), which have been found to influence vaccination uptake (36,38–41). By controlling for these specific demographics, the distinguishing feature between groups was the presence/absence of daughter cancer history. Eligibility criteria for participants included: 1) the mother or female primary caregiver of a female 9–17 years of age, 2) proficient in reading and writing English, 3) cognitively able to understand and complete the study questionnaire, and 4) willing and able to provide informed consent per institutional review board (IRB) guidelines. Over an 18-month interval, a total of 235 mothers with daughters with a history of childhood cancer ("cancer survivor" group; daughter *Mage* = 13.2 years, *SD* = 2.69) and 70 mothers with daughters without cancer ("acquaintance control;" daughter *Mage* = 13.3 years, *SD* = 2.47) were enrolled in the study and returned questionnaires (Figure 1). Cancer survivors and acquaintance controls did not significantly differ on any of the measured demographic variables (Table 1).

Among the cancer survivor group, maternal caregivers were recruited during their daughter's regularly scheduled ACT Clinic visit. A trained member of the research team approached mothers, explained the purpose of the study, and obtained informed consent as approved by the IRB. After consent was obtained, participants completed paper-and-pencil questionnaires, which took approximately 15–30 minutes. Potential acquaintance control participants were contacted via telephone based on contact information provided by the mothers with daughters with a cancer history (typically by accessing information stored on their cellular phones). Controls who verbally consented via telephone were provided the option of completing either an online questionnaire or a mailed paper-and-pencil questionnaire. Questionnaires were identical across the two groups, aside from identifying the St. Jude daughters as "patients." After completing questionnaires, all participants were provided with an information sheet on HPV and HPV vaccination. Questionnaires were collected in 2010 and 2011.

**Outcome Variables—**HPV vaccine initiation/non-initiation was defined as a binary outcome variable such that mothers who reported their daughters have received one or more HPV vaccine doses were categorized as "initiated," and those having received zero doses were categorized as "non-initiated." HPV vaccine completion/non-completion was defined as a binary outcome variable such that mothers who reported their daughters have received all three doses of HPV vaccine were categorized as complete, and those who have received at least one dose but less than three doses of HPV vaccine were categorized as incomplete. Participants whose daughters have received zero doses of the HPV vaccine were excluded in the modeling of HPV vaccination completion.

**Independent Variables—**All participants completed questionnaires regarding their daughters' socio-demographic and medical history, HPV-specific knowledge and communication, and health beliefs.

### Medical and Socio-Demographic Variables

Mothers provided familial demographic information, including maternal and child age, race/ethnicity, marital status, education level, and annual household income, along with medical history of gynecological care and cervical cancer screening. Items were adapted from instruments previously used in the HPV vaccine literature (42–44) (Table 1). Items measuring maternal perceptions of daughter's sexual activity and relationship status were also adapted from previous self-report questionnaires (41).

### HPV Knowledge and Communication

Knowledge of HPV, cervical cancer, and HPV vaccination was measured by a scale adapted from Brabin and colleagues (42). Correct responses to 10 multiple choice items were summed for a total knowledge score, with higher scores representing greater knowledge. The questionnaire content was abstracted from the CDC's HPV vaccination information website as well as other sources (42,45). Familial communication regarding the messages and purpose of HPV vaccination was assessed via a 4-item scale also adapted from Brabin and colleagues (42). The 18 item Mother-Adolescent Sexual Communication Instrument assessed maternal-adolescent sexual behavior and development communication (46). Internal reliability in our sample was high ($\alpha$ =.92) and convergent and discriminant validity have been previously established and described (46). Communication scores were recoded into binary variables (median splits) prior to model inclusion: HPV communication (*Mdn* = 14, *Range* = 4–16), and sexual communication (*Mdn* = 68, *Range* = 18–90).

### Health Beliefs

The HPV Vaccine Health Beliefs Questionnaire (47) is a validated instrument designed to measure maternal perceptions of daughters' vulnerability to HPV, severity of HPV, barriers to, benefits of, and self-efficacy for initiating/completing the vaccine. Internal reliability was acceptable for all subscales in our sample: Vulnerability ($\alpha$ = .95), Severity ($\alpha$ = .87), Barriers ($\alpha$ = .81), Benefits ($\alpha$ = .82), and Self-Efficacy ($\alpha$ = .91). Cox and colleagues (47) also found the internal reliabilities of these factors to be robust which contributed to establishing the predictive validity of health belief factors as it relates to HPV vaccination acceptability among mothers of girls aged 11–16 years. Additional measures of vaccine-

related Cues to Action and Social Environmental Influence were also considered with scales adapted from previously validated surveys (42–44,47). Health belief scores were recoded into binary variables (median splits) prior to model inclusion: Vulnerability (*Mdn* = 12.0, *Range* = 5–25), severity (*Mdn* = 32, *Range* = 8–40), barriers (*Mdn* = 25, *Range* = 12–52), benefits (*Mdn* = 23, *Range* = 8–35), and self-efficacy (*Mdn* = 24, *Range* = 6–30).

### Statistical Analysis

Univariate analyses were utilized to examine differences between groups (cancer history/no history) in HPV vaccine initiation and completion. Univariate differences were also assessed as a function of socio-demographic, medical, knowledge and communication, as well as health belief factors. Comparisons with *p*-values less than .10 were included in each of the two multivariate models (vaccine initiation and completion). Differences for continuous variables were assessed using univariate one-way analysis of variance (ANOVA). Differences in categorical variables were assessed using Chi-square and Fisher's Exact tests. Multivariable logistic regression models were used to calculate odds ratios (OR) and 95% confidence intervals (CI) for vaccine outcomes. Given that no differences emerged between groups on vaccination outcomes, cancer survivors and acquaintance control participants were combined in the presented multivariate models. Participant status (cancer vs. control) was also retained as a factor in both models.

