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Human Papillomavirus (HPV) Vaccination in 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 the cause of cervical cancer, the second most common cancer among women worldwide. HPV vaccine uptake is particularly important for females surviving cancer, some of whom are at high risk for HPV complications due to the direct and indirect effects of cancer treatment. Thus, Version 3.0 of the Children's Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent and Young Adult Cancer recommends HPV vaccination for all eligible females surviving childhood cancer. Because this vaccine was only FDA approved in 2006, little is known about the complexity of vaccination uptake among those surviving cancer. The purpose of this article is to describe the HPV vaccine and its usefulness in the survivorship population, provide a rationale for describing cancer survivors as being at increased risk for HPV complications, identify factors which associate with HPV vaccination, and discuss the utilization of these predictors in designing strategies to promote adherence to HPV vaccination recommendations within the survivorship context.

Genital human papillomavirus (HPV) is the most common sexually transmitted infection 1, 2, and epidemiological studies indicate that approximately 80% of sexually active women contract HPV during their lifetime 3–5. Among young women, the prevalence of HPV has been estimated to be as high as 40% among 14- to 19-year-olds and 49% among 20- to 24-year-old sexually active females 6. The United States Youth Risk Behavior Surveillance of 2007, a national school-based survey of health-risk behaviors among high school students, reports 48% of all students and 46% of female students have engaged in sexual intercourse 7. Women who begin having sex at younger ages and those with more sexual partners are at highest risk for HPV exposure. HPV infection rates are highest in younger women and rise sharply soon after the median age of first sexual activity, 16.9 years for females 8.

Of the over 100 identified types of HPV, approximately 40 affect the genital tract 9. Oncogenic HPV strains have been etiologically linked to cervical, vaginal, vulvar, penile, anal and oral cancers. Cervical cancer (which is caused by HPV) is the second most common cancer among women worldwide and is the leading cause of cancer-related deaths among women in developing countries 10. In 2004, 11,892 women in the US were diagnosed with cervical cancer, which resulted in 3,850 disease specific deaths. Because

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cervical cancer is commonly asymptomatic until it is has progressed beyond the point where effective treatment is possible, primary prevention is the best approach for reducing the expression of this and other HPV-related malignancies. Regular screening using the Papanicolaou (Pap) test has been the most successful tactic for identifying cervical intraepithelial neoplasia, which is a precursor to cervical cancer.

Approximately 55 million Pap tests are performed each year in the US, and of these, 3.5 million (6 percent) yield abnormal results which require medical follow-up 11. HPV infections are primarily asymptomatic and infected women typically have normal Pap test results as infections usually clear without abnormality 11. However, all HPV strains have the potential to produce precancerous cells in the cervix that can be identified by Pap screening.

Genital HPV is transmitted by skin or mucosal contact, almost exclusively through sexual contact. Most commonly, the virus is transmitted through vaginal or anal intercourse. Oral and digital infection with genital HPV strains also occurs; however, the risk of transmission by digital-genital or oral-genital contact appears minimal 12. Although most HPV infections clear spontaneously, persistent infection with a high risk human papillomavirus type is necessary to cause cervical cancer 13. In particular, HPV types 16 and 18 are responsible for the majority of worldwide invasive cervical cancers 14. Progression from HPV infection to precancerous abnormal cell growth to cervical cancer is a slow process which may take decades to complete. Thus, although HPV occurs most often in sexually active adolescents and women aged 15 to 24 years, cervical cancer most often occurs in women over the age of 40, with median age at diagnosis for all cervical cancer patients being 47–48 years 15, 16.

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 clinically effective 17–19. In June of 2006, the US Food and Drug Administration 20 approved Gardasil (Merck & Co., Inc), a quadrivalent vaccine protecting recipients from HPV types 6, 11, 16, and 18, HPV types which account for 70% of cervical cancers and 90% of genital warts cases 21. Cervarix (GlaxoSmithKline), a bivalent vaccine which is currently available in Australia, the Philippines, and the European Union, protects against HPV types 16 and 18 and is predicted to gain FDA approval in 2009. In clinical trials, these vaccines (when administered as directed) demonstrated 98% efficacy in protecting females against the specified HPV types, thus eliminating the risk of grade 2/3 cervical intraepithelial neoplasia, adenocarcinoma in situ, and other HPV-type specific complications 19, 20, 22–24. Furthermore, these vaccines appear to be relatively safe. Specific to Gardasil, injection-site adverse experiences were reported to be generally mild to moderate in intensity for pain, swelling, and erythema. Systemic adverse events were reported to be mild to moderate with 1.5% of vaccine and 1.1% of placebo recipients experiencing fever ≥ 102°F, with no differences emerging across vaccine and placebo groups 4. Vaccine-related serious adverse events occurred in <0.1% of all study participants, and included events such as bronchospasm, gastroenteritis, headache/hypertension, vaginal hemorrhage, and injection site pain/movement impairment. There were no deaths in these trials secondary to the HPV vaccine or delivery procedures 24. Contraindications for vaccination include pregnancy and hypersensitivity to active substances/excipients in the vaccine.

Based on these favorable findings, routine HPV vaccination is currently recommended by the Advisory Committee on Immunization Practices (ACIP) for adolescent girls aged 11- and 12-years, but the injection series can be started for those as young as 9 years of age as Gardasil has been FDA approved for females between 9 and 26 years of age 19. It is recommended that girls receive the series of injections prior to the onset of sexual activity due to the mechanism of HPV transmission 20. HPV vaccination is not licensed in the US

for males of any age, although the European Union, Mexico, Australia, New Zealand, Indonesia, Costa Rica and Korea have approved Gardasil for use in males 25, 26, and a recent Merck-funded Phase III trial found that Gardasil was effective in preventing 90% of HPV-related external genital lesions among adolescent and young adult males 27. These findings suggest that in the US, HPV vaccine recommendations may one day include males since they are HPV carriers, are vulnerable to HPV-related cancers, and may respond favorably to the HPV vaccine 24.

