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Assessing Knowledge and Attitudes of the Human Papillomavirus Infection and Vaccine among Adolescents in Hartford, CT

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Assessing Knowledge and Attitudes of the Human Papillomavirus
Infection and Vaccine among Adolescents in Hartford, CT

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B.S., University of Maryland, 2010

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APPROVAL PAGE

Masters of Public Health Thesis

Assessing Knowledge and Attitudes of the Human Papillomavirus Infection and Vaccine among Adolescents in Hartford, CT

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Table of Contents

Chapter 1—Introduction.....	1
<i>A. The pathophysiology and biological mechanisms of HPV.....</i>	<i>2</i>
<i>B. Epidemiology.....</i>	<i>4</i>
<i>C. The HPV vaccine.....</i>	<i>9</i>
<i>D. Health education.....</i>	<i>35</i>
<i>E. Specific aims.....</i>	<i>38</i>
Chapter 2—Setting.....	39
Chapter 3—Methodology.....	45
Chapter 4—Results.....	60
Chapter 5—Discussion and Conclusion.....	91
References.....	104
Appendix I—Physician Interview Protocol.....	112
Appendix II—Survey Instrument.....	114
Appendix III—Focus Group Questions.....	117

Chapter 1: Introduction

Human papillomavirus (HPV) is the most common sexually transmitted infection both globally and nationally. It is an infection with a significant public health impact, contributing to the development of a variety of cancers, including cervical squamous cell carcinoma, cervical adenocarcinoma, anal cancers, vulvar, vaginal, and penile cancers, and oral and pharyngeal cancers. While there is no cure for HPV infection, the HPV vaccine, marketed both as *Gardasil*® by Merck & Co. and *Cervarix*® by GlaxoSmithKline, has been proven to be a highly efficacious tool for prevention. However, rates of vaccination among both females and males in the United States remain exceedingly low.

Nationally, there has been very little research conducted on knowledge and attitudes regarding HPV and its vaccine. Using a variety of qualitative and quantitative methods, this thesis aims to contribute to the research gap through the study of the knowledge and attitudes of Hartford, Connecticut adolescents, in collaboration with the City of Hartford Department of Health and Human Services. The specific purpose of this study is to investigate the barriers, facilitators, and beliefs concerning the HPV vaccine, with respect to the intent to be vaccinated among adolescents. This study also pilot tests a didactic intervention to address some of the misconceptions surrounding the HPV vaccine, allowing adolescents to have the knowledge to gain control of their health and make vaccine-related decisions. Ultimately, this study is meant to highlight key areas for intervention that will increase knowledge regarding and access to the HPV vaccine, and increase vaccination rates among Hartford's youth. The research was conducted with

adolescents utilizing various community resources in the City of Hartford over the course of the 2013-2014 and 2014-2015 academic years.

The pathophysiology and biological mechanisms of HPV

HPV is a non-enveloped, double-stranded, icosahedral DNA virus. Its virion is an 8-kb circular genome¹, whose relevant proteins are major capsid protein (L1) and minor capsid protein (L2), coding for early genes E1-E7 and late structural genes.^{2,3}

The presence of epidermal or mucosal epithelial cells is a prerequisite for HPV infection.⁴ HPV enters basal cells of stratified squamous epithelium by utilizing viral capsid L1. It is thought that this initial step requires microtrauma or mild abrasion of the epidermis, such as that that occurs during sexual intercourse.⁵ The virion then replicates episomally, meaning via DNA fragments outside of the chromosome.⁶ It eventually integrates into human DNA within the human cell's nucleus and uses the host cell's protein-producing organelles to make its infectious proteins. Proteins E1 through E4 disrupt cytoskeleton networks, while subtypes of protein E5 bind the epidermal growth factor (EGF) receptor, the platelet-derived growth factor beta (PDGF β) receptor, and vacuolar ATPase, interfering with numerous cell functions including MHC class I expression and cell-cell communication. E6 and E7 maintain proliferation of the host cell. Specifically, E6 binds the p53 tumor-suppressor gene and degrades it via ubiquitination.⁸ E7 binds hypophosphorylated Rb and degrades it, resulting in an overexpression of p16, used as a biomarker of disease.⁹⁻¹¹

Normally, p53 senses the cell's damaged DNA, stops the cell from dividing, and either activates the cell's repair systems or triggers "programmed cell death" by apoptosis, insuring that a damaged or infected cell does not replicate.⁵ When p53 is

silenced by E6, the cell replicates even if its DNA is damaged. Rb, meanwhile, normally prevents uncontrolled cell proliferation, so when it is silenced by E7, cell division progresses unchecked. Thus, cells are essentially “immortalized,” which can lead to the formation of a tumor.