## RESULTS

### Univariate Cancer/Control Comparisons

Univariate differences emerged between cancer/no cancer groups on risk factors including vulnerability to HPV infection and complication ($P = .04$) and prediction of daughter's sexual activity ($P = .09$). Specifically, mothers of daughters with a cancer history perceived their child to be more susceptible to HPV infection and complication, but were less likely to predict that their daughters would be sexually active by high school graduation. No other significant cancer/control differences were found on any other socio-demographic and medical history variables, HPV-specific knowledge and communication variables, or health belief variables.

### Prevalence

Overall, 32.6% (75/230) of cancer survivors and 34.3% (24/70) healthy controls had initiated the HPV vaccine series. Among those who had initiated, 56.0% (42/75) of cancer survivors and 58.3% (14/24) of healthy controls had completed the vaccine series. In the overall sample, 17.9% (42/230) of survivors and 20% (14/70) of controls had completed the vaccine. No significant differences emerged in the rates of vaccine initiation or completion between cancer survivors and healthy controls.

### HPV Vaccine Initiation

Univariate analyses revealed significant differences between those who have/have not initiated the HPV vaccine (see Tables 2 and 3). Based on the univariate findings, the multivariate model for HPV vaccine initiation included the following variables: race, daughter's age, adolescent history of gynecological care, adolescent history of annual Pap

smear, doctor recommendation for vaccine, parental permission to date socially, maternal perception of daughter's past and current relationship status, maternal perception of daughter's sexual activity status, maternal-adolescent sexual communication, and maternal health beliefs of vulnerability, barriers to vaccination, benefits of vaccinating, and self-efficacy regarding HPV vaccination (Table 4). The final multivariate logistic regression model predicting binary vaccine initiation outcome indicated that older daughter age and physician recommendation for vaccination were associated with an increased likelihood of HPV vaccine initiation. Furthermore, mothers who perceived greater barriers to having their daughter receive the HPV vaccine (e.g., financial or religious conflicts, concerns about vaccine promoting sexual activity in daughter, historical lack of vaccination endorsement, etc.) were less likely to have initiated the vaccine.

### HPV Vaccine Completion

Univariate analyses for participants who had initiated the vaccine revealed significant differences between those who have/have not completed the vaccine series (Tables 2 and 3). Based on these differences, the final multivariate logistic regression model for HPV vaccine completion included the following variables: Race, daughter's age, physician recommendation for HPV vaccination, parental permission for dating socially, and maternal health beliefs of vulnerability, severity, and barriers regarding HPV vaccination (Table 5). Among vaccine-initiated participants, those who were non-white, held perceptions of greater HPV severity, and who perceived greater barriers to vaccination were less likely to have completed the HPV vaccine series post initiation.

## DISCUSSION

Advances in the treatment of childhood cancer have resulted in the majority of survivors living into adulthood (48–49). Given the reduction of mortality associated with cancer treatment, increased attention has been placed on promoting health and quality of life in survivorship (29, 50). HPV vaccination is one tool to assist in these efforts, and as such, a need exists to better understand vaccine prevalence and determinants in this vulnerable group.

Based on maternal report, the results of our study found that 32.6% of cancer survivors have initiated the vaccine series, whereas 17.9% have completed it. No differences in vaccine rates were identified between cancer survivors and acquaintance control groups, but univariate differences in known risk factors for vaccine initiation and completion did emerge. Specifically, mothers of survivors perceived greater vulnerability to HPV-related complication upon patient exposure but were less likely to believe that their daughters would engage in sexual activity prior to high school graduation. Although survivors are at increased risk for HPV-related complication, they did not engage in higher rates of vaccination. Cancer survivors and control participants were similar on many risk factors previously identified as being predictive of vaccination status, including age (39) physician recommendation (51–54) and race (36,38,55). The similarities between groups are consistent with previous research which identified no differences in risky sexual behavior between adolescent childhood cancer survivors and healthy siblings (56). Conceivably, interventions

designed to increase vaccine uptake in the healthy population may be generalizable for utilization among childhood cancer survivor populations as well based on these similarities.

Among the entire sample, the modeling of determinants associated with vaccine initiation found that older daughter age and physician recommendation were both related to increased vaccine uptake, whereas perceptions of high vaccine barriers were associated with decreased initiation. Our study aligns with previous research demonstrating that physician recommendation for HPV immunization is a robust predictor of vaccine uptake (52,57). It is interesting to note that only half of all mothers endorsed physician recommendation for HPV vaccination. Amidst the non-significant cancer/control differences described in the results, a trend was seen in which a minority of survivor families received a physician recommendation for vaccination, whereas a majority of controls reported receiving one. This is discouraging given survivors' frequency of medical encounters and their increased risk for HPV-related complication (58). These data suggest potential confusion in vaccine management in that some primary care physicians may assume that oncologists are managing this aspect of care and *vice versa*. This lack of clarity may account for these less than optimal vaccine rates in the cancer group, and physician communication/ recommendation may be targets of future intervention, particularly in light of physician recommendation being predictive of vaccine initiation. Physician endorsement of HPV vaccination, as well as problem-solving specific to perceived barriers to vaccine initiation or completion, may also be mechanisms to increase vaccine uptake in adolescents (59).