The public health benefits of HPV immunization are considerable. The American Cancer Society estimates a possible reduction of cervical cancer risk by over 70% during the next decade with the implementation of the HPV vaccine 24. Such a decline in cervical cancer rates will depend on the number of carcinogenic HPV types eventually targeted by the vaccines, durability of protection by vaccination, degree of vaccination coverage among at-risk populations, and whether the medical community and the public continue to follow recommended screening guidelines 24. Therefore, promotion of HPV vaccine uptake is critical particularly among those populations at increased risk for HPV-related complications.

Women surviving childhood cancer are at increased risk for HPV-related complications

Although it is well known that survivors of childhood cancer are at increased risk for second malignancies, an increased incidence of cervical carcinoma and other HPV-related cancers has not been uniformly observed across diagnostic groups in this population. This finding begs the question as to whether women surviving childhood cancer are at increased risk for HPV-related complications like cervical cancer. As the median age for the expression of cervical cancer is 47–48 years of age 16, and only 2.8% of the female survivors in the Childhood Cancer Survivor Study cohort (which systematically monitors for second malignancies) are over 51 years of age, the relative risk of cervical and other HPV-related complications among women surviving childhood cancer risk is not definitively known. As treatment for childhood cancer continues to improve and the life expectancy of childhood cancer survivors continues to rise, it is likely that the expression of cervical carcinoma and other HPV-related cancers will increase in this population. Yet, for those females receiving specific types of cancer therapy in childhood, evidence for HPV-related vulnerability is already mounting, indicating the increased need for HPV vaccination in these high risk groups.

Immunosuppression

It has been well established that women who have undergone renal, liver or lung transplantation are at increased risk for HPV-related genital and oral disease, including cancer 28–33, and persistent HPV infection resulting from impaired immune clearance has been implicated as the mechanism responsible for these sequelae. Women with human immunodeficiency virus (HIV) are also at increased risk for HPV-associated malignancies, are more frequently diagnosed with advanced and difficult to treat cervical cancers, and are more likely to experience recurrence after treatment 34–39. As impaired immune function appears to be responsible for the increased rates of cervical and oral dysplasia experienced by these groups, we will target our review on female childhood cancer patients with persistent immune compromise (particularly those treated with hematopoietic stem cell transplantation or pelvic irradiation and those diagnosed with Hodgkin lymphoma). The implications of HPV vaccination in these groups will also be discussed.

Hematopoietic stem cell transplantation (HSCT)—Children and adolescents undergoing HSCT experience extreme immunosuppression as a result of pretransplant conditioning. This conditioning (which includes high dose chemotherapy, with or without total body irradiation) is necessary to achieve tumor control and, in allogeneic graft recipients, sustained hematopoietic engraftment. Although most patients will have complete immune reconstitution by two years post transplant, the duration and severity of immunodeficiency depends on several factors including type of the stem cells and their pre-transplant manipulation, graft vs. host disease (GVHD), and the age of the transplant recipient. Chronic GVHD, for example, adversely affects immune system reconstitution due to the aberrant T-cell function associated with the GVHD process as well as the immunosuppressive drugs required for GVHD control. Typically, patients who receive T-cell replete autologous or allogeneic grafts will develop near normal CD3+ cells three months post transplant. Yet during this period, CD4+ is decreased while higher proportions of CD8+ cells exist. This inverted CD4+/CD8+ ratio for those with chronic GVHD may continue for more than one year, and this delay in immune recovery increases the likelihood of infectious complications from bacteria, fungi and viruses, such as HPV 40.

Women who undergo bone marrow transplant as part of cancer treatment are at significantly increased risk for cervical dysplasia and second cancers, including cervical cancers. When Socie and colleagues 41 examined second malignancies among 3182 children who received allogeneic bone marrow transplant as part of treatment for acute lymphoblastic leukemia, the estimated cumulative risk for a new solid cancer was 11% by 15 years post transplant, which represented a 34-fold increased risk as compared to expected population-based rates. Those who were transplanted at earlier ages and those who received higher doses of total body irradiation as part of transplant conditioning were more likely to develop solid tumors post transplant. Female survivors of bone marrow transplantation are also at significantly increased risk for cervical dysplasia, a precancerous marker of cervical cancer. Whereas the proportion of abnormal Pap smears is typically 3%–6% among healthy women, those 3 years post bone marrow transplantation had a disproportionate rate of abnormal Pap smears which ranged from 14%–54% and 4%–33% for allogeneic and autologous transplant recipients, respectively 42. At 7 years post allogeneic transplant, 43% of females had abnormal Pap cytology smear findings, with 20% experiencing HPV-related high grade (and 14% experiencing low grade) squamous intraepithelial lesions. Those women experiencing chronic GVHD post transplant, which required prolonged systematic immunosuppressive therapy for greater than 3 years, were at the highest risk for dysplasia and more aggressive abnormalities of the cervix. Specific to cervical cancer, Bhatia and colleagues 43 conducted a retrospective study examining the occurrence of new solid cancers among 2129 patients who received bone marrow transplantation between 1976 and 1998. Similar to the findings reported by Socie et al., the cumulative probability for developing a solid cancer was almost 15% at 15 years post bone marrow transplantation. Transplant recipients had a 13-fold increased risk for the development of cervical cancer as compared to expected population-based rates. Pre-treatment conditioning factors were not found to be associated with the expression of new cervical cancers, and the authors concluded that immunodeficiency in combination with HPV exposure best explained the elevated rates of cervical dysplasia and cancer in this population.

