

DNP Project Final Report:

Increasing Provider Knowledge of HPV Vaccine Recommendations

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Introduction

Purpose

Human papillomavirus (HPV), the most common sexually transmitted infection (STI) in the United States, is estimated to infect 14 million people between the ages of 15 – 59 annually (Asiaf, Ahmad, Mohammad, & Zargar, 2014; Fu, Bonhomme, Cooper, Joseph, & Zimet, 2014; Markowitz et al., 2014; Moreira et al., 2014; Rosenthal et al., 2011). Approximately 75% of sexually active adults will have at least one HPV infection during their lifetime, which can cause dysplasia of the squamous epithelium of the oropharynx and various anogenital sites (Asiaf et al., 2014; Dominiak-Felden et al., 2013).

Most HPV infections are transient, asymptomatic, and cause no clinical problems (Asiaf et al., 2014; Dominiak-Felden et al., 2013; Markowitz et al., 2014; Nelson & Stockdale, 2013). Approximately 70% of people with new cervical HPV infections will clear the infection within 1 year and 90% will clear the infection within 2 years (Markowitz et al., 2014). It is unknown whether HPV infections are resolved by complete viral clearance or by a prolonged maintenance phase where the virus replicates at low levels in the basal epithelium without clinical evidence of infection (Dochez, Bogers, Verhelst, & Rees, 2014). While most HPV infections are self-limited, persistent infection with HPV can cause cervical, vulvar, vaginal, anal, and oropharyngeal cancers, precancerous dysplasia, and genital warts (Jemal et al., 2013; Markowitz et al., 2014; World Health Organization, 2014).

Two HPV vaccines are licensed for use in the United States that have the potential to drastically decrease the prevalence of HPV-associated diseases. Gardasil, a quadrivalent HPV vaccine (HPV4), protects against HPV 6, 11, 16, and 18 and is licensed for use in females and males aged 9 through 26 years. Cervarix, a bivalent HPV vaccine (HPV2), protects against HPV

16 and 18 and is licensed for use in females aged 9 through 25 years. Both vaccines consist of a 3-shot series and neither contains live virus. See Table A1 in the appendix for more information on HPV vaccine characteristics.

Despite the availability of safe, effective vaccines against HPV since 2006, vaccination rates are low. In 2013, just over half (57.3%) of girls age 13-17 years had received at least one dose of the series and only 37.6% had received all three doses (Markowitz et al., 2014). Vaccination rates in males are even lower. In 2013, 34.6% of males age 13-17 years had received at least one dose (Markowitz et al., 2014). Several factors contribute to low vaccination rates, including concern about side effects, belief that the vaccine is not necessary, and limited knowledge about HPV (Laz, Rahman, & Berenson, 2012; Stokley et al., 2014). However, the most important factor in vaccine acceptance is recommendation from a healthcare provider (Hopkins & Wood, 2013; Markowitz et al., 2012; Rambout, Tashkandi, Hopkins, & Tricco, 2014; Rosenthal et al., 2011; Vadaparampil et al., 2014).

In an effort to improve provider knowledge of HPV vaccines, this DNP project is designed to effectively educate primary care providers (PCPs) with the latest evidence surrounding HPV-associated diseases, the indications for HPV vaccination, and the importance of provider recommendation. Through PCP education, this DNP project aims to increase HPV vaccination rates in the Portland, Oregon metro via evidence-based recommendations for healthcare providers.

Literature Review

A literature search on HPV-associated diseases and HPV vaccines was conducted in August and September 2014 using three electronic databases: Ovid MEDLINE without revisions (1996-current), Cumulative Index of Nursing and Allied Health Literature (CINAHL), and

Cochrane Database of Systematic Reviews. Search terms included *human papillomavirus*, *papillomavirus infections*, *vulva neoplasms*, *vagina neoplasms*, *anal neoplasms*, *oropharyngeal neoplasms*, *vaccine*, and *cervical screening*. Search results were limited to articles published in the English language from January 1, 2000-October 31, 2014. A manual review of the bibliographies of selected articles was also conducted to identify relevant primary articles.

A second literature review on education techniques for healthcare providers was conducted in October and November 2014 using three electronic databases: Ovid MEDLINE without revisions (1996-current), Cumulative Index of Nursing and Allied Health Literature (CINAHL), and Cochrane Database of Systematic Reviews. Search terms included *continuing medical education*, *continuing professional education*, *continuing professional development*, and *vaccine*. Search results were limited to articles published in the English language from January 1, 2000-current. A manual review of the bibliographies of selected articles was also conducted to identify relevant primary articles.