Once the vaccine has been initiated, the series must be completed to achieve maximum protection (6). Being non-white and perceiving high barriers and severity associated with HPV infection/complication are all risk factors decreasing the likelihood of vaccine completion. The interpretation of the finding regarding high perceptions of HPV severity and its association with non-completion, while unexpected, is primarily a function/limitation of the cross sectional study design. It appears that mothers whose daughters have completed the vaccine series are least concerned about the severity of future HPV complications. This is presumably due to the comfort associated with full vaccine protection. This also suggests that an awareness of HPV-related complications could act as a motivator for vaccine completion. Modifiable variables consistent with the Health Belief Model (60) such as perceived severity and barriers to vaccination (and to a lesser extent vulnerability to HPV infection), should be prioritized in vaccine promotion efforts. Furthermore, there may be other modifiable variables which, though significant at the univariate level, did not reach significance in the multivariate models. Given the opportunity, interventionists may consider targeting such variables, like HPV communication or health beliefs, as part of vaccine promotion efforts in the future.

This is the first study to report the prevalence and correlates of HPV vaccination in childhood cancer survivors; however, this work was limited by a) inclusion of females from a single-site, b) survivors greater than 5 years post diagnosis, and c) utilized maternal report of child vaccination only. Furthermore, with cross-sectional study designs, only associations (not causalities) can be determined between the considered risk factors and vaccine outcomes. This literature is in the early stages of quantifying HPV-specific risk profiles among survivors of childhood cancer (61), necessitating additional research in this

population. Additionally, our definition of incompletion did not differentiate pending versus intentionally incomplete participants. It is possible that our incomplete group is heterogeneous in their intentions to complete the vaccine series. Related to this point, although all adolescents in the study were within the age indication for receiving the vaccine, the time since vaccine initiation and questionnaire completion may have been less than 6 months. As such, it is possible that the reported rates of vaccine completion in this sample may vary as a function of time since vaccination initiation.

Despite the COG recommendation for vaccination, the immunogenicity of the HPV vaccine among childhood cancer survivors has not yet been demonstrated. Among children living with HIV, for example, differences have been noted in quadrivalent HPV vaccine seroconversion, as titers against HPV subtypes 6 and 18 were demonstrated to be 30–50% lower than age matched controls (62). In response, a Phase II study is warranted examining the safety, immunogenicity, and tolerability (as well as scheduling and dosing of vaccine) among survivors of childhood cancer. In addition, future research should examine cancer-specific factors (e.g. diagnosis, treatment, etiology) and their associations with HPV vaccine outcomes among survivors. As the HPV vaccine is also approved for young adults and males, examining factors contributing to vaccinations in these groups are warranted as well.

In conclusion, cancer survivors are at increased risk for adverse late effects including second malignancies and organ compromise, and as such, would benefit from HPV vaccination. Findings of the current study establish the prevalence and identification of factors influencing HPV vaccination among adolescent females surviving childhood cancer and their peers. A minority of adolescents surviving childhood cancer have initiated or completed HPV vaccination despite their increased risk for HPV complication. Future interventions designed to increase vaccination among childhood cancer survivors may draw upon these study findings to enhance immunization rates and promote their daughters' health in the future.

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## References

1. Weinstock H, Berman S, Cates W. Sexually transmitted diseases among American youth: Incidence and prevalence estimates, 2000. Perspect Sex Reprod Health. 2004; 36:6–10. [PubMed: 14982671]
2. Cogliano V, Baan R, Straif K, Grosse Y, Secretan B, El Ghissassi F, et al. Carcinogenicity of human papillomaviruses. Lancet Oncol. 2005; 6:204. [PubMed: 15830458]
3. Myers ER, McCrory DC, Nanda K, Bastian L, Matchar DB. Mathematical model for the natural history of human papillomavirus infection and cervical carcinogenesis. Am J Epidemiol. 2000; 151:1158–1171. [PubMed: 10905528]
4. Hariri S, Unger ER, Sternberg M, Dunne EF, Swan D, Patel S, et al. Prevalence of genital human papillomavirus among females in the United States, the national health and nutrition examination survey, 2003–2006. J Infect Dis. 2011; 204:566–573. [PubMed: 21791659]
5. Haydon AA, Herring AH, Prinstein MJ, Halpern CT. Beyond age at first sex: patterns of emerging sexual behavior in adolescence and young adulthood. J Adolesc Health. 2012; 50:456–463. [PubMed: 22525108]