Hodgkin Lymphoma—Hodgkin lymphoma is characterized by malignant transformation of lymphocytes. Generalized immune deficiency/suppression is a classic disease feature of Hodgkin lymphoma and is associated with persistent deficits in cellular immunity relating to enhanced sensitivity to suppressor monocytes and T-suppressor cells and abnormal interleukin-2 production 44, 45. This immune deficiency is worsened by cancer treatments (like chemotherapy, radiation therapy or splenectomy), and often persists long after treatment. Clinically, the immune deficiency associated with Hodgkin lymphoma results in

increased susceptibility and persistence of bacterial, fungal, and viral infections like HPV. Therefore, vaccinations and prompt treatment of infections are particularly important in this population.

It is not yet clear whether patients develop Hodgkin lymphoma because of these deficits in cellular immunity or as a result of the disease, and specific to HPV-related complications, there appears to be evidence for both etiologies. A premorbid history of genital warts or herpes zoster has, for example, been associated with the later development of Hodgkin lymphoma 46, whereas HPV-related epidermodysplasia verruciformis and cervical cancers have also been reported in patients after treatment for Hodgkin's lymphoma 47, 48. In the largest study of HPV infection among women with Hodgkin lymphoma, the medical charts of 666 patients consecutively treated at M.D. Anderson Cancer Center between 1963 and 1982 were retrospectively reviewed. Records which included the results of Pap testing, cervical biopsy, colposcopy, or related exam were included in the study 49. Among the 85 participants who met the study entry criteria, 46% had HPV infection and related neoplasia of the cervix or anogenital region. Specifically, 38% had unicentric or multicentric condylomatous lesions either with (n=14) or without (n= 19) intraepithelial neoplastic lesions, while 7% (n=6) had experienced invasive carcinoma of the cervix and/or vulva. Furthermore, being HPV positive was associated with a 2.88 excess risk for having high-grade Hodgkin lymphoma (stage III or IV) and with being more likely to receive combined radiation and chemotherapy treatment. These findings suggest that women with Hodgkin lymphoma have increased vulnerability to HPV-related complications, and that this susceptibility is due to the compromised immune functioning associated with Hodgkin lymphoma.

Pelvic Irradiation—Initiation of the immune response to genital HPV infection is largely orchestrated by epithelial cells within the lower genital tract. Genital tract epithelial cells play a key role in immunity to HPV by means of pathogen recognition, expression of antimicrobial mediators, and production of cytokines and chemokines that direct the immune response 50. Female cancer patients treated with therapies toxic to mucosal surfaces, such as anthracyclines and radiotherapy, may be more prone to HPV infection simply on the basis of impaired genital tract epithelial cell function. Similarly, survivors with chronic GVHD that involves the genital tract mucosa may have impaired epithelial cell function. When considering the potential for an underlying genetic predisposition to malignancy in patients treated for childhood cancer, who may then acquire impaired epithelial cell function after radiotherapy, one can argue that it is important for females undergoing pelvic irradiation as part of childhood cancer treatment to undergo HPV vaccination to prevent HPV-related complications.

Women who have received pelvic irradiation, as with those treated for Hodgkin lymphoma or with HSCT, are significantly more likely to experience HPV-related cervical and vaginal dysplasia and carcinomas of the genital tract. When examining lesions of postirradiation dysplasia among 17 women previously treated with pelvic irradiation due to malignancies of the uterine cervix, vagina and endometrium, one or more types of HPV DNA was identified in 8 (47%) of the lesions, and in 5 of 11 (46%) cases condyloma acuminatum was found 51. Similarly, 43 of 88 (49%) of women developed colposcopy-verified vaginal dysplastic lesions post pelvic irradiation, with high-risk HPV being identified in 42 (98%) of the lesions 52. One-third of women who experienced gynecological cancers after irradiation for cervical, endometrial, vulvar or colon cancer had HPV-related tumors 10 to 37 years after radiotherapy exposure.

Among women treated with pelvic irradiation, the etiology of post treatment cervical dysplasia and cancers has been attributed to recurrence of original malignancy, mutation of

cervicovaginal mucosa cells due to radiation exposure, natural HPV dysplastic processes, or a combination of these mechanisms driven by treatment-induced immunosuppression 51. Although it is difficult to isolate one process primarily responsible for these dysplastic and neoplastic outcomes, the higher than expected HPV infection rates, multiple types of HPV DNA identified in cervical lesions developing after radiotherapy, and the similarities between naturally occurring cervical dysplasia and cancers reinforces the notion that HPV (in combination with immunosuppression) is primarily responsible for these post treatment events 51–53. Although the HPV vaccine has yet to be tested among women who received pelvic irradiation as part of their cancer treatment, murine models examining the effect of pelvic radiotherapy and cisplatin on HPV vaccine responsiveness found that previous cancer treatment does not prevent the induction of an effective immune response by a peptide vaccine. This finding suggests that HPV vaccine efficacy should not be compromised among girls who receive pelvic radiation prior to vaccine administration. Although the impact of chemotherapy-related immunosuppression on antibody response to the HPV vaccine has not been evaluated, these preclinical data also suggest that HPV vaccination may be effective even in women who have had previous chemotherapy. Further studies are needed to confirm the efficacy of the HPV vaccine in this group.