There is evidence that chemotherapy or radiation can reactivate p53 in HPV-positive tumors, resulting in better outcomes for those with HPV-positive oropharyngeal cancer.¹² Newer research shows that E6 also interferes with several PSD-95/DLG/ZO-1 (PDZ) domain-containing proteins, resulting in altered cell polarity, a quality associated with tumor progression. This process occurs when E6 binds to and interferes with a key protein involved in tight junctions.¹³

In the late phase of productive viral infection, the L1 and L2 proteins allow for the creation of new virions, which are shed from the cell surface to infect another host. L1 is responsible for the icosahedral shape of the HPV virion, can self-assemble into empty virus-like particles (VLPs), and is a target for HPV vaccines. L2 enhances the assembly of VLPs, facilitates encapsidation of the viral genome into host cells, and after being cleaved by the enzyme furin, allows for endosome escape. It then accompanies the viral genome to the host cell’s nucleus, where the virus’s genetic material is integrated into host DNA.¹⁴

There are more than 150 genotypes of HPV¹⁵, classified by sequence of the gene encoding the major capsid protein L1.¹⁶ HPV types 1-4 are associated with benign skin warts. Low-risk types, HPV-6 and HPV-11, are associated with genital warts (condylomata), lower-grade squamous intraepithelial lesions of the cervix (LSIL), and vulvar intraepithelial neoplasia (VIN 1). High-risk types include HPV-16 and HPV-18,

and are associated with cervical intraepithelial neoplasia (CIN) and cervical cancer, as well as anal cancer and close to half of all vaginal, vulvar, and penile cancers.¹⁷ It appears that low-risk types are cleared more easily by the immune system than high-risk types¹⁸— only the E6 and E7 genes of high-risk types are able to immortalize human cells.^{4,5} As HPV infection requires the presence of epidermal or mucosal epithelial cells, it only infects areas where these cells are present, which are the skin, throat, urogenital tract, and anus. With respect to cervical cancer specifically, lesions are typically found at the squamo-columnar junction, the border between different layers of cervical cell types.¹⁹

Epidemiology

Data show that over half of all sexually active men and 80% of sexually active women will become infected at some point in their lives.^{1,20} HPV is an infection that is transmitted by direct contact, which can include genital-to-genital skin contact, as well as vaginal, anal, or oral sex. Condoms provide some protection, but regular and consistent condom use has shown to only accomplish about 60% protection against infection.²¹ HPV can still be transmitted through contact with areas of unprotected genital skin such as the vulva or scrotal sacs²¹, though circumcision has been shown to greatly reduce genital HPV prevalence in men.²² Nonsexual routes of transmission are uncommon, but can include vertical transmission to an infant at the time of birth.

Risk factors for HPV infection are related to sexual behavior, such as number of concurrent sex partners, lifetime history of sex partners, and partners' sexual history.²⁰ One study found that HPV prevalence among women aged 18–25 years was directly correlated with the number of lifetime sex partners: prevalence was 14.3% in those with

one lifetime partner, 22.3% for those with two, and 31.5% for those with three or more lifetime partners.¹⁵ A higher risk of infection is associated with a younger age of sexual initiation, an increased frequency of sexual intercourse, and the practice of anal sex.¹ A prospective study of college women revealed that total incidence of HPV infection was 40% by 2 years after the onset of sexual activity, with high-risk subtype 16 accounting for 10.4% of these infections.²⁰ Age is also an important determinant of risk of HPV infection. A review of global data on age-specific prevalence revealed that HPV incidence in women is bimodal, with two peak points at <25 and around 45, while in men, prevalence and incidence remain consistently high at all ages.²³ Other risk factors for infection include low socioeconomic status, alcohol and tobacco use, increased number of pregnancies, lack of circumcision in male partners, and oral contraceptive use.¹

In the United States, the CDC estimates that 79 million individuals are currently infected, and 14 million new infections occur each year. Approximately half of these new infections occur among those aged 15–24 years.¹⁵ Based on data from numerous studies, estimates of the prevalence of infection in asymptomatic women among the general population in the U.S. range between 2% and 44%, varying based on study samples and data collection methods.¹ The 2011 National Health and Nutrition Examination Survey (NHANES), using polymerase chain reactions (PCR) on self-collected cervicovaginal samples from over 4,000 US women between the ages of 14 and 49, placed the overall prevalence of HPV infection at 42.5%.²² Prevalence differed by age group, with the highest level of infection among females aged 20-24 (53.8%).²² In this age group, prevalence of HPV types 6, 11, 16, or 18 was 18.5%.¹⁵ Lower levels of infection were

seen among those between the ages of 14 and 19 (32.9%).²² As had been seen in previous studies, infection was also found to be more prevalent among those of Hispanic or African American ethnicity. Prevalence was estimated at 59.2% among non-Hispanic Blacks and 44.2% among Mexican Americans, versus 39.2% among non-Hispanic Whites.²²