Burden of HPV-Associated Diseases

Both high-risk and low-risk HPV types contribute to significant morbidity and mortality in the United States. Persistent high-risk HPV infections are associated with cancers of the cervix, vagina, vulva, anus, penis, and oropharynx. An estimated 33,200 HPV-associated cancers occur annually in the United States with 20,600 among females and 12,600 among males (Markowitz et al., 2014). Cervical cancer is the most common HPV-associated cancer in women with 12,000 cases annually (Centers for Disease Control and Prevention, 2012). Epidemiologic studies demonstrate that HPV is responsible for 99% of cervical cancer and that HPV 16 and 18 alone cause 70% of cases (Asiaf et al., 2014). Oropharyngeal squamous cell carcinoma (OPSCC) is the most common HPV-associated cancer in men with 7,200 cases annually (Centers for

Disease Control and Prevention, 2012). It is estimated that 70% of all OPSCC is associated with HPV infection (Chaturvedi et al., 2011; Jemal et al., 2013), particularly OPSCC of the tonsils and base of the tongue, and that HPV 16 causes more than 90% of HPV-associated OPSCC (Herrero et al., 2013). Similar to the cervix and oropharynx, the majority of HPV-associated cancers of the anus, vagina, vulva, and penis are attributed to HPV 16 and 18. It is estimated that ~40% of vulvar carcinoma, 60% of vaginal carcinoma, and 80% of anal carcinoma could be avoided by prophylactic vaccination against HPV 16/18 (De Vuyst, Clifford, Nascimento, Madeleine, & Franceschi, 2009).

Low-risk HPV types are responsible for all cases of genital warts, particularly HPV 6 and 11, which cause more than 90% of cases (Goldstone et al., 2013; Markowitz et al., 2014; Nelson & Stockdale, 2013; World Health Organization, 2014). Genital warts are common in the United States with 500,000 to 1,000,000 new cases annually (Nelson & Stockdale, 2013). While benign in nature, genital warts are associated with psychosocial distress, including increased anxiety and depression, negative impacts on personal relationships, and decreased quality of life (Dominiak-Felden et al., 2013; Markowitz et al., 2014). Genital warts also have a high rate of treatment failure and recurrent treatments are costly and often painful (Giuliano et al., 2011).

Vaccine Efficacy and Safety

The efficacy of HPV2 and HPV4 has been repeatedly demonstrated in large, randomized, double blind, placebo-controlled clinical trials of men and women (Markowitz et al., 2014).

HPV4 is over 98% effective at preventing genital warts and dysplasia and cancer of the cervix and anus associated with types 6, 11, 16, and 18. Similarly, HPV2 is 95% effective at preventing HPV 16- and 18-associated dysplasia and cancer of the cervix and anus. No benefit of HPV4 or HPV2 was observed in females or males against HPV types that they were already infected with,

highlighting the need for early vaccination, ideally before sexual debut. Long-term efficacy of HPV vaccines has been demonstrated at five years (Villa et al., 2006) and is currently being evaluated in men and women 10-14 years after vaccination (Markowitz et al., 2014).

The safety of HPV2 and HPV4 is well established. From June 2006 through March 2014, 67 million doses of HPV4 have been distributed in the United States. The most commonly reported adverse-events are syncope, dizziness, nausea, pallor, headache and fever. While 96 deaths occurred in children post-vaccination, there was no causal relationship established with HPV4 (Markowitz et al., 2014). Additionally, no statistically significant increased risks were observed for Guillain-Barre syndrome, stroke, seizure, anaphylaxis, or venous thromboembolism (Markowitz et al., 2014).

Recommendations for Use of HPV Vaccines

The Advisory Committee on Immunization Practices (ACIP) recommends routine vaccination at age 11 or 12 years with HPV4 or HPV2 for females and with HPV4 for males (Markowitz et al., 2014). Vaccination is also recommended for females aged 13 through 26 years and for males aged 13 through 21 years who have not been vaccinated previously or who have not completed the 3-dose series. Males up to 26 years may be vaccinated; see section on special populations. The HPV vaccine series should be started even if a person will turn 27 years of age prior to completion of the 3-shot series (Markowitz et al., 2014).

Special populations.

Immunocompromised. People who are immunocompromised have higher rates of HPV acquisition and progression to clinical disease, including genital warts, dysplasia, and carcinoma. Vaccination with HPV4 is recommended for immunocompromised men and women through age 26 who have not been previously vaccinated or who have not completed all 3 doses of the series

(Markowitz et al., 2014).

Men who have sex with men. Men who have sex with men (MSM) are at higher-risk for HPV infection and associated conditions, including genital warts and anal cancer. Vaccination with HPV4 is recommended through age 26 for all MSM who have not been previously vaccinated or who have not completed all 3 doses of the series (Markowitz et al., 2014).

Abnormal Pap test, known HPV infection, or HPV-associated lesion. HPV vaccination can provide protection against other HPV types even if a person already has a known or suspected HPV-related infection or lesion. Only a small percentage of people are infected with both HPV 16 and 18 or all four vaccine types. HPV vaccination will not have any therapeutic effect on existing infections, but may help prevent further infection (Markowitz et al., 2014).