Behavioral, Cognitive-Behavioral, and Demographic Risk Factors

Behavioral Risk Factors—Despite their increased risk for cervical dysplasia and cancers, female survivors of childhood cancer are not engaging in cervical cancer screening at rates recommended by the American Cancer Society. After adjusting for age, ethnicity, education, income and health insurance, women surviving childhood cancer were found to be significantly less likely than their healthy siblings to have undergone a Pap smear within the previous three years 54, with Hispanic survivors being the least likely to have undergone this screening 55. Survivors of childhood cancer without insurance and those over the age of 30 are already less likely to report secured medical care, and this risk increases as the survivor ages and time since diagnosis increases 56. It has also been suggested that survivors who perceive themselves to be infertile as a result of cancer therapy may engage in riskier sexual behaviors, which in turn, increases HPV exposure risk 57.

Cognitive-Behavioral Risk Factors—Up to 40% of survivors of childhood cancer have neurocognitive deficits, with inattention and hyperactivity being among the most commonly reported late effects of treatment 58, 59. Within the general population, evidence exists linking inattention and/or hyperactivity to increased risky sexual behavior. For example, Flory and colleagues 60 found that young adults who were diagnosed with Attention Deficit Hyperactivity Disorder (ADHD) as children were more likely to engage in behaviors such as earlier initiation of sexual activity and intercourse, increased number of sexual partners, increased casual sexual encounters, and increased partner pregnancies (among men) as compared to unaffected community peers. Similarly, those experiencing hyperactivity in childhood are more likely to become parents and to have been treated for a sexually transmitted disease 61. Because survivors of childhood cancer are more likely to experience inattention and/or hyperactivity, they are consequently at risk for increased engagement in risky sexual behaviors and contracting sexually transmitted infections such as HPV.

Demographic Risk Factors—In US population-based studies, the occurrence of cervical cancer has been associated with lower education, lower household income, and Hispanic ethnicity 62. Socioeconomic differences in male and female sexual behavior, along with access to cervical cancer screening, have been suggested to potentially explain these findings 63. Among childhood cancer survivors, women who are college educated, medically insured and older are more likely to have undergone Pap testing within the previous 3 years as compared to survivors who are less educated, without insurance, and

younger 54. As survivors of childhood cancer are more likely to report unemployment, lower educational attainment, and lower annual incomes as compared to their siblings 64, they are at increased risk for cervical cancer and suboptimal cervical cancer screening as a socioeconomic consequence of their childhood cancer treatment.

Rates and Predictors of HPV Vaccination

As of yet, there are no studies on rates of vaccination in the childhood cancer survivor population; thus, findings must be extrapolated from the healthy population. Although adolescents in the general population report high levels of acceptance regarding HPV vaccination, the actual rates of vaccination initiation and completion are reportedly low ranging from 5–25% 65¯67. Although differences in reported vaccination rates may be attributed to time since the vaccine's FDA approval, in addition to variability in regard to sampling methods, sexual history, and age of female participants, the reported HPV vaccination rates are significantly lower than the 90% target established by the Healthy People 2010 initiative.

Acceptability

Despite relatively low rates of HPV vaccination, between 66%–74% of adolescent/young adult females report intentions for HPV vaccination in the future 66, 68. Although encouraging, the majority of females in this age range are already HPV-positive, underscoring the importance of vaccination prior to infection. As with adolescents, parents are also accepting of HPV vaccination for their daughters. Specifically, 55% to 100% of parents are willing to vaccinate adolescents, and brief educational interventions have been found to increase acceptability among parents who were initially opposed or undecided regarding HPV vaccine utilization 69¯71.

Physician Recommendation

Adolescents surviving childhood cancer are often monitored by medical teams specializing in cancer survivorship, and it is well-known that medical providers have considerable influence on their patients' immunization decisions 72, 73. Although 90% of pediatricians endorse HPV immunization, many report parental barriers to HPV vaccination administration including concerns regarding vaccine safety, reluctance to immunize their child for a sexually transmitted infection and to have discussions regarding sexuality and HPV transmission, belief that their child already receives too many vaccines, denial that their child may be at risk for HPV, and concerns that vaccination would lead to riskier adolescent behaviors 74, 75. Of the 10% of physicians who report being unlikely to recommend HPV vaccination, factors such as being male, discomfort discussing sexuality issues with patients, and not routinely prescribing oral contraceptives are associated with being unlikely to recommend the vaccine 76. Physician factors associated with intent to recommend the HPV vaccine included personal and professional characteristics (e.g., age, race, practice location, HPV knowledge), office procedures (e.g., vaccinating children during sports physicals, ill visits, reminder calls), and vaccine cost and reimbursement 75. Finally, pediatricians' intent to recommend the HPV vaccine may be influenced by the endorsement of trusted sources (e.g., American Cancer Society, Center for Disease Control and Prevention, American Academy of Pediatrics, Advisory Committee for Immunization Practices) 74. The recent inclusion of HPV vaccination in the new version of the COG Long-Term Follow-Up guidelines for childhood cancer survivors may promote successful vaccine delivery in this patient population.

Familial Decision Making in the Cancer Survivorship Context

Despite physician influence, immunization against HPV is ultimately a familial decision-making process. As the recommended age for vaccination is relatively young, child attitudes about HPV vaccination are typically consistent with those of their parents who often determine whether to vaccinate their daughters 73. Familial predictors of HPV vaccination approval include family history of cancer, older age of daughter, familial communication regarding cervical cancer and other HPV-related topics, in addition to increased perceived vulnerability to and severity of HPV-related complication 68, 77, 78. Based on this cluster of predicative factors, HPV vaccine implementation in the context of cancer survivorship visits seems plausible in that all of these families will have a history of cancer, which is frequently accompanied by an increased sense of health vulnerability among both cancer survivors and their parents 79. Physician recommendation of HPV vaccine within the oncology setting may maximize the likelihood of HPV vaccination, in that this vaccine provides primary prevention of cervical and other HPV-related cancers.