HPV infection is also common in men, and as a result is inextricably linked to infection in women. Clinic-based studies among heterosexual men have shown that prevalence is often upwards of 20%, though this number is highly determined by the site and method of specimen collection.²⁰ In contrast to women, HPV infection is present on keratinized surfaces in men, often resulting in poor yield when sampling.²² A large U.S.-based study examining HPV infection in men revealed a prevalence of 61%, greater than that found in women by the NHANES, with the high-risk subtypes of 6, 11, 16, and 18 found in 23% of the study population.²² Incidence of oral HPV infection is also higher in men than women, and NHANES data has demonstrated that men have an incidence rate of 10%, versus 4% in women. Unlike in women, there has been no correlation noted with age.²² An international study done on men between the ages of 18-70 seeking information about sexually transmitted disease testing from clinics in the U.S., Mexico, and Brazil, revealed a genital HPV prevalence range of 52-69% by country, again with no age correlation.¹⁵

Despite its high prevalence, most HPV infections are cleared by the immune system. And once cleared, very few cases reappear, and even fewer lead to clinically relevant disease: 70% of all new HPV infections resolve within one year, and 90% within two years with no medical treatment.¹ A study done of U.S. female college students

revealed that the median duration of new HPV infections was only 8 months.¹ Numerous other studies have shown that the 1 year clearance rate of infection ranges from 40-70%, while the 2 year clearance rate ranges from 70-100%.²² Therefore, only a minority of HPV cases progress to clinical disease. In these cases, over a course of approximately 12-15 years, persistent high-risk HPV infection leads to progression through several stages: low-grade (LSIL) and high-grade intraepithelial lesions (HSIL), seen cytologically, and cervical intraepithelial neoplasia (CIN) grade I-III, seen histologically.¹ In cross-sectional studies, an estimated 3-5% of women eventually develop cervical cancer without any clinical intervention.²² Evidence suggests that those who progress in this way are not able to mount a successful cell-mediated immune response against the virus, specifically to major capsid protein L1.¹⁶ Since L1 determines the viral genotype, previous exposure and clearance of HPV infection may confer long-term immunity, certainly to the same genotype and perhaps across sub-types as well, though this is not certain due to the localized nature of infection.^{24, 25}

HPV infection alone, therefore, is not sufficient to trigger progression from infection to tumor. Numerous factors have shown to be positively associated with persistent infection and the transition from HPV infection to invasive disease. Initial infection with a high-risk HPV subtype increases the risk of both persistence and progression. The longest course of persistent infection has been seen with HPV subtypes 16, 31, 54, and 53.²² The E6 and E7 genes play crucial roles in this process. HPV-induced carcinogenesis is a multi-step process, so often regular screening can prevent the transition to cancer. Therefore, factors associated with infrequent health maintenance visits, such as low socioeconomic status, increase the risk of developing HPV-associated

cancer. Those of African American or Hispanic ethnicity are also more likely to develop malignancy. Since the infection is normally cleared by the immune system, factors that cause failure of this control also increase risk. These include older age, tobacco smoking, poor nutrition, immunodeficiency, and concurrent infections.¹ One trial showed no clearance of high-risk HPV infections in women over the age of 70.²² Clearance of infection also seems to occur faster in men, with an average clearance time of about 6 months. One study showed that almost 75% of HPV infections in men were cleared within 1 year.²²

Overall, HPV is responsible for approximately 5.2% of all cancers.¹ It is a necessary, but not sufficient, cause of cervical squamous cell carcinoma (SCC) and cervical adenocarcinoma. A study done in 1999 demonstrated that HPV DNA could be found in 99.7% of cervical cancer specimens.²⁶ In 2008, the American Cancer Society estimated that 11,070 new cases of cervical cancer were diagnosed in the U.S., resulting in 3,870 deaths. HPV subtypes 16 and 18 caused approximately 70% of these cases.²⁰ Additionally, HPV is responsible for approximately 90% of anal cancers, 40% of vulvar, vaginal, and penile cancers, and 12% of oral and pharyngeal cancers.²⁰ In the United States, 91% of anal cancers have been found to be positive for HPV, 77% of which have been HPV 16.¹⁵ Of vulvar, vaginal, or penile cancers, the prevalence of HPV 16 and 18 is 47.9%.²⁷

According to the CDC, approximately 3,500 cases of HPV-associated vulvar cancer and 730 cases of HPV-associated vaginal cancer occur each year.^{21,28} With regards to oropharyngeal cancer, rates have steadily increased for men since the 1970s and for females from 2000-2009 in the United States.¹⁵ Although the use of tobacco and alcohol

are strong risk factors for oropharyngeal cancers, a recent U.S. study reported that approximately 72% were positive for HPV, 61% of which had HPV 16. Prevalence of HPV 16 and 18 in these cancers was higher in males than females, and lower in non-Hispanic blacks than in other racial/ethnic groups.¹⁵