Barriers to Vaccination

The most commonly cited reasons for low HPV vaccine utilization include lack of recommendation for vaccination by a healthcare provider, insufficient knowledge about HPV, and the belief that HPV vaccination is not needed (Laz et al., 2012; Stokley et al., 2014). In 2012, only 64.4% of adolescent females and 41.6% of males reported receiving an recommendation for HPV vaccination from their providers (Stokley et al., 2014) yet healthcare provider recommendation is consistently cited as one of the most important factors in accepting HPV vaccination (Hopkins & Wood, 2013; Markowitz et al., 2012; Rambout et al., 2014; Rosenthal et al., 2011; Vadaparampil et al., 2014). A recent study by Rosenthal et al. (2011) showed that women who do not receive a strong recommendation for HPV vaccination from their physician are four times less likely to accept vaccination.

Next to provider recommendation, receipt of more in-depth information on HPV vaccination increases vaccine acceptance (Hopkins & Wood, 2013). Patients are often not aware

that HPV causes cancer and may not be familiar with the ability of the HPV vaccine to prevent precancerous lesions and to decrease mortality from HPV-associated cancers (Wegwarth, Kurzenhauser-Carstens, & Gigerenzer, 2014). HPV education can be simple; evidence-based leaflets on HPV vaccination are effective at increasing patients' knowledge about the HPV vaccine, improving perceived risk judgments, and lead to increased vaccine uptake (Wegwarth et al., 2014). Additionally, HPV vaccine education at the time the first dose is administered increases compliance with completion of the 3-dose series (Fu et al., 2014).

Other barriers to vaccination include concern about side effects and feeling that the vaccine is not necessary (Hopkins & Wood, 2013; Rambout et al., 2014). The HPV vaccine has also raised philosophical and social concerns in the United States, particularly in states where HPV vaccination is mandated in only one gender (i.e., females) (Hawkes, Kismodi, Larson, & Buse, 2014) and in people who believe the HPV vaccination may lead to riskier sexual behaviors in adolescents and young adults (Hopkins & Wood, 2013; Markowitz et al., 2012). These barriers can be addressed with education on HPV from providers and by following the current ACIP recommendations to vaccinate both males and females.

Another potential barrier to increasing HPV vaccination rates is lack of provider knowledge of vaccine benefits. Providers have been found to underestimate the benefit of HPV vaccination, including protection against non-cervical anogenital and oropharyngeal cancers (Hopkins & Wood, 2013; Saraiya, Rosser, & Cooper, 2012). Additionally, physicians have been found to rate their knowledge of HPV higher than it is scored objectively (Hopkins & Wood, 2013), therefore, they may not feel like they need to seek out further education on HPV.

Provider Education

Continuing education (CE) activities are commonly used in professional practice settings to improve clinical practice and patient outcomes. Three systematic reviews and one meta-analysis demonstrate that CE interventions have a small to moderate effect on professional practice and patient outcomes (Bloom, 2005; Bluestone et al., 2013; Forsetlund et al., 2009; Mansouri & Lockyer, 2007). Evidence from these studies suggests that education interventions are more effective when they are interactive and learners are engaged, such as case-based learning and clinical simulations. Didactic instruction and providing printed materials alone, such as a lecture, have little to no impact on learning outcomes (Bloom, 2005; Bluestone et al., 2013). The combination of interactive and didactic material has the greatest effect on professional practice (Forsetlund et al., 2009). When interactive learning techniques are utilized, educational outcomes are similar between computer-based and live instruction (Bluestone et al., 2013).

The most commonly reported barrier to completion of CE activities by providers is lack of time (Ikenwilo & Skåtun, 2014). One way to address this barrier is through online CE activities, which offer flexible timing and easy access at low cost (Lam-Antoniades, Ratnapalan, & Tait, 2009). Use of an online platform can also increase CE participation from rural locations (Schoen et al., 2009). Internet-based CE activities have similar results to traditional, in-person methods; providers who complete online CE activities are more likely to choose evidence-based answers to case vignettes than non-participants, suggesting that internet-based CE activities are effective in improving clinical practice (Casebeer et al., 2010; Cook et al., 2008).

For an online CE activity to be effective, learners must perceive the topic as directly applicable to clinical practice (Dalal, Brancati, & Sisson, 2012; Schoen et al., 2009; Young, Kim, Yeung, Sit, & Tobe, 2011). While face-to-face CE is preferred for new or controversial content,

online CE is preferred for reviewing updated guidelines and filling gaps in knowledge (Young et al., 2011). Additionally, credibility of the source of online information is essential in order to engage providers. Credibility is increased by affiliation with known, trusted organizations and decreased by affiliation with pharmaceutical companies (Young et al., 2011). Providers also prefer to have some control of online media content, such as being able to navigate quickly to relevant content and to have content available in a variety of formats (e.g., text, audio, video) (Young et al., 2011). In addition, learners report higher satisfaction with online CE activities when they score higher on post-tests regardless of pre-test scores (Dalal et al., 2012), emphasizing the need for participants to successfully gain knowledge from an online CE activity.