Future Directions

Although the Advisory Committee on Immunization Practices recommends the HPV vaccine for “those immunosuppressed as a result of disease or medications,” the immunogenicity of the HPV vaccine has not yet been established among immunocompromised individuals. Antibody titers for HPV types 6 and 18 have been found to be significantly lower among vaccinated HIV-infected children as compared to healthy controls 80 suggesting that longitudinal trials are necessary in immunocompromised groups to determine long-term efficacy, appropriate dosing, and timing of vaccine administration. For immunocompromised survivors of childhood cancer, longitudinal studies will not only allow for the development of informed recommendations related both to vaccine administration and safer sexual behavior, but will also allow for close monitoring of vaccine-related long term side effects.

In addition to vaccine safety and efficacy, research is needed to determine whether specific factors, such as perceived vulnerability for second cancers, familial history of cancer and physician recommendation, are particularly relevant in decision-making about the HPV vaccine for childhood cancer survivors and their parents. These factors could then be utilized in interventions designed to increase rates of vaccination in this high risk group. Examination of barriers to vaccine completion (cost, access to healthcare, physician and parent education) would also be beneficial in reducing potential health care disparities specific to the HPV vaccine. The behavioral impact of the vaccine in terms of sexual behavior and cervical cancer screening should also be studied.

Conclusion

The HPV vaccine is an important public health tool which has specific benefits relating to the primary prevention of cervical and other cancers. The Children's Oncology Group's Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent and Young Adult Cancer Version 3.0, which serve as the gold standard in the screening for late effects that may arise due to treatment of pediatric cancer, has recommended HPV vaccination for all eligible females surviving childhood cancer. Survivors at the highest risk for HPV infection and its related complications include those undergoing hematopoietic stem cell transplantation, those with Hodgkin lymphoma, those treated with pelvic irradiation, and those receiving other treatments resulting in sustained immunosuppression. This risk profile is further potentiated by suboptimal cervical cancer screening, cognitive late effects, and declines in socioeconomic status commonly observed in childhood cancer survivors. The endorsement of the HPV vaccine by these guidelines is an important first step in addressing

the need for HPV vaccination in childhood cancer survivors, but interventions are needed to translate these recommendations into a successful HPV vaccination strategy.

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References

1. Sauvageau C, Duval B, Gilca V, Lavoie F, Ouakki M. Human Papilloma Virus vaccine and cervical cancer screening acceptability among adults in Quebec, Canada. BMC Public Health. 2007; 7(1): 304. Available from http://www.biomedcentral.com/1471-2458/7/304. [PubMed: 17961209]
2. Weinstock H, Berman S, Cates W Jr. Sexually transmitted diseases among American youth: incidence and prevalence estimates, 2000. Perspect Sex Reprod Health. 2004; 36(1):6–10. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14982671. [PubMed: 14982671]
3. Mariam A. Cervical cancer vaccines available in 2007. Drug Discovery Today. 2005; 10(14):949–50. Available from http://www.sciencedirect.com/science/article/B6T64-4GMB0F0-2/2/a770e318da358964dd13ef5c3083bc13. [PubMed: 16023048]
4. Markowitz LE, Dunne EF, Saraiya M, Lawson HW, Chesson H, Unger ER. Quadrivalent Human Papillomavirus Vaccine: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep. 2007; 56(RR-2):1–24. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=17380109. [PubMed: 17380109]
5. 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(12):1158–71. Available from http://aje.oxfordjournals.org/cgi/content/abstract/151/12/1158. [PubMed: 10905528]
6. 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(8):813–19. Available from http://jama.ama-assn.org/cgi/content/abstract/297/8/813. [PubMed: 17327523]
7. Eaton DK, Kann L, Kinchen S, Shanklin S, Ross J, Hawkins J, et al. Youth risk behavior surveillance--United States, 2007. MMWR Surveill Summ. 2008; 57(4):1–131. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=18528314. [PubMed: 18528314]
8. Wulf, D. In their own right: Addressing the sexual and reproductive health needs of American men. Alan Guttmacher Institute; New York: 2002.
9. Munoz N, Bosch FX, de Sanjose S, Herrero R, Castellsague X, Shah KV, et al. Epidemiologic Classification of Human Papillomavirus Types Associated with Cervical Cancer. N Engl J Med. 2003; 348(6):518–27. Available from http://content.nejm.org/cgi/content/abstract/348/6/518. [PubMed: 12571259]
10. American Cancer Society. Cancer Facts & Figures, 2008. American Cancer Society; 2008.
11. 2007. National Cancer Institute Fact Sheet 5.16, ed. The Pap Test: Questions and Answers
12. Burchell AN, Winer RL, de Sanjose S, Franco EL. Chapter 6: Epidemiology and transmission dynamics of genital HPV infection. Vaccine. 2006; 24(Suppl 3):S52–61. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=16950018.
13. Ault KA. Long-term efficacy of human papillomavirus vaccination. Gynecologic Oncology. 2007; 107(2, Supplement 1):S27–S30. Available from http://www.sciencedirect.com/science/article/B6WG6-4PWF3M2-7/2/4845f60e3f9fc6115f3e7feea1c1118d. [PubMed: 17938016]
14. Paavonen J, Lehtinen M. Introducing human papillomavirus vaccines - questions remain. Ann Med. 2008; 40(3):162–6. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=18382882. [PubMed: 18382882]