The HPV vaccine

In June 2006, *Gardasil*®, developed by Merck & Co., became the first vaccine approved by the U.S. Food and Drug Administration (FDA) for HPV prevention.²⁹ It was licensed for use in girls and women ages 9 to 26 years, and provides protection against HPV types 16, 18, 6, and 11. *Cervarix*®, developed by GlaxoSmithKline, was not approved by the FDA until three years later, in October 2009, though it had been in use in Europe, Australia, and the Philippines prior to that time.²⁹ It was approved for use in girls and women ages 10 to 25 years, and provides protection against HPV types 16 and 18.¹⁵

In October 2009, the same month that the bivalent Cervarix was approved for use in females, the quadrivalent Gardasil was approved by the FDA for use in boys and men between the ages of 9 and 26 years for the prevention of genital warts. The Advisory Committee on Immunization Practices (ACIP) added the vaccine to its recommended routine vaccination schedule in October 2011 for males aged 11-12 years, with catch-up vaccination up to the age of 21.³⁰

Pathophysiology

Like any vaccine, both Gardasil and Cervarix work by generating immunologic memory. By exposing individuals to virus subcomponents through vaccination, antibodies and cell-mediated immunity develop that protect from natural infection.

Although several of these mechanisms are clearly delineated with in vitro and theoretical models, it remains unclear exactly how these vaccines specifically prevent natural infection from HPV.¹⁶ However, several different mechanisms have been explored, and each probably plays a role in the protection the HPV vaccine provides.

Both Gardasil and Cervarix are composed of L1 coat proteins, which is the viral component specific to different HPV genotypes.¹⁶ These proteins spontaneously self-assemble into empty viral protein shells, also called virus-like particles (VLPs).²⁹ VLPs are non-infectious, as they contain no viral DNA or infectious viral components.³¹ As with any protein-based vaccine, adjuvants are used to increase immunogenicity. Similar to other prophylactic pediatric vaccines, such as Pedvax Hib for *Haemophilus influenzae* and Recombivax for hepatitis B, Gardasil uses an aluminum salt adjuvant, aluminum hydroxyphosphate sulfate, which stimulates a Type 2 humoral response in human T cells.²⁹ Cervarix uses aluminum hydroxides as well as a bacterial lipid called ASO₄³², which stimulates both Type 1 cell-mediated and Type 2 immune responses.²⁹ Gardasil is quadrivalent, meaning it protects against four strains of HPV: 6, 11, 16, and 18. Strains 6 and 11 cause for 90% of genital warts and strains 16 and 18 cause most cases of cervical cancer. Cervarix is bivalent and only contains L1 proteins of HPV types 16 and 18 for protection from these cervical cancer-causing strains.¹⁶

After the vaccine is injected, VLPs are detected as a foreign protein by phagocytes that are programmed to attack non-self proteins. Certain phagocytes, specifically called antigen-presenting cells (APCs), break down the proteins, then migrate to the draining lymph nodes. In the draining lymph nodes, the APCs can activate specific

B-cells that have the potential to make antibodies against the L1 protein.¹⁶ After the first vaccine, antibodies against the HPV L1 proteins are created.

Since HPV infection occurs in the epithelium of the cervix (or other epithelial surfaces in cases of anogenital infection) with low levels of inflammation, repeat vaccinations are necessary to increase antibody levels and to select for more specific antibodies. The HPV vaccine is given in 3 doses at 0, 1 or 2, and 6 months.³³ After the second vaccine dose, the process of affinity maturation selects for activated B-cells that produce more specific antibodies against the L1 protein.³⁴ Very specific antibodies to the specific strains in each vaccine develop in high titers after the third dose to protect from infection.¹⁶

Months after the third and final dose is given, long-living plasma cells in the bone marrow create persistent low levels of antibodies against HPV. Additionally, memory B cells circulate that can recognize HPV antigens and create high levels of antibody upon re-exposure. Mathematical models have shown that immunity from infection can theoretically last decades after vaccination based on antibody levels after vaccination.³⁵ Using a conventional power law model, it was estimated that detectable antibodies would be found for a median duration of 32 years following three doses of HPV-16 vaccine in women ages 16-23 years; a modified power law model predicted life-long persistence of antibodies above the level of detection (>5.9 mMU/mL).²³

It remains unclear how circulating antibodies can prevent in vivo infection in the epithelium, since the HPV virus occurs in a low-inflammatory state and rarely causes viremia.¹⁶ Because of the localized infection, natural infection with an HPV strain is not thought to lead to natural immunity.¹⁶ However, through the process of repeated

vaccination, high enough levels of circulating antibodies in the bloodstream may prevent initial infection by preventing the HPV virus from attaching to the epithelial basement membrane.³⁶ It appears that up to 40% of vaccinated individuals have antibody levels that fall off to background levels, but clinical trials have shown that immunity persists despite low antibody levels.³⁶ Presumably, low levels of very specific antibodies after three vaccinations can prevent infection and memory B cells may be easily activated upon natural infection.¹⁶ Regardless of the exact mechanism of the HPV vaccine, both clinical trials and population based studies have shown marked decreases in strain-specific HPV infection after vaccination.