One highly effective method for teaching providers is case-based learning, whether the CE activity is face-to-face or online (Andolsek, Rosenberg, Abdolrasulnia, Stowell, & Gardner, 2013). Case studies help to reinforce and validate concepts (Young et al., 2011) and are most effective when they incorporate typical patient scenarios (Andolsek et al., 2013). In follow up after a CE activity, case vignettes can also be used to assess application of knowledge and to predict actual clinical practice patterns (Andolsek et al., 2013).

Approach to the Conduct of the Project

Setting

This project consisted of an online CE activity, *HPV Vaccination: Current Evidence and Recommendations*, initially offered to providers practicing in the Portland, Oregon metro and then nationally via the American Association of Nurse Practitioners (AANP) CE website. The CE activity included a 38-minute lecture with integrated case studies and 10-question pre- and post-tests. It was available on a public web address from 4/1/2014 to 5/31/2015 and providers

were able to complete the activity at a time of their choosing. On June 10, 2015, the activity was released to the AANP for use on their CE website.

The online setting was chosen for this project so that the information could be efficiently and cost-effectively distributed on a large scale. Additionally, considering that many providers cite lack of time as a barrier to completing CE activities (Ikenwilo & Skåtun, 2014), the online platform allowed providers to select their preferred time for participation and to pause the activity and return later to complete it. To distribute the project efficiently, several key facilitators were identified, including clinical preceptors, the OHSU School of Nursing (SON) graduate program assistants for access to email list serves, the Nurse Practitioners of Oregon (NPO) organization for access to state email list serves of practicing advanced practice registered nurses (APRNs), and the AANP for national distribution. Anticipated barriers to project distribution and participation included no response from facilitators and low participation rates. The facilitators were contacted via email with a link to the project website and, if no response, also contacted by telephone.

Participants

As most HPV vaccines are administered in the primary care setting (Markowitz et al., 2012), the intended population for this project was PCPs, including APRNs, physicians, and physician assistants. Of note, only licensed APRNs were eligible to receive CE credit for the activity but any healthcare provider (HCP) could complete the activity. Participation was voluntary and could be anonymous; participants did not need to include their name or email on the pre-test or post-test unless they wished to receive CE credit. Additionally, the course evaluation was anonymous. This project did not require institutional review board (IRB) approval thus formal participant protection protocols were not applicable.

The inclusion criteria for this project were professional licensure as a healthcare provider and access to a computer with Internet capabilities. To achieve a widespread distribution, several APRNs in Portland, OR were contacted to share the project with their colleagues, the OHSU SON DNP and FNP faculty email list serves were utilized, and the NPO was contacted for statewide distribution. An application for inclusion on the AANP CE website was also submitted in March 2015 and accepted for national distribution of the project. Additionally, the Portland Veterans Affairs Medical Center (PVAMC) education department was contacted for distribution to HCPs in the VA system.

Implementation and Outcome Evaluation

Implementation

The first step in implementation of this project was obtaining CE accreditation. The AANP was chosen as an accrediting body because it is a reputable, professional organization and providers have demonstrated higher participation rates when a CE activity it is affiliated with a credible source (Young et al., 2011). An application for CE approval was submitted to the AANP on 3/17/2015 and CE approval was granted on 3/20/15. The program was approved for 1 hour of CE credit, including 0.3 hours of pharmacology and can be referenced by program number 1503157. After obtaining CE accreditation, the activity was posted to a public web address hosted by the Sakai platform (https://sakai.ohsu.edu/access/content/group/horak-dnp-project/hpv_vaccination_CE) on 4/1/2015 and remained accessible online through 5/31/2015. To be granted 1 CE unit, participants were required to watch the 38-minute lecture and score at least 70% on the post-test. A certificate of completion was emailed to them within 72 hours of successfully completing the post-test.

After receiving accreditation from the AANP and officially posting the CE activity on a public web address, three clinical preceptors were contacted to distribute the project to their colleagues at the OHSU Family Medicine at Richmond Walk-In Clinic, Rose City Urgent Care and Family Practice, and the Center for Women Veterans Health at the PVAMC. Project information was also emailed to current OHSU DNP students and to all DNP faculty at OHSU. For statewide distribution, the NPO was contacted multiple times via email for access to their email list serve, however they did not respond. For national distribution, an application for inclusion on the AANP CE Center website was submitted in March 2015. Upon follow-up correspondence in May 2015, they agreed to include the learning activity with CE on their website with the understanding that they could not host it on their website while it was also available on a public web address. Ultimately, the CE activity will be posted on the AANP website sometime after June 10, 2015.