15. National Cancer Institute. SEER Cancer Statistics Review, 1975–2003. In: Ries, LAG.; Melbert, D.; Krapcho, M., et al., editors. National Cancer Institute. Vol. vol. 2008. National Cancer Institute; Bethesda, MD: 2006.
16. Watson M, Saraiya M, Ahmed F, Cardinez CJ, Reichman ME, Weir HK, et al. Using population-based cancer registry data to assess the burden of human papillomavirus-associated cancers in the United States: overview of methods. Cancer. 2008; 113(10 Suppl):2841–54. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=18980203. [PubMed: 18980203]
17. 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(9518):1247–55. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=16631880. [PubMed: 16631880]
18. Koutsky LA, Harper DM. Chapter 13: Current findings from prophylactic HPV vaccine trials. Vaccine. 2006; 24(Suppl 3):S114–21. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=16949998.
19. CDC. Quadrivalent human papillomavirus vaccine: Recommendations of the Advisory Committee on Immunization Practices (ACIP). Morbidity and Mortality Weekly Report. 2007; 56(No. RR-2): 1–26. Available from http://www.cdc.gov/mmwr/preview/mmwrhtml/rr56e312a1.htm?s_cid=rr56e312a1_e. [PubMed: 17218934]
20. FDA. HPV (human papillomavirus). Health OoWs. , editor. Vol. vol. 2008. 2006.
21. Villa LL, Costa RL, Petta CA, Andrade RP, Ault KA, Giuliano AR, 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(5):271–8. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15863374. [PubMed: 15863374]
22. Villa LL. Overview of the clinical development and results of a quadrivalent HPV (types 6, 11, 16, 18) vaccine. International Journal of Infectious Diseases. 2007; 11(Supplement 2):S17–S25. Available from http://www.sciencedirect.com/science/article/B7CPT-4RDXJ1M-4/2/ced67413d7f597c71af27bf67caf64c9. [PubMed: 18162241]
23. Villa LL, Costa RL, Petta CA, Andrade RP, Paavonen J, Iversen OE, et al. High sustained efficacy of a prophylactic quadrivalent human papillomavirus types 6/11/16/18 L1 virus-like particle vaccine through 5 years of follow-up. Br J Cancer. 2006; 95(11):1459–66. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=17117182. [PubMed: 17117182]
24. Saslow, D.; Castle, PE.; Cox, JT.; 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. Vol. vol. 57. 2007. p. 7-28.
25. Twombly R. U.S. Girls To Receive HPV Vaccine but Picture Unclear on Potential Worldwide Use, Acceptance. J. Natl. Cancer Inst. 2006; 98(15):1030–32. Available from http://jnci.oxfordjournals.org http://jnci.oxfordjournals.org/cgi/content/full/98/15/1030. [PubMed: 16882936]
26. Hoffman, J. Vaccinating Boys For Girls' Sake?. New York Times; New York: 2008.
27. MERCK. Gardasil, Merck's Cervical Cancer Vaccine, Demonstrated Efficacy in Preventing HPV-Related Disease in Male in Phase III Study Research & Development News. Vol. vol. 2009. 2008.
28. 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(7): 894–7. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15261186. [PubMed: 15261186]
29. 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(4):570–3. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=16926603. [PubMed: 16926603]
30. 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(2):647–52. Available

from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=18952575. [PubMed: 18952575]

31. Vacher-Coponat H, Dussol B, Berland Y. [Neoplastic disorders and organ transplantation]. Rev Med Interne. 1999; 20(11):992–1003. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=10586438. [PubMed: 10586438]
32. Mass K, Quint EH, Punch MR, Merion RM. Gynecological and reproductive function after liver transplantation. Transplantation. 1996; 62(4):476–9. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=8781613. [PubMed: 8781613]
33. 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(2–4):92–5. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=12593446. [PubMed: 12593446]
34. Hagensee ME, Cameron JE, Leigh JE, Clark RA. Human papillomavirus infection and disease in HIV-infected individuals. Am J Med Sci. 2004; 328(1):57–63. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15254442. [PubMed: 15254442]
35. Fruchter RG, Maiman M, Arrastia CD, Matthews R, Gates EJ, Holcomb K. Is HIV infection a risk factor for advanced cervical cancer? J Acquir Immune Defic Syndr Hum Retrovirol. 1998; 18(3):241–5. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=9665501. [PubMed: 9665501]
36. Palefsky JM, Minkoff H, Kalish LA, Levine A, Sacks HS, Garcia P, et al. Cervicovaginal human papillomavirus infection in human immunodeficiency virus-1 (HIV)-positive and high-risk HIV-negative women. J Natl Cancer Inst. 1999; 91(3):226–36. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=10037100. [PubMed: 10037100]
37. Di Stefano L, Coppola G, Moro S, Colageo E, Cellini A, Coletti G. Cervical-vaginal disease in HIV immunosuppressed patients: management and present screening programme. Eur J Gynaecol Oncol. 2006; 27(3):267–70. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=16800255. [PubMed: 16800255]
38. Parham GP, Sahasrabuddhe VV, Mwanahamuntu MH, Shepherd BE, Hicks ML, Stringer EM, et al. Prevalence and predictors of squamous intraepithelial lesions of the cervix in HIV-infected women in Lusaka, Zambia. Gynecol Oncol. 2006; 103(3):1017–22. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=16875716. [PubMed: 16875716]
39. Sirivongrangson P, Bollen LJ, Chaovavanich A, Suksripanich O, Virapat P, Tunthanathip P, et al. Screening HIV-infected women for cervical cancer in Thailand: findings from a demonstration project. Sex Transm Dis. 2007; 34(2):104–7. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=16755274. [PubMed: 16755274]
40. Bunin, N.; DiDomenico, C.; Guzikowski, V. Hematopoietic stem cell transplantation. In: Schwartz, CL.; Hobbie, WL.; Constine, LS.; Ruccione, KS., editors. Survivors of Childhood and Adolescent Cancer. Springer; Berlin Heidelberg: 2005. p. 271-82.
41. Socie G, Curtis RE, Deeg HJ, Sobocinski KA, Filipovich AH, Travis LB, et al. New malignant diseases after allogeneic marrow transplantation for childhood acute leukemia. J Clin Oncol. 2000; 18(2):348–57. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=10637249. [PubMed: 10637249]
42. Sasadeusz J, Kelly H, Szer J, Schwarer AP, Mitchell H, Grigg A. Abnormal cervical cytology in bone marrow transplant recipients. Bone Marrow Transplant. 2001; 28(4):393–7. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=11571513. [PubMed: 11571513]
43. Bhatia S, Louie AD, Bhatia R, O'Donnell MR, Fung H, Kashyap A, et al. Solid cancers after bone marrow transplantation. J Clin Oncol. 2001; 19(2):464–71. Available from http://