Efficacy and Safety

The HPV vaccine has now been available to the public for approximately 8 years. In that time, vaccination programs have been broadly implemented, initially targeting only adolescent girls and then including boys by 2009. Both efficacy and safety of the vaccine have been extensively researched. The risk of HPV exposure theoretically exists throughout one's sexual life, so overall effectiveness is highly dependent on the duration of protection of the vaccine. As of December 2014, the bivalent Cervarix had been followed for 9.4 years, while the quadrivalent Gardasil had been followed for 8 years, without breakthroughs.³⁷ Through a variety of studies, differing in the methods used in the assessment of immunogenicity, sample size, and endpoints, including HPV-associated disease and persistent infection, efficacy has been widely demonstrated for both Gardasil and Cervarix.¹⁵

Phase III trials were initially conducted to demonstrate efficacy in preventing both HPV infection and pre-neoplastic lesions secondary to infection.³⁷ Gardasil was

evaluated by the FUTURE I8 and FUTURE II9 trials, while Cervarix was evaluated by the PATRICIA and the Costa Rica HPV Vaccine trials.³⁷ All four were randomized control trials made up of young women aged 15-26 years (mean 20 years); sample sizes ranged from 5,500-18,500.³⁷ Pre-enrollment, participants were tested by PCR for HPV DNA to determine both prior and current infection status, though the results did not affect enrollment.¹⁵ The primary endpoint in all four trials, and the basis for licensure in females for both vaccines, was the incidence rate of CIN 2/3 or adenocarcinoma in situ (AIS) associated with HPV 16 and 18, serving as a surrogate marker for cervical cancer.¹⁵ Incidence rates of vaginal intraepithelial neoplasia (VaIN2/3), vulvar intraepithelial neoplasia (VIN2/3), and anal intraepithelial neoplasia (AIN2/3) were used as secondary endpoints and surrogate markers for vaginal, vulvar, and anal cancers, respectively.¹⁵ Invasive cancer could not be used as an endpoint as the standard of care is to screen for and treat the above-mentioned dysplastic, pre-neoplastic states.¹⁵

High efficacy of the vaccine against all measured end points was demonstrated in all four studies. Those participants who received all three doses, had no evidence of current or past infection with HPV upon enrollment, and followed the assigned protocol of doses at 0, 1 or 2, and 6 months, demonstrated the greatest efficacy when cases were counted 1 month after the third dose.¹⁵ In the PATRICIA trial, efficacy in this cohort against HPV 16- or 18-related CIN 3 was estimated at 100%.³⁷ In comparison, in the same trial, the efficacy among all participants regardless of baseline HPV status with cases counted one day after the first dose was 45.7%.³⁷ The difference was attributed to the fact that some participants had pre-existing HPV infection at the time of enrollment, and the vaccines do not prevent progression of disease in those already infected.¹⁵ Prior

infection with one HPV type, however, did not diminish efficacy against the other HPV types covered by the vaccine.²⁰ In the FUTURE I and II trials, efficacy for HPV 16- or 18-related CIN2/3 or AIS was 97%, while efficacy against any CIN secondary to HPV 6, 11, 16, or 18 was 95%.²⁰ Greater than 95% efficacy was observed against VIN2/3 or VaIN2/3 and genital warts in the infection-naïve cohort, while greater than 75% efficacy was observed in all participants.³⁷ The duration of protection following HPV vaccine is not known, but for both vaccines, from all four trials, a subset of participants have been followed for greater than 60 months with no breakthrough.²⁰

Throughout the first three phases of clinical research, antibody titers for the two vaccines were measured by different immunoassays, as two different adjuvants are used. As mentioned previously, Gardasil uses an aluminum salt adjuvant, aluminum hydroxyphosphate sulfate²⁹, while Cervarix uses aluminum hydroxides as well as a bacterial lipid called ASO₄.³² For both vaccines, greater than 99% of recipients develop an antibody response to the HPV subtypes covered 1 month after completing the three-dose series, indicating that the vaccines are highly immunogenic.²⁰ However, there is no known minimal titer determined to be protective or a known serologic component that can be measured to test for immunity. It is also difficult to compare the immunogenicity of the two vaccines, given the difference in the assays used to measure antibody titers.¹⁵ One study that compared the two vaccines directly by using the same serologic assay found that Cervarix provided 2.3-4.8 times higher anti-HPV-16 neutralizing-antibody levels and 6.8-9.1 times higher anti-HPV-18 neutralizing-antibody levels than Gardasil one month after the 3-dose series completion. Longer-term effectiveness, however, was not addressed in this study.³⁸