6. Centers for Disease Control and Prevention. Quadrivalent human papillomavirus vaccine: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep. 2007; 56:1–24.
7. Klein NP, Hansen J, Chao C, Velicer C, Emery M, Slezak J, et al. Safety of quadrivalent human papillomavirus vaccine administered routinely to females. Arch Pediatr Adolesc Med. 2012; 166:1140–1148. [PubMed: 23027469]
8. Harper DM, Franco EL, Wheeler CM, Moscicki AB, Romanowski B, Roteli-Martins CM, et al. Sustained efficacy up to 4–5 years of a bivalent L1 virus-like particle vaccine against human papillomavirus types 16 and 18: Follow-up from a randomised control trial. Lancet. 2006; 367:1247–1255. [PubMed: 16631880]
9. Muñoz N, Kjaer SK, Sigurdsson K, Iversen OE, Hernandez-Avila M, Wheeler CM, et al. Impact of human papillomavirus (HPV)-6/11/16/18 vaccine on all HPV-associated genital diseases in young women. J Natl Cancer Inst. 2010; 102:325–339. [PubMed: 20139221]
10. Garland SM, Hernandez-Avila M, Wheeler CM, Perez G, Harper DM, Leodolter S, et al. Quadrivalent vaccine against human papillomavirus to prevent anogenital diseases. N Engl J Med. 2007; 356:1928–1943. [PubMed: 17494926]
11. U.S. Food and Drug Administration. FDA licenses new vaccine for prevention of cervical cancer and other diseases in females caused by human papillomavirus. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2006/ucm108666.htm
12. Villa LL, Costa RL, Petta CA, Andrade RP, Paavonen J, Iversen OE, et al. Prophylactic quadrivalent human papillomavirus (types 6, 11, 16, and 18) L1 virus-like particle vaccine in young women: a randomised double-blind placebo-controlled multicentre phase II efficacy trial. Lancet Oncol. 2005; 6:271–278. [PubMed: 15863374]
13. U.S. Food and Drug Administration. FDA approves new indication for Gardasil to prevent genital warts in men and boys. http://www.fda.gov/newsevents/newsroom/pressannouncements/ucm187003.htm
14. Centers for Disease Control and Prevention. Recommended immunization schedules for persons aged 0 through 18 years - United States, 2012. MMWR Morb Mortal Wkly Rep. 2012; 61:1–4.
15. Muñoz N, Bosch FX, Castellsague X, Díaz M, de Sanjose S, Hammouda D, et al. Against which human papillomavirus types shall we vaccinate and screen? The international perspective. Int J Cancer. 2004; 111:278–285. [PubMed: 15197783]
16. Saslow D, Castle E, Cox T, Davey DD, Einstein MH, Ferris DG, et al. American Cancer Society Guideline for human papillomavirus (HPV) vaccine use to prevent cervical cancer and its precursors. CA Cancer J Clin. 2007; 57:7–28. [PubMed: 17237032]
17. Bunin, N.; DiDomenico, C.; Guzikowski, V. Hematopoietic stem cell transplantation. In: Schwartz, CL.; Hobbie, WL.; Constine, LS., et al., editors. Survivors of childhood and adolescent cancer: a multidisciplinary approach. 2. New York, NY: Springer; 2005. p. 271-282.
18. Gross G, Ellinger K, Roussaki A, Fuchs PG, Peter HH, Pfister H. Epidermodysplasia verruciformis in a patient with hodgkin's disease: Characterization of a new papillomavirus type and interferon treatment. J Invest Dematol. 0988; 91:43–48.
19. Hennig EM, Nesland JM, Di Lonardo A, Venuti A. Multiple primary cancers and HPV infection: Are they related? J Exp Clin Cancer Res. 1999; 18:53–54. [PubMed: 10374677]
20. Barzon L, Pizzighella S, Corti L, Mengoli C, Palù G. Vaginal dysplastic lesions in women with hysterectomy and receiving radiotherapy are linked to high-risk human papillomavirus. J Med Virol. 2002; 67:401–405. [PubMed: 12116034]
21. Fujimura M, Ostrow RS, Okagaki T. Implication of human papillomavirus in postirradiation dysplasia. Cancer. 1991; 68:2181–2185. [PubMed: 1655204]
22. Courtney AE, Leonard N, O'Neill CJ, McNamee PT, Maxwell AP. The uptake of cervical cancer screening by renal transplant recipients. Nephrol Dial Transplant. 2009; 24:647–652. [PubMed: 18952575]
23. Malouf MA, Hopkins PM, Singleton L, Chhajed PN, Plit ML, Glanville AR. Sexual health issues after lung transplantation: importance of cervical screening. J Heart Lung Transplant. 2004; 23:894–897. [PubMed: 15261186]

24. Mass K, Quint EH, Punch MR, Merion RM. Gynecological and reproductive function after liver transplantation. Transplantation. 1996; 62:476–479. [PubMed: 8781613]
25. Rose B, Wilkins D, Li W, Tran N, Thompson C, Cossart Y, et al. Human papillomavirus in the oral cavity of patients with and without renal transplantation. Transplantation. 2006; 82:570–573. [PubMed: 16926603]
26. Seshadri L, George SS, Vasudevan B, Krishna S. Cervical intraepithelial neoplasia and human papilloma virus infection in renal transplant recipients. Indian J Cancer. 2001; 38:92–95. [PubMed: 12593446]
27. Yeazel MW, Oeffinger KC, Gurney JG, Mertens AC, Hudson MM, Emmons KM, et al. The cancer screening practices of adult survivors of childhood cancer: A report from the Childhood Cancer Survivor Study. Cancer. 2004; 100:631–640. [PubMed: 14745882]
28. Campbell LK, Scaduto M, Sharp W, Dufton L, Van Slyke D, Whitlock JA, et al. A meta-analysis of the neurocognitive sequelae of treatment for childhood acute lymphocytic leukemia. Pediatr Blood Cancer. 2007; 49:65–73. [PubMed: 16628558]
29. Krull KR, Huang S, Gurney JG, Klosky JL, Leisenring W, Termuhlen A, et al. Adolescent behavior and adult health status in childhood cancer survivors. J Cancer Surviv. 2010; 4:210–217. [PubMed: 20383785]
30. Moleski M. Neuropsychological, neuroanatomical, and neurophysiological consequences of CNS chemotherapy for acute lymphoblastic leukemia. Arch Clin Neuropsychol. 2000; 15:603–630. [PubMed: 14590198]
31. Mulhern RK, Fairclough D, Ochs J. A prospective comparison of neuropsychologic performance of children surviving leukemia who received 18-gy, 24-gy, or no cranial irradiation. Am J Clin Oncol. 1991; 9:1348–1356.
32. Pietilä S, Korpela R, Lenko HL, Haapasalo H, Alalantela R, Nieminen P, et al. Neurological outcome of childhood brain tumor survivors. J Neurooncol. 2012; 108:153–161. [PubMed: 22350432]
33. Gurney JG, Krull KR, Kadan-Lottick N, Nicholson HS, Nathan PC, Zebrack B, et al. Social outcomes in the Childhood Cancer Survivor Study cohort. Am J Clin Oncol. 2009; 27:2390–2395.
34. Children's Oncology Group. Long-Term Follow-Up Guidelines for survivors of childhood, adolescent, and young adult cancers. http://www.survivorshipguidelines.org/pdf/LTFUGuidelines.pdf
35. Centers for Disease Control and Prevention. National and state vaccination coverage among adolescents aged 13 through 17 years – United States, 2010. MMWR Morb Mortal Wkly Rep. 2011; 60:1117–1123. [PubMed: 21866084]
36. Centers for Disease Control and Prevention. National and state vaccination coverage among adolescents aged 13–17 years - United States, 2011. MMWR Morb Mortal Wkly Rep. 2012; 61:671–677. [PubMed: 22932301]
37. U.S. Department of Health and Human Services. Healthy people 2020: Immunization and infectious diseases. http://www.healthypeople.gov/2020/topicsobjectives2020/objectiveslist.aspx?topicid=23
38. Keenan K, Hipwell A, Stepp S. Race and sexual behavior predict uptake of the human papillomavirus vaccine. Health Psychol. 2012; 31:31–34. [PubMed: 22229933]
39. Dorell CG, Yankey D, Santibanez TA, Markowitz LE. Human papillomavirus vaccination series initiation and completion, 2008–2009. Pediatrics. 2011; 128:830–839. [PubMed: 22007006]
40. Crosby RA, Casey BR, Vanderpool R, Collins T, Moore GR. Uptake of free HPV vaccination among young women: A comparison of rural versus urban rates. J Rural Health. 2011; 27:380–384. [PubMed: 21967381]
41. Rosenthal SL, Rupp RR, 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; 43:239–235. [PubMed: 18710678]
42. Brabin L, Roberts SA, Farzaneh F, Kitchener HC. Future acceptance of adolescent human papillomavirus vaccination: A survey of parental attitudes. Vaccine. 2006; 24:3087–3094. [PubMed: 16500736]