www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=11208840. [PubMed: 11208840]

44. Slivnick DJ, Ellis TM, Nawrocki JF, Fisher RI. The impact of Hodgkin's disease on the immune system. Semin Oncol. 1990; 17(6):673–82. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=2251514. [PubMed: 2251514]
45. Slivnick DJ, Nawrocki JF, Fisher RI. Immunology and cellular biology of Hodgkin's disease. Hematol Oncol Clin North Am. 1989; 3(2):205–20. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=2663823. [PubMed: 2663823]
46. Serraino D, Franceschi S, Talamini R, Barra S, Negri E, Carbone A, et al. Socioeconomic indicators, infectious diseases and Hodgkin's disease. Int J Cancer. 1991; 47(3):352–7. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=1993542. [PubMed: 1993542]
47. 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 Dermatol. 1988; 91(1):43–8. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=2838553. [PubMed: 2838553]
48. 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(1):53–4. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=10374677. [PubMed: 10374677]
49. Katz RL, Veanattukalathil S, Weiss KM. Human papillomavirus infection and neoplasia of the cervix and anogenital region in women with Hodgkin's disease. Acta Cytol. 1987; 31(6):845–54. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=2827413. [PubMed: 2827413]
50. Quayle AJ. The innate and early immune response to pathogen challenge in the female genital tract and the pivotal role of epithelial cells. J Reprod Immunol. 2002; 57(1–2):61–79. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=12385834. [PubMed: 12385834]
51. Fujimura M, Ostrow RS, Okagaki T. Implication of human papillomavirus in postirradiation dysplasia. Cancer. 1991; 68(10):2181–5. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=1655204. [PubMed: 1655204]
52. Barzon L, Pizzighella S, Corti L, Mengoli C, Palu G. Vaginal dysplastic lesions in women with hysterectomy and receiving radiotherapy are linked to high-risk human papillomavirus. J Med Virol. 2002; 67(3):401–5. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=12116034. [PubMed: 12116034]
53. Seidman JD, Kumar D, Cosin JA, Winter WE 3rd, Cargill C, Boice CR. Carcinomas of the female genital tract occurring after pelvic irradiation: a report of 15 cases. Int J Gynecol Pathol. 2006; 25(3):293–7. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=16810069. [PubMed: 16810069]
54. 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(3):631–40. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14745882. [PubMed: 14745882]
55. Castellino SM, Casillas J, Hudson MM, Mertens AC, Whitton J, Brooks SL, et al. Minority adult survivors of childhood cancer: a comparison of long-term outcomes, health care utilization, and health-related behaviors from the childhood cancer survivor study. J Clin Oncol. 2005; 23(27):6499–507. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=16170159. [PubMed: 16170159]
56. Oeffinger KC, Mertens AC, Hudson MM, Gurney JG, Casillas J, Chen H, et al. Health care of young adult survivors of childhood cancer: a report from the Childhood Cancer Survivor Study. Ann Fam Med. 2004; 2(1):61–70. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15053285. [PubMed: 15053285]