While the initial Phase III trials were only conducted in women, the quadrivalent Gardasil has been shown to be efficacious against HPV-related disease in men as well. A large-scale randomized controlled study done in 2009 among 4065 healthy males between 16 and 26 years of age, 602 of whom were self-reported to have sex with other men (MSM), recruited from 18 different countries, demonstrated high efficacy of Gardasil against HPV-related external genital lesions.²³ Among all participants, efficacy against any external genital lesion related to HPV 6, 11, 16, or 18 was found to be 90.4%, while efficacy against genital warts and penile intraepithelial neoplasia was 89.4% and 100%, respectively.³⁹ When broken down by self-reported sexual orientation, the vaccine had an efficacy of 92.7% against genital warts among heterosexuals, and 79% among MSM; for persistent infection, the vaccine had an efficacy of 50.4% for heterosexuals and 43.6% for MSM.²³ Against AIN in MSM, efficacy was 77.5%.²³ This study demonstrated the direct benefits men can receive from the vaccine, but other studies have also demonstrated that the vaccine also has an indirect effect on males with only female vaccination. In 2007, a study was done in Australia in which females aged 12 to 26 were vaccinated with Gardasil with a coverage rate between 65% and 75%. Women and heterosexual men under the age of 28 demonstrated a large decrease in incidence rate of genital warts from 2004-2007 to 2008, with a prevalence ratio of 0.83 compared to 0.52, respectively. This decrease was not seen in MSM or women older than 28, suggesting a herd immunity effect.³⁹

Post-marketing studies have demonstrated the long-term clinical significance of HPV vaccination in specific communities. One ecological study conducted in Victoria, Australia, compared the incidence rate of CIN 2+ lesions in girls less than 18 years of age

both before and after the initiation of a vaccination program with Gardasil in 12-to-13 year olds. With a vaccination coverage rate of 71-79%, incidence rate has progressively decreased by 0.38%.²³ Similar studies have been conducted in New Zealand and California; coverage rates were under 50% in both regions, but there was a reduction of 60% and 30% in genital warts, respectively.²³

In addition to being effective, both HPV vaccines have been proven to be well-tolerated and safe. The vaccines do not contain mercury, thimerosal, live viruses, or dead viruses, but only virus-like particles, which cannot reproduce in humans.³² Similar to other protein subunit-based vaccines, like tetanus and hepatitis B, the most common reported adverse reaction during the Phase III trials was pain at the site of injection, which was reported by 91% of those receiving Cervarix, 85% of those receiving Gardasil, and 75-78% of those receiving a placebo. Fever was next most common, and was reported by 15% of those receiving Gardasil, 12% of those receiving Cervarix, and 11-12% of those receiving a placebo.²⁹ Rates of serious adverse events, such as autoimmune disorders and death, did not differ between those receiving the vaccine and those receiving a placebo.¹⁵

Gardasil has been on the market since June 2006, and from then through March 2014, approximately 67 million doses of the vaccine were distributed in the United States. In that same time period, the CDC's Vaccine Adverse Event Reporting System (VAERS) received a total of 25,063 adverse event reports secondary to the vaccine. 92.4% of those reports were classified as non-serious, which included generalized symptoms such as headache, fever, syncope, dizziness, and pallor, as well as localized pain. The rate of serious events, classified as those resulting in hospitalization, permanent

disability, life-threatening illnesses, or death, peaked in 2009 at 12.8%, but was down to 7.4% by 2013. Additionally, no statistically significant increased risk has been observed for Guillain-Barré syndrome, motor neuron disease, stroke, venous thromboembolism, appendicitis, seizures, syncope, allergic reactions, or anaphylaxis.¹⁵ In 2008, the media targeted Gardasil after reports between June 2006 and December 2008 revealed increased numbers of syncopal episodes and venous thromboembolic events (VTEs) following vaccination compared to background rates. However, of the 31 women that had confirmed cases of VTEs, 28 had underlying risk factors, such as obesity, oral contraceptive use, and hypercoagulability disorders.⁴⁰ The vaccine's overall safety profile is comparable to that of other childhood vaccinations.²⁹ There is less data regarding the safety and tolerability of Cervarix, as it was licensed more recently in October 2009, and from that time through March 2014, only an estimated 719,000 doses were distributed.¹⁵ In this time period, 113 reports were submitted to VAERS, with 93.8% classified as non-serious.¹⁵ As with Gardasil, these included generalized symptoms such as dizziness and headache, as well as localized pain.