43. Constantine NA, Jerman P. Acceptance of human papillomavirus vaccination among Californian parents of daughters: A representative statewide analysis. J Adolesc Health. 2007; 40:108–115. [PubMed: 17259050]
44. Dempsey AF, Zimet GD, Davis RL, Koutsky L. Factors that are associated with parental acceptance of human papillomavirus vaccines: A randomized intervention study of written information about HPV. Pediatrics. 2006; 117:1486–1493. [PubMed: 16651301]
45. Center for Diseases Control. HPV vaccination information for young women. http://www.cdc.gov/std/hpv/STDFact-HPV-vaccine-young-women.htm
46. Cox MF, Fasolino TK, Tavakoli AS. Factor analysis and psychometric properties of the Mother-Adolescent Sexual Communication (MASC) instrument for sexual risk behavior. J Nurs Meas. 2008; 16:171–183. [PubMed: 19886470]
47. Cox DS, Cox AD, Sturm L, Zimet G. Behavioral interventions to increase HPV vaccination acceptability among mothers of young girls. Health Psychol. 2010; 29:29–39. [PubMed: 20063933]
48. Mariotto AB, Rowland JH, Yarbroff KR, Scoppa S, Hachey M, Ries L, et al. Long-term survivors of childhood cancers in the United States. Cancer Epidemiol Biomarkers Prev. 2009; 18:1033–1040. [PubMed: 19336557]
49. Reis, LA.; Melbert, D.; Krapcho, M., editors. SEER cancer statistics review, 1975–2004. Bethesda, MD: National Cancer Institute; http://seer.cancer.gov/csr/1975_2004/
50. Stolley MR, Restrepo J, Sharp LK. Diet and physical activity in childhood cancer survivors: A review of the literature. Ann Behav Med. 2010; 39:232–249. [PubMed: 20559768]
51. Guerry SL, De Rosa CJ, Markowitz LE, Walker S, Liddon N, Kerndt PR, et al. Human papillomavirus vaccine initiation among adolescent girls in high-risk communities. Vaccine. 2011; 29:2235–2241. [PubMed: 21288799]
52. Ylitalo KR, Hedwig L, Mehta NK. Health care provider recommendation, human papillomavirus vaccination, and race/ethnicity in the US National Immunization Survey. Am J Public Health. 2013; 103:164–169. [PubMed: 22698055]
53. Kester LM, Zimet GD, Fortenberry JD, Kahn JA, Shew ML. A national study of HPV vaccination of adolescent girls: Rates, predictors, and reasons for non-vaccination. Matern Child Health J. 2013; 17:879–885. [PubMed: 22729660]
54. Griffioen AM, Glynn S, Mullins TK, Zimet GD, Rosenthal SL, Fortenberry JD, et al. Perspectives on decision making about human papillomavirus vaccination among 11- to 12- year-old girls and their mothers. Clin Pediatr. 2012; 51:560–568.
55. Cook RL, Zhang J, Mullins J, Kauf T, Brumback B, Steingraber H, et al. Factors associated with initiation and completion of human papillomavirus vaccine series among young women enrolled in medicaid. J Adolesc Health. 2010; 47:596–599. [PubMed: 21094437]
56. Klosky JL, Howell CR, Li Z, Mertens AC, Robison LL, Ness KK. Risky health behavior among adolescents in the childhood cancer survivors study cohort. J Pediatr Psychol. 2012; 37:634–646. [PubMed: 22427699]
57. Reiter PL, Brewer NT, Gottlieb SL, McRee AL, Smith JS. Parents' health beliefs and HPV vaccination of their adolescent daughters. Soc Sci Med. 2009; 69:475–480. [PubMed: 19540642]
58. Ojha RP, Tota JE, Offutt-Powell TN, Klosky JL, Ashokkumar R, Gurney JG. Human papillomavirus-associated subsequent malignancies among long-term survivors of pediatric and young adult cancers. PLOS One. 2013; 23:281–285.
59. Vadaparampil ST, Kahn JA, Salmon D, Lee JH, Quinn GP, Roetzheim R, et al. Missed clinical opportunities: Provider recommendations for HPV vaccination for 11–12 year old girls are limited. Vaccine. 2011; 29:8634–8641. [PubMed: 21924315]
60. Champion, VL.; Skinner, CS. The health belief model. In: Glanz, K.; Rimer, BK.; Viswanath, K., editors. Health behavior and health education: Theory, research, and practice. 4. San Francisco, CA: Jossey-Bass; 2008. p. 45-65.
61. Klosky JL, Gamble HL, Spunt SL, Randolph ME, Green DM, Hudson MM. Human papillomavirus (HPV) vaccine in survivors of childhood cancer. Cancer. 2009; 115:5627–5636. [PubMed: 19813272]