57. Zebrack BJ, Casillas J, Nohr L, Adams H, Zeltzer LK. Fertility issues for young adult survivors of childhood cancer. Psychooncology. 2004; 13(10):689–99. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15386645. [PubMed: 15386645]
58. Moleski M. Neuropsychological, neuroanatomical, and neurophysiological consequences of CNS chemotherapy for acute lymphoblastic leukemia. Arch Clin Neuropsychol. 2000; 15(7):603–30. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14590198. [PubMed: 14590198]
59. 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. J Clin Oncol. 1991; 9(8):1348–56. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=2072138. [PubMed: 2072138]
60. Flory K, Molina BSG, Pelham WE Jr. Gnagy E, Smith B. Childhood ADHD Predicts Risky Sexual Behavior in Young Adulthood. Journal of Clinical Child and Adolescent Psychology. 2006; 35(4): 571–77. Available from floryk@gwm.sc.edu 10.1207/s15374424jccp3504_8 http://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2006-13073-008&site=ehost-live. [PubMed: 17007602]
61. Barkley RA, Fischer M, Smallish L, Fletcher K. Young adult outcome of hyperactive children: Adaptive functioning in major life activities. J. Am. Acad. Child Adolesc. Psychiatry. 2006; 45(2): 192–202. [PubMed: 16429090]
62. Benard VB, Johnson CJ, Thompson TD, Roland KB, Lai SM, Cokkinides V, et al. Examining the association between socioeconomic status and potential human papillomavirus-associated cancers. Cancer. 2008; 113(10 Suppl):2910–8. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=18980274. [PubMed: 18980274]
63. Parkin DM, Bray F. Chapter 2: The burden of HPV-related cancers. Vaccine. 2006; 24(Suppl 3):S3/11–25. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=16949997. [PubMed: 16949997]
64. Gurney JG, Krull KR, Kadan-Lottick N, Nicholson HS, Nathan PC, Zebrack B, et al. Social Outcomes in the Childhood Cancer Survivor Study Cohort. J Clin Oncol. 2009 Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=19224833.
65. Kahn JA, Rosenthal SL, Jin Y, Huang B, Namakydoust A, Rosemore J, et al. 32: Vaccine-Type HPV Infection and Post-Licensure Attitudes About HPV Vaccination in Young Women. Journal of Adolescent Health. 2008; 42(2, Supplement 1):28–29. Available from http://www.sciencedirect.com/science/article/B6T80-4RR2XPS-25/1/750d8c0b0cdbe6b4d172f9a72076830a. [PubMed: 18155027]
66. 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(5):1103–10. Available from http://www.greenjournal.org/cgi/content/abstract/111/5/1103. [PubMed: 18448742]
67. CDC. Vaccination coverage among adolescents aged 13–17 years - United States, 2007. MMWR Morb Mortal Wkly Rep. 2008; 57(40):1100–3. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=18846032. [PubMed: 18846032]
68. Boehner CW, Howe SR, Bernstein DI, Rosenthal SL. Viral sexually transmitted disease vaccine acceptability among college students. Sex Transm Dis. 2003; 30(10):774–8. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14520177. [PubMed: 14520177]
69. Brewer NT, Fazekas KI. Predictors of HPV vaccine acceptability: A theory-informed, systematic review. Preventive Medicine. 2007; 45(2–3):107–14. Available from http://www.sciencedirect.com/science/article/B6WPG-4NWNCNW-1/2/f584c1721e64de30b7867fce1ad9ac6d. [PubMed: 17628649]
70. Davis K, Dickman ED, Ferris D, Dias JK. Human papillomavirus vaccine acceptability among parents of 10- to 15-year-old adolescents. J Low Genit Tract Dis. 2004; 8(3):188–94. Available

from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15874862. [PubMed: 15874862]

71. Gerend MA, Lee SC, Shepherd JE. Predictors of human papillomavirus vaccination acceptability among underserved women. Sex Transm Dis. 2007; 34(7):468–71. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=17139233. [PubMed: 17139233]
72. Ziv A, Boulet JR, Slap GB. Utilization of physician offices by adolescents in the United States. Pediatrics. 1999; 104(1 Pt 1):35–42. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=10390257. [PubMed: 10390257]
73. Zimet GD, Mays RM, Winston Y, Kee R, Dickes J, Su L. Acceptability of Human Papillomavirus Immunization. J of Women's health & Gender-based medicine. 2000; 9(1):47–50. Available from http://web.ebscohost.com/ehost/detail?vid=1&hid=109&sid=8de4ce9b-9b72-4396-abf4-3142565b5884%40sessionmgr107&bdata=JnNpdGU9ZWhvc3QtbGl2ZQ%3d%3d#db=nxh&A N=5323775.
74. Kahn JA, Zimet GD, Bernstein DI, Riedesel JM, Lan D, Huang B, et al. Pediatricians' intention to administer human papillomavirus vaccine: the role of practice characteristics, knowledge, and attitudes. Journal of Adolescent Health. 2005; 37(6):502–10. Available from http://www.sciencedirect.com/science/article/B6T80-4HMV7J7-B/2/45d4c2bfbd260e0dd6281f12c2c38f4e. [PubMed: 16310128]
75. Kahn JA, Rosenthal SL, Tissot AM, Bernstein DI, Wetzel C, Zimet GD. Factors Influencing Pediatricians' Intention to Recommend Human Papillomavirus Vaccines. Ambulatory Pediatrics. 2007; 7(5):367–73. Available from http://www.sciencedirect.com/science/article/B7XMV-4PNDBSB-7/2/cc3a8bdb4d4422db4137b4b58d03efa3. [PubMed: 17870645]
76. Daley MF, Liddon N, Crane LA, Beaty BL, Barrow J, Babbel C, et al. A National Survey of Pediatrician Knowledge and Attitudes Regarding Human Papillomavirus Vaccination. Pediatrics. 2006; 118(6):2280–89. Available from http://pediatrics.aappublications.org/cgi/content/abstract/118/6/2280. [PubMed: 17142510]
77. Marlow LA, Waller J, Wardle J. Parental attitudes to pre-pubertal HPV vaccination. Vaccine. 2007; 25(11):1945–52. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=17284337. [PubMed: 17284337]
78. 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(5):1486–93. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=16651301. [PubMed: 16651301]
79. Mulhern RK, Tyc VL, Phipps S, Crom D, Barclay D, Greenwald C, et al. Health-related behaviors of survivors of childhood cancer. Med Pediatr Oncol. 1995; 25(3):159–65. Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=7623724. [PubMed: 7623724]
80. Weinberg, A.; Song, LY.; Handelsman, E.; Moscicki, A.; Patterson, J.; Saah, A., et al. Safety and immunogenicity of a quadrivalent vaccine to prevent human papilloma virus infection in HIV-infected children: IMPAACT P1047. 15th Conference on Retroviruses and Opportunistic Infections; 2008.