The only absolute contraindication to receiving the HPV vaccine is a severe allergic reaction either to a vaccine component or following a prior dose. Deferral of vaccination is recommended for those with a moderate or severe acute illness until symptom improvement. Both Gardasil and Cervarix are classified as Pregnancy Category B meaning they are not recommended for use during pregnancy due to limited data in pregnant women, though no risk has been found in animal studies.²⁰

Initial Rollout and Controversies

The Food and Drug Administration licensed Merck & Co., Inc.'s Gardasil for use in females aged 9 to 26 years on June 8, 2006. Prior to its approval, it was touted as a product with both significant public health and immense blockbuster potential. Merck launched a widespread ad campaign, "Tell Someone," which educated viewers about the prevalence of HPV and its link to cervical cancer and resulted in Gardasil being dubbed the "Cervical Cancer Vaccine".⁴¹ Later that month, the ACIP issued their recommendations for routine HPV vaccination.⁴² Because the vaccine has the greatest benefit when given before sexual debut, the committee recommended three doses of the vaccine for 11 and 12 year old females, and vaccination for females between 13 and 26 years of age who had not been vaccinated previously or who had not completed the 3-dose series.⁴² The committee did not take a position on whether vaccination should be mandatory by law as such policy decisions are left up to the individual states.⁴³

These recommendations were met with polarizing debates, fueled by substantial media coverage, which overshadowed the vaccine's public health potential. Some of the opposition to Gardasil stemmed from the history of resistance to vaccination and specifically, the growing trend of parental refusal of childhood vaccines. One of the recent consequences of growing vaccination avoidance was the early 2015 measles outbreak in the United States, originating in Disneyland, California, and then spreading to multiple other states. The most discussed and feared complication of vaccination has been the development of neurological complications, and specifically, autism spectrum disorders. This fear originated in 1998, when doctors from London's Royal Free Hospital, led by Andrew Wakefield, released a study published in the *Lancet* that

suggested a link between the MMR vaccination and inflammatory bowel disease, leading to autism. Two follow-up studies, commissioned by the British Department of Health in 1999, could not confirm this link. However, panic among parents increased exponentially.⁴⁴

In the following years, multiple advocacy groups, such as SafeMinds, and public figures, such as Jenny McCarthy, continued to propagate the idea of a linkage between childhood vaccinations and autism.⁴⁴ A report by the Institute of Medicine (IOM), “Immunization Safety Review: Vaccines and Autism,” released in 2004, concluded that “the evidence favors rejection of a causal relationship between thimerosal-containing vaccines and autism,” also rejecting any link between MMR and inflammatory bowel disease. The CDC supported the IOM conclusion.⁴⁵ Ten of the 13 authors that wrote the 1998 study published in the *Lancet* retracted their work in 2004, and Andrew Wakefield, the lead author, was stripped of his medical license in 2010.⁴⁴ Furthermore, a study published in 2013 in *The Journal of Pediatrics* analyzed data from a case-control study conducted in three managed care organizations (MCOs) consisting of close to 1000 children, and studying the possible connection between exposure to total antibody-stimulating proteins and polysaccharides from vaccines and risk of autism. Exposure to these antigens in the first 2 years of life was not found to be linked to risk of developing an ASD.⁴⁶ The American Academy of Pediatrics publishes a yearly document summarizing all studies and publications on vaccine safety to date; the 2013 report continues to show no link between autism and the MMR vaccine, thimerosal, multiple vaccines given at once, fevers, or seizures.⁴⁷

Gardasil received increased scrutiny because it was approved based on the results of four clinical trials that only averaged three years in length, leaving questions about the duration of its protection and potential long-term adverse effects. Additionally, Merck, in its urgency to outcompete the yet-to-be-approved Cervarix by GlaxoSmithKline, participated in aggressive lobbying to convince state legislatures to make the vaccine mandatory for adolescent girls. Texas was the first state to mandate the vaccine in February 2007, when an executive order was issued by Governor Rick Perry requiring vaccination for all girls to enter middle school. The media extensively covered the fact that Merck partially financed Perry's reelection campaign and that members of Perry's staff had ties to Merck lobbyists. The order was eventually overturned by a landslide decision of 181-3 by the state legislature.⁴⁸ Additional reports emerged that Merck was funding lobbyists in more than 20 other states to work towards mandatory vaccination, which led the company to eventually stop funding lobbying on the issue.⁴⁸ In May 2007, Arizona's legislature approved a bill prohibiting the state's health department from requiring the vaccine, while nationally, a Republican congressman introduced the *Parental Right to Decide Protection Act*, meant to prohibit the use of federal money to establish mandatory HPV vaccination programs.⁴⁹ By the end of May 2007, the only state to make Gardasil a legal requirement was Virginia.⁵⁰