Outcome Evaluation

Fourteen participants completed the CE activity between 4/1/15 and 5/21/15; all participants successfully scored 70% or higher on the post-test on the first attempt. A dependent samples t-test was conducted to identify whether the CE activity effectively increased providers' knowledge of HPV vaccine recommendations. There was a statistically significant increase in scores from the pre-test ($M=5.6$, $SD=1.52$) to the post-test ($M=8.6$, $SD=1.10$) ($t(13)=7.09$, $p=0.000194$), demonstrating that the CE activity was an effective educational activity.

Other outcomes evaluated for this project included the feasibility and acceptability of an online learning module for HCPs. From a feasibility perspective, the project was successful. The CE activity was developed using basic software, distributed online via a public web address, and accredited by the AANP. The project was developed at low cost (\$50 total for the CE

application) and was widely distributed to HCPs, demonstrating that the online setting is a good option for professional CE activities.

The acceptability, or how well the activity was received by participants and met the needs of participants, was also assessed using course evaluations. A total of 10 course evaluations were submitted with a mean score of 9.6 out of 10 points (range 8 to 10 points) with 10 being the most effective/satisfactory experience. The high course evaluation scores reflect participant satisfaction with the CE activity experience, indicating that the activity objectives were met.

Practice-Related Implications

This project demonstrated that developing an online CE activity is feasible for APRNs and that, overall, online CE activities are well accepted by providers. When developing online CE activities, topic selection is important to the acceptability of the activity. HPV vaccination recommendations was an appropriate choice for the online setting because it was an update on existing guidelines rather than a new or controversial topic, which are more suited for in-person lectures (Young et al., 2011). It is also essential to have an affiliation with a credible source, such as a certifying body or a trusted medical organization, to increase participation. The online setting is a low-cost option for CE activities that allows for widespread distribution, making it a practical option for APRNs who are interested in creating a CE activity. Online CE activities may also be of particular value to providers in rural areas where access to professional education opportunities may be limited (Schoen et al., 2009).

Summary

Despite the availability of safe and effective vaccines, HPV vaccination rates are low in the United States, contributing to the increasing prevalence of HPV-related diseases (Markowitz et al., 2014). Several barriers to vaccination exist, including insufficient knowledge about HPV

and the belief that HPV vaccination is not needed (Laz et al., 2012). However, the most important factor in increasing HPV vaccine acceptance is provider recommendation (Stokley et al., 2014).

In an effort to improve provider knowledge of HPV vaccines, this DNP project was designed to effectively educate HCPs with the latest evidence surrounding HPV-associated diseases, the indications for HPV vaccination, and the importance of provider recommendation via an online CE activity. The CE activity, *HPV Vaccination: Current Evidence and Recommendations*, included a 38-minute lecture with integrated case studies and 10-question pre- and post-tests which was accredited by the AANP for 1 CE credit. The free CE activity was released on a public web address between 4/1/15 and 5/31/15. Fourteen HCPs completed the activity with a statistically significant increase in post-test scores, demonstrating a meaningful increase in provider knowledge. Following removal from the public web address, it will be posted on the AANP CE Center website for national distribution.

This project demonstrates the feasibility of an APRN developing an online CE activity and the acceptability of a CE activity in the online format. The online setting is an economical option for developing CE activities that allows for widespread distribution of educational materials. Additionally, providers often prefer the online setting for scheduling flexibility (Lam-Antoniades et al., 2009). Online CE activities are effective in increasing provider knowledge and should be utilized by APRNs to provide evidence-based educational opportunities for colleagues.

References

- Andolsek, K., Rosenberg, M. T., Abdolrasulnia, M., Stowell, S. A., & Gardner, A. J. (2013). Complex cases in primary care: Report of a CME-certified series addressing patients with multiple comorbidities. *International Journal of Clinical Practice*, *67*(9), 911-917.
doi:<http://dx.doi.org/10.1111/ijcp.12175>
- Asiaf, A., Ahmad, S. T., Mohammad, S. O., & Zargar, M. A. (2014). Review of the current knowledge on the epidemiology, pathogenesis, and prevention of human papillomavirus infection. *European Journal of Cancer Prevention*, *23*(3), 206-224.
doi:10.1097/CEJ.0b013e328364f273
- Bloom, B. S. (2005). Effects of continuing medical education on improving physician clinical care and patient health: A review of systematic reviews. *International Journal of Technology Assessment in Health Care*, *21*(3), 380-385.
- Bluestone, J., Johnson, P., Fullerton, J., Carr, C., Alderman, J., & BonTempo, J. (2013). Effective in-service training design and delivery: Evidence from an integrative literature review. *Human Resources for Health*, *11*(1)
- Casebeer, L., Brown, J., Roepke, N., Grimes, C., Henson, B., Palmore, R., . . . Salinas, G. D. (2010). Evidence-based choices of physicians: A comparative analysis of physicians participating in internet CME and non-participants. *BMC Medical Education*, *10*(1)
doi:10.1186/1472-6920-10-42
- Centers for Disease Control and Prevention. (2012). Human papillomavirus-associated cancers - united states, 2004-2008. *MMWR - Morbidity & Mortality Weekly Report*, *61*, 258-261.