62. Levin MJ, Moscicki A, Song L. Safety and immunogenicity of quadrivalent human papillomavirus (types 6, 11, 16, and 18) vaccine in HIV-infected children 7 to 12 years old. J Acquir Immune Defic Syndr. 2010; 55:197–204. [PubMed: 20574412]

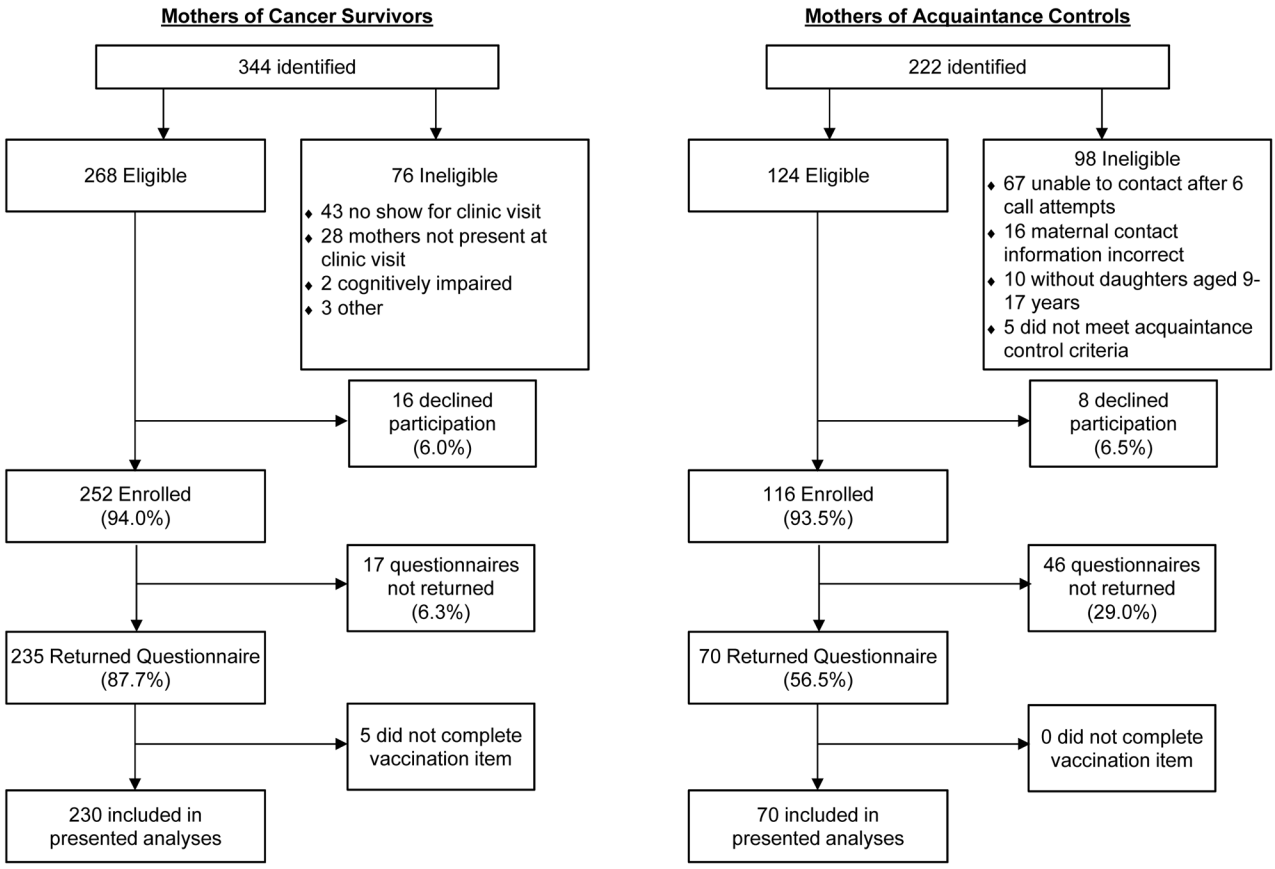


**Figure 1.**

Flowchart depicting recruitment and questionnaire completion for mothers of cancer survivors and mothers of controls