Other controversies arose regarding the idea of mandatory vaccination, particularly because HPV is a sexually transmitted infection.⁵¹ Opponents of a vaccine mandate argued that HPV is not spread by casual contact or airborne droplets, and therefore, there is no immediate risk of infection in schools.⁴⁸ Rather than creating herd immunity, then, a mandate would only protect the individual vaccinated, which has been

argued is an invasion of individual and parental rights.⁵² Similar arguments in the past had been raised regarding vaccination against hepatitis B, which is spread by sexual contact and intravenous drug use. In both cases, targeting specific at-risk groups to receive the vaccine would be less effective than universal vaccination.⁴³ Some raised moral objections to making a vaccine for a sexually transmitted disease mandatory.⁵⁰ Organizations such as Focus on the Family and the Christian Medical Association took a stand against mandatory vaccine, preferring that the decision to vaccinate be a parental one, though ultimately came to support availability of the vaccine itself.⁴⁸ Other parents argued that due to religious values or other personal beliefs, their children would remain abstinent, and therefore uninfected, until marriage, making a vaccine mandate unnecessary.⁵² However, according to the CDC, 13% of girls in the United States are sexually experienced by the age of 15, 43% by the age of 17, and 70% by the age of 19. Additionally, the rate at which adolescents drop out of school starts increasing at the age of 13. Therefore, to reach the majority of vulnerable women while they are still in school, a mandatory vaccine program would ideally begin at age 12.⁵² The University of Michigan C.S. Mott Children's Hospital National Poll on Children's Health, conducted online in March 2007, found that only 44% of parents supported the idea of a HPV vaccine mandate⁴⁸, compared to 68% for the tetanus-diphtheria-pertussis (Tdap) vaccine.⁴⁹ Allowing religious or philosophical exemptions to the vaccine would have alleviated some of the concern over a vaccine mandate, though studies with other vaccines have found greatly reduced vaccination rates when this is an option.⁴³

The most vocal opponents maintained that the use of Gardasil would promote promiscuity among teenagers. The argument was that there would be "disinhibition,"

defined by the CDC as "an increase in unsafe behaviors in response to perceptions of safety caused by introduction of a preventive or therapeutic intervention." The same argument has been made regarding needle exchange centers and rates of drug use, as well as condom distribution and rates of unwanted pregnancies and sexually transmitted diseases.⁴¹ This idea was perpetuated by the media, with such headlines as "Cervical Cancer Vaccine Gets Injected with a Social Issue: Some Fear a Shot for Teens Could Encourage Sex" in the Washington Post.⁴¹ However, this concern has been proven to not be the case. Numerous studies have shown that the HPV vaccine does not promote promiscuity.⁵¹ Most recently, a study published in the *Canadian Medical Association Journal* in December 2014 demonstrated similar rates of pregnancy and sexually transmitted infections, used as surrogate markers of increased unsafe sexual activity, in two cohorts of vaccinated (n= 128,712) and unvaccinated (n= 131,881) girls in Ontario.⁵³

Finally, concerns were raised by both providers and patients regarding barriers to access. Some argued that additional populations that could benefit were not included in the ACIP's recommendations, which at the time, only included females. By only recommending routine vaccination for girls aged 11-12 prior to first sexual contact, older and sexually active people, as well as males, were being deprived of the potential benefits of the vaccine.⁵⁴ On the other hand, some argued that it was a matter of gender inequity that only girls were compelled to submit to the new vaccine.⁴⁹

When GlaxoSmithKline's bivalent Cervarix vaccine was licensed in the United States in 2009, the ACIP revised their recommendation to include both vaccines.⁴² Prior to receiving approval in the United States, Cervarix had been licensed in over 100 countries.⁵⁵ Cervarix proved to be as safe and effective as Gardasil against HPV 16 and

18, but regulatory delays kept it out of the U.S. for several years.⁵⁵ While both HPV vaccines had been recommended for girls since 2009, it was not until 2011 that the ACIP recommended routine use of Gardasil for males as well⁴², which had been licensed for male use in 2009.⁵⁶ The ACIP added Gardasil to its recommended routine vaccination schedule for males aged 11-12 years, with vaccination up to the age of 21 for those who had not been vaccinated previously or who had not completed the 3-dose series.³⁰

Debate following Gardasil's approval and recommendation for male use was muted compared to that which followed recommendations for females in 2006. This lesser reaction is perhaps due to the double standard that exists in which early sexual activity in boys is more accepted than it is in girls. Controversy primarily centered on the fact that some HPV-related cancers in men, such as anal or oral cancer, result from male to male sex, and that there is a higher prevalence of HPV infection among gay men.⁴⁹

Additionally, cost was an issue. The price of Gardasil is steep, totaling approximately \$360 for three doses plus associated office visits.⁴⁸ It was estimated that vaccinating all 11 and 12-year-old boys in the United States would cost approximately \$140 million annually, while catch-up vaccination among males ages 13 to 21 years would cost hundreds of millions more. Generally, the U.S. government pays for about half of all vaccinations, which was a source of contention.⁵⁷ A study authored by Bogaards et al. (2011) used mathematical models to determine cost effectiveness of the vaccine among both genders, and concluded that increasing vaccine uptake among preadolescent girls would be more effective than starting routine vaccination for preadolescent boys in decreasing