Chaturvedi, A. K., Engels, E. A., Pfeiffer, R. M., Hernandez, B. Y., Xiao, W., Kim, E., . . .

Gillison, M. L. (2011). Human papillomavirus and rising oropharyngeal cancer incidence in the united states. *Journal of Clinical Oncology*, 29(32), 4294-4301.

Cook, D. A., Levinson, A. J., Garside, S., Dupras, D. M., Erwin, P. J., & Montori, V. M. (2008).

Internet-based learning in the health professions: A meta-analysis. *JAMA - Journal of the American Medical Association*, 300(10), 1181-1196. doi:10.1001/jama.300.10.1181

Dalal, D., Brancati, F. L., & Sisson, S. D. (2012). Factors affecting learner satisfaction with an

internet-based curriculum. *Southern Medical Journal*, 105(8), 387-391.

doi:10.1097/SMJ.0b013e31825d9abb

De Vuyst, H., Clifford, G. M., Nascimento, M. C., Madeleine, M. M., & Franceschi, S. (2009).

Prevalence and type distribution of human papillomavirus in carcinoma and intraepithelial neoplasia of the vulva, vagina and anus: A meta-analysis. *International Journal of Cancer*, 124(7), 1626-1636.

Dochez, C., Bogers, J. J., Verhelst, R., & Rees, H. (2014). HPV vaccines to prevent cervical

cancer and genital warts: An update. *Vaccine*, 32(14), 1595-1601.

Dominiak-Felden, G., Cohet, C., Atrux-Tallau, S., Gilet, H., Tristram, A., & Fiander, A. (2013).

Impact of human papillomavirus-related genital diseases on quality of life and psychosocial wellbeing: Results of an observational, health-related quality of life study in the UK. *BMC Public Health*, 13, 1065.

Forsetlund, L., Bjørndal, A., Rashidian, A., Jamtvedt, G., O'Brien, M. A., Wolf, F. M., . . .

Oxman, A. D. (2009). Continuing education meetings and workshops: Effects on professional practice and health care outcomes. *Cochrane Database of Systematic Reviews*, (2) doi:10.1002/14651858.CD003030.pub2.

Fu, L. Y., Bonhomme, L. A., Cooper, S. C., Joseph, J. G., & Zimet, G. D. (2014). Educational interventions to increase HPV vaccination acceptance: A systematic review. *Vaccine*, 32(17), 1901-1920.

Giuliano, A. R., Palefsky, J. M., Goldstone, S., Moreira, E. D., Jr, Penny, M. E., Aranda, C., . . .
Guris, D. (2011). Efficacy of quadrivalent HPV vaccine against HPV infection and disease in males. *New England Journal of Medicine*, 364(5), 401-411.

Goldstone, S. E., Jessen, H., Palefsky, J. M., Giuliano, A. R., Moreira, E. D., Jr, Vardas, E., . . .
Garner, E. (2013). Quadrivalent HPV vaccine efficacy against disease related to vaccine and non-vaccine HPV types in males. *Vaccine*, 31(37), 3849-3855.

Hawkes, S., Kismodi, E., Larson, H., & Buse, K. (2014). Vaccines to promote and protect sexual health: Policy challenges and opportunities. *Vaccine*, 32(14), 1610-1615.

Herrero, R., Quint, W., Hildesheim, A., Gonzalez, P., Struijk, L., Katki, H. A., . . . CVT Vaccine,
G. (2013). Reduced prevalence of oral human papillomavirus (HPV) 4 years after bivalent HPV vaccination in a randomized clinical trial in costa rica. *PLoS ONE [Electronic Resource]*, 8(7), e68329.