## Table 1

Demographic and Treatment Characteristics of Study Participants*

| Maternal Caregiver | Cancer Survivors n = 230 *Freq (%)* | Controls n = 70 *Freq (%)* | Combined N = 300 *Freq (%)* |
|---|---|---|---|
| Race/Ethnicity | | | |
| White | 175 (76.1) | 54 (77.1) | 229 (76.3) |
| Non-White | 55 (23.9) | 16 (22.9) | 71 (23.7) |
| Marital Status | | | |
| Married | 159 (69.1) | 54 (77.1) | 213 (71.0) |
| Divorced/Separated/Widowed | 39 (17.0) | 12 (17.1) | 51 (17.0) |
| Other | 29 (12.6) | 4 (5.7) | 33 (11.0) |
| Missing | 3 (1.3) | 0 (0) | 3 (1.0) |
| Education Level | | | |
| Less than College Degree | 152 (65.1) | 44 (62.9) | 196 (65.3) |
| College Degree or more | 72 (31.3) | 26 (37.1) | 98 (32.7) |
| Missing | 6 (2.6) | 0 (0) | 6 (2.0) |
| Household Income | | | |
| Less than $20,000 | 37 (16.1) | 5 (7.1) | 42 (14.0) |
| $20,000 to $59,999 | 74 (32.2) | 24 (34.3) | 98 (32.7) |
| $60,000 and above | 108 (47.0) | 36 (51.4) | 144 (48.0) |
| Missing | 11 (4.8) | 5 (7.1) | 16 (5.3) |
| Age (*in Years*) | | | |
| 18–40† | 107 (46.5) | 31 (44.3) | 138 (46.0) |
| 41–62 | 123 (53.5) | 39 (55.7) | 162 (54.0) |
| Age of Daughter (*in Years*) | | | |
| 9–13 | 113 (49.1) | 38 (54.3) | 151 (50.3) |
| 14–17 | 117 (50.9) | 32 (45.7) | 149 (49.7) |
| Daughter’s Cancer Diagnosis | | | |
| Leukemia/Lymphoma | 88 (38.3) | -- | -- |
| Brain/CNS Tumor | 44 (19.1) | -- | -- |
| Solid Tumor | 98 (42.6) | -- | -- |
| Time from Diagnosis (*in Years*) | | | |
| 5–7 | 53 (23.0) | -- | -- |
| 8–11 | 117 (50.9) | -- | -- |
| 12–15 | 48 (20.9) | -- | -- |
| 16–19 | 12 (5.2) | -- | -- |
| Age at Diagnosis (*in Years*) | | | |
| 0–4 | 173 (75.2) | -- | -- |
| 5–8 | 48 (20.9) | -- | -- |
| 9–12 | 9 (3.9) | -- | -- |

*Note: There were no cancer/control group differences among variables presented in Table 1.

[†]One self-identified “maternal caregiver” in this group was an older sister 18 years of age. The next youngest mother was 27 years of age.

## Table 2

Univariate Analysis for Socio-demographic and Medical Factors by HPV Vaccination Status

| | Not Initiated n = 201‡ | Initiated n = 99 | Incomplete† n = 43 | Complete n = 56 |
|---|---|---|---|---|
| | *Freq (%)* | *Freq (%)* | *Freq (%)* | *Freq (%)* |
| Health Status | | | | |
| Cancer Survivor | 155 (67.4) | 75 (32.6) | 33 (44) | 42 (56) |
| Healthy Control | 46 (65.7) | 24 (34.3) | 10 (41.7) | 14 (58.3) |
| Race of Maternal Caregiver | | | | |
| White | 160 (69.9) | 69 (30.1) * | 25 (36.2) | 44 (63.8) ** |
| Non-White | 41 (57.7) | 30 (42.3) | 18 (60) | 12 (40) |
| Age of Daughter (*in Years*) | | | | |
| 9–13 | 123 (81.5) | 28 (18.5) *** | 15 (53.6) | 13 (46.4) ** |
| 14–17 | 78 (52.3) | 71 (47.7) | 28 (39.4) | 43 (60.6) |
| Daughter Sees OB/GYN | | | | |
| No | 173 (72.7) | 65 (27.3) *** | 28 (43.1) | 37 (56.9) |
| Yes | 24 (45.3) | 29 (54.7) | 12 (41.4) | 17 (58.6) |
| Daughter Gets Yearly Pap Test | | | | |
| No | 185 (70.9) | 76 (29.1) *** | 32 (42.1) | 44 (57.9) |
| Yes | 10 (37.0) | 17 (63) | 7 (41.2) | 10 (58.8) |
| Doctor Recommended Vaccine | | | | |
| No | 126 (88.7) | 16 (11.3) *** | 10 (62.5) | 6 (37.5) * |
| Yes | 64 (45.1) | 78 (54.9) | 30 (38.5) | 48 (61.5) |
| Allowed to Date | | | | |
| No | 151 (76.6) | 46 (23.4) *** | 24 (52.2) | 22 (47.8) * |
| Yes | 39 (45.3) | 47 (54.7) | 16 (34) | 31 (66) |
| Current Relationship | | | | |
| No | 174 (70.4) | 73 (29.6) ** | 34 (46.6) | 39 (53.4) |
| Yes | 23 (52.3) | 21 (47.7) | 6 (28.6) | 15 (71.4) |
| Past Relationship | | | | |
| No | 172 (72.6) | 65 (27.4) *** | 30 (46.2) | 35 (53.8) |
| Yes | 18 (40) | 27 (60) | 11 (40.7) | 16 (59.3) |
| Sexually Active, Current | | | | |
| No | 185 (68.8) | 84 (31.2) * | 37 (44) | 47 (56) |
| Yes | 7 (46.7) | 8 (53.3) | 3 (37.5) | 5 (62.5) |
| Sexually Active, Past | | | | |
| No | 179 (69.6) | 78 (30.4) *** | 35 (44.9) | 43 (55.1) |
| Yes | 10 (38.5) | 16 (61.5) | 5 (31.3) | 11 (68.8) |
| Predict Sexual Activity by H.S. Grad | | | | |
| No | 121 (70.3) | 51 (29.7) ** | 20 (39.2) | 31 (60.8) |
| Yes | 27 (50.9) | 26 (49.1) | 12 (46.2) | 14 (53.8) |

| | Not Initiated n = 201‡ | Initiated n = 99 | Incomplete† n = 43 | Complete n = 56 |
|---|---|---|---|---|
| | *Freq (%)* | *Freq (%)* | *Freq (%)* | *Freq (%)* |
| Not Sure | 45 (72.6) | 17 (27.4) | 9 (52.9) | 8 (47.1) |

*** $p<.01$;

** $p<.05$;

* $p<.10$; These p-values are associated with Chi-square tests which examined group differences on the variables.