- Hopkins, T. G., & Wood, N. (2013). Female human papillomavirus (HPV) vaccination: Global uptake and the impact of attitudes. *Vaccine*, *31*(13), 1673-1679.
- Ikenwilo, D., & Skåtun, D. (2014). Perceived need and barriers to continuing professional development among doctors. *Health Policy*, *117*(2), 195-202.
- Jemal, A., Simard, E. P., Dorell, C., Noone, A. -, Markowitz, L. E., Kohler, B., . . . Edwards, B. K. (2013). Annual report to the nation on the status of cancer, 1975-2009, featuring the burden and trends in human papillomavirus (HPV)-associated cancers and HPV vaccination coverage levels. *Journal of the National Cancer Institute*, *105*(3), 175-201.
doi:10.1093/jnci/djs491
- Lam-Antoniades, M., Ratnapalan, S., & Tait, G. (2009). Electronic continuing education in the health professions: An update on evidence from RCTs. *Journal of Continuing Education in the Health Professions*, *29*(1), 44-51. doi:10.1002/chp.20005
- Laz, T. H., Rahman, M., & Berenson, A. B. (2012). An update on human papillomavirus vaccine uptake among 11-17 year old girls in the united states: National health interview survey, 2010. *Vaccine*, *30*(24), 3534-3540.
- Mansouri, M., & Lockyer, J. (2007). A meta-analysis of continuing medical education effectiveness. *Journal of Continuing Education in the Health Professions*, *27*(1), 6-15.
- Markowitz, L. E., Dunne, E. F., Saraiya, M., Chesson, H. W., Curtis, C. R., Gee, J., . . . Unger, E. R. (2014). Human papillomavirus vaccination: Recommendations of the advisory

committee on immunization practices (ACIP). *Morbidity & Mortality Weekly Report*, 63(RR-05), 1-30.

Markowitz, L. E., Tsu, V., Deeks, S. L., Cubie, H., Wang, S. A., Vicari, A. S., & Brotherton, J. M. (2012). Human papillomavirus vaccine introduction--the first five years. *Vaccine*, 30(Suppl 5), F139-48.

Moreira, E. D., Jr, Giuliano, A. R., Palefsky, J., Flores, C. A., Goldstone, S., Ferris, D., . . . Haupt, R. M. (2014). Incidence, clearance, and disease progression of genital human papillomavirus infection in heterosexual men. *Journal of Infectious Diseases*, 210(2), 192-199.

Nelson, E. L., & Stockdale, C. K. (2013). Vulvar and vaginal HPV disease. *Obstetrics & Gynecology Clinics of North America*, 40(2), 359-376.

Rambout, L., Tashkandi, M., Hopkins, L., & Tricco, A. C. (2014). Self-reported barriers and facilitators to preventive human papillomavirus vaccination among adolescent girls and young women: A systematic review. *Preventive Medicine*, 58, 22-32.

Rosenthal, S. L., Weiss, T. W., Zimet, G. D., Ma, L., Good, M. B., & Vichnin, M. D. (2011). Predictors of HPV vaccine uptake among women aged 19-26: Importance of a physician's recommendation. *Vaccine*, 29(5), 890-895.

Saraiya, M., Rosser, J. I., & Cooper, C. P. (2012). Cancers that U.S. physicians believe the HPV vaccine prevents: Findings from a physician survey, 2009. *Journal of Women's Health*, 21(2), 111-117.

Schoen, M. J., Tipton, E. F., Houston, T. K., Funkhouser, E., Levine, D. A., Estrada, C. A., . . .

Kiefe, C. I. (2009). Characteristics that predict physician participation in a web-based CME activity: The MI-plus study. *Journal of Continuing Education in the Health Professions*, 29(4), 246-253. doi:10.1002/chp.20043

Stokley, S., Jeyarajah, J., Yankey, D., Cano, M., Gee, J., Roark, J., . . . Markowitz, L. (2014).

Human papillomavirus vaccination coverage among adolescents, 2007-2013, and postlicensure vaccine safety monitoring, 2006-2014--united states. *Morbidity & Mortality Weekly Report*, 63(29), 620-624.

Vadaparampil, S. T., Malo, T. L., Kahn, J. A., Salmon, D. A., Lee, J. H., Quinn, G. P., . . .

Giuliano, A. R. (2014). Physicians' human papillomavirus vaccine recommendations, 2009 and 2011. *American Journal of Preventive Medicine*, 46(1), 80-84.

Villa, L. L., Costa, R. L., Petta, C. A., Andrade, R. P., Paavonen, J., Iversen, O. E., . . . Barr, E.

(2006). 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. *British Journal of Cancer*, 95(11), 1459-1466.

Wegwarth, O., Kurzenhauser-Carstens, S., & Gigerenzer, G. (2014). Overcoming the

knowledge-behavior gap: The effect of evidence-based HPV vaccination leaflets on understanding, intention, and actual vaccination decision. *Vaccine*, 32(12), 1388-1393.

World Health Organization. (2014). Human papillomavirus vaccines: WHO position paper,

october 2014. *Weekly Epidemiological Record*, 89(43), 465-491.