† Percent based on number having received at least one dose of HPV vaccine.

‡ All n's may not equal 300 or 99 due to missing data.

## Table 3

Univariate Analysis for Communication and Health Belief Factors by HPV Vaccination Status

| | **Not Initiated n = 201**[‡] | **Initiated n = 99** | **Incomplete**[†] **n = 43** | **Complete n = 56** |
|---|---|---|---|---|
| | ***Freq (%)*** | ***Freq (%)*** | ***Freq (%)*** | ***Freq (%)*** |
| Maternal-Adolescent Communication | | | | |
| Low | 105 (80.2) | 26 (19.8) *** | 9 (34.6) | 17 (65.4) |
| High | 80 (55.6) | 64 (44.4) | 29 (45.3) | 35 (54.7) |
| HPV Communication | | | | |
| Low | 89 (76.7) | 27 (23.3) *** | 9 (33.3) | 18 (66.7) |
| High | 87 (58.4) | 62 (41.6) | 28 (45.2) | 34 (54.8) |
| Health Belief Factor: Vulnerability | | | | |
| Low | 87 (57.6) | 64 (42.4) *** | 24 (37.5) | 40 (62.5) * |
| High | 105 (79.5) | 27 (20.5) | 14 (51.9) | 13 (48.1) |
| Health Belief Factor: Severity | | | | |
| Low | 85 (63.9) | 48 (36.1) | 16 (33.3) | 32 (66.7) ** |
| High | 110 (70.5) | 46 (29.5) | 23 (50.0) | 23 (50.0) |
| Health Belief Factor: Barriers | | | | |
| Low | 75 (53.6) | 65 (46.4) *** | 22 (33.8) | 43 (66.2) * |
| High | 120 (82.8) | 25 (17.2) | 17 (68.0) | 8 (32.0) |
| Health Belief Factor: Benefits | | | | |
| Low | 105 (80.8) | 25 (19.2) *** | 12 (48.0) | 13 (52.0) |
| High | 89 (56.0) | 70 (44) | 29 (41.4) | 41 (58.6) |
| Health Belief Factor: Self-Efficacy | | | | |
| Low | 110 (74.8) | 37 (25.2) *** | 16 (43.2) | 21 (56.8) |
| High | 86 (60.1) | 57 (39.9) | 25 (43.9) | 32 (56.1) |

*** $p<.01$;

** $p<.05$;

* $p<.10$; These p-values are associated with Chi-square tests which examined group differences on the variables.

[†] Percent based on number having received at least one dose of HPV vaccine.

[‡] All n's may not equal 300 or 99 due to missing data.

## Table 4

Multivariate Logistic Regression for Factors Associating with HPV Vaccination Initiation†

| Variable | *OR* | 95% CI* | *p* |
|---|---|---|---|
| Health Status | | | |
| Cancer Survivor | 1.00 | | |
| Healthy Control | 1.14 | 0.43 to 2.98 | .796 |
| Daughter's Age | | | |
| Preadolescents, 9–13 years | 1.00 | | |
| Adolescents, 14–17 years | 5.82 | 2.00 to 16.91 | .001 |
| Doctor Recommended Vaccine | | | |
| No | 1.00 | | |
| Yes | 6.54 | 2.56 to 16.73 | .000 |
| Health Belief Factor: Vulnerability | | | |
| Low | 1.00 | | |
| High | 0.45 | 0.19 to 1.04 | .062 |
| Health Belief Factor: Barriers | | | |
| Low | 1.00 | | |
| High | 0.26 | 0.10 to 0.70 | .008 |

*CI = confidence interval for odds ratio (OR)

†Only variables that were significant or marginally significant predictors in the multivariate analyses are included in this table, with the exception of the cancer/no cancer groups.

## Table 5

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

| Variable | *OR* | 95% CI[*] | *p* |
|---|---|---|---|
| Health Status | | | |
| Cancer Survivor | 1.00 | | |
| Healthy Control | 1.13 | 0.36 to 3.58 | .839 |
| Race of Maternal Caregiver | | | |
| White | 1.00 | | |
| Non-White | 0.26 | 0.07 to 0.89 | .032 |
| Daughter's Age | | | |
| Preadolescents, 9–13 years | 1.00 | | |
| Adolescents, 14–17 years | 4.83 | 0.93 to 25.05 | .061 |
| Health Belief Factor: Vulnerability | | | |
| Low | 1.00 | | |
| High | 0.27 | 0.07 to 1.11 | .069 |
| Health Belief Factor: Severity | | | |
| Low | 1.00 | | |
| High | 0.17 | 0.05 to 0.61 | .007 |
| Health Belief Factor: Barriers | | | |
| Low | 1.00 | | |
| High | 0.21 | 0.06 to 0.74 | .015 |

[*] CI = confidence interval for odds ratio (OR)

[†] Only variables that were significant or marginally significant predictors in the multivariate analyses are included in this table, with the exception of the cancer/no cancer groups.