Young, K. J., Kim, J. J., Yeung, G., Sit, C., & Tobe, S. W. (2011). Physician preferences for accredited online continuing medical education. *Journal of Continuing Education in the Health Professions*, 31(4), 241-246. doi:<http://dx.doi.org/10.1002/chp.20136>

Appendix A

Table A1

Human Papillomavirus Vaccines Licensed in the United States

Characteristic	Quadrivalent (HPV4)	Bivalent (HPV2)
Brand name	Gardasil	Cervarix
Manufacturer	Merck and Co, Inc.	GlaxoSmithKline
HPV types	HPV 6, 11, 16, 18	HPV 16, 18
Year of licensure (age range)	Females: 2006 (9-26 years) Males: 2009 (9-26 years)	Females: 2009 (9-25 years) Males: not licensed for use
Vaccine composition	20 µg HPV 6 40 µg HPV 11 40 µg HPV 16 20 µg HPV 18	20 µg HPV 16 20 µg HPV 18
Manufacturing	<i>Saccharomyces cerevisiae</i> (Baker's yeast) expressing L1, the major capsid protein of HPV	<i>Trichoplusia ni</i> insect cell line infected with L1 encoding recombinant baculovirus
Adjuvant	225 µg amorphous aluminum hydroxyphosphate sulfate	500 µg aluminum hydroxide 50 µg 3-O-desacyl-4' monophosphoryl lipid A
Preservatives	None	None
Volume per dose	0.5 ml	0.5 ml
Other content	Sodium chloride, L-histidine, polysorbate 80, sodium borate, and water	Sodium chloride, sodium dihydrogen phosphate dehydrate, and water
Administration	Intramuscular	Intramuscular
Vaccine schedule	3-dose series 0, 2, and 6 months	3-dose series 0, 1, and 6 months
Storage	Store refrigerated at 2° to 8°C, do not freeze	Store refrigerated at 2° to 8°C, do not freeze

Appendix B

HPV Vaccine Pretest/Posttest Questionnaire

1. A 26-year-old male presents in your clinic for a routine checkup. He has never been vaccinated for HPV and his birthday is next month. When gathering his sexual history, you learn that he has sex with both men and women and has a history of genital warts. Would you recommend the HPV vaccine to this patient?
 - a. No, because he will be over the age of 26 by the time the 3-shot series is completed
 - b. No, because he already has a history of genital warts
 - c. Yes, because he is in a high-risk population and meets criteria for catch-up vaccination
 - d. Yes, because routine HPV vaccination is recommended for all men up to age 26

2. Which of the following are facts about anal cancer relating to HPV?
 - a. 30% of anal cancer is associated with HPV infection
 - b. HPV-associated dysplasia and cancer of the anus can occur in both men and women who have never had anal sex
 - c. Most women with HPV-associated anal cancer have had anal sex with multiple partners
 - d. All of the above

3. The Gardasil HPV vaccine protects against:
 - a. Low grade HPV infection
 - b. High grade HPV infection
 - c. Low and high grade HPV infection

4. A 21-year-old male presents in your clinic for a routine checkup. He has never been vaccinated for HPV. He has been sexually active with female partners only since age 16. Is an HPV vaccine recommended for this patient?
 - a. No, because he is over age 18
 - b. No, because he is sexually active with female partners only
 - c. Yes, because routine HPV vaccination is recommended for all men up to age 21
 - d. Yes, because routine HPV vaccination is recommended for all men up to age 26

5. For protection against HPV, men may receive:
 - a. Gardasil vaccine only
 - b. Cervarix vaccine only
 - c. Either Gardasil or Cervarix
 - d. Neither, no HPV vaccine has been approved for use in men

6. Common reasons patients do not accept HPV vaccination include:
 - a. Concerns about vaccine safety
 - b. Lack of provider recommendation
 - c. Belief that the vaccine is not necessary
 - d. a and c
 - e. All of the above

7. A 19-year-old female patient presents in your clinic for an annual exam. She has never been vaccinated for HPV. She has a history of CIN 2 and had a LEEP in 2012. Should she receive the HPV vaccine?
 - a. No, because she has a history of a high-grade cervical lesion
 - b. No, because she has had a LEEP
 - c. Yes, because the HPV vaccine can help reverse high-grade cervical lesions
 - d. Yes, because the HPV vaccine may help protect against strains of HPV she has not yet been exposed to

8. All of the following are common side effects of Gardasil *except*
 - a. Nausea
 - b. Vomiting
 - c. Syncope
 - d. Dizziness

9. Approximately what percent of HPV infections are transient and resolve spontaneously without symptoms?
 - a. 25%
 - b. 50%
 - c. 75%
 - d. 90%

10. Vaccination with Gardasil has been demonstrated to:
 - a. Prevent HPV-associated dysplasia and cancer of the cervix, vulva, vagina, and anus
 - b. Prevent HPV-associated dysplasia of the oropharynx from progressing to squamous cell carcinoma
 - c. Prevent existing genital warts from spreading
 - d. All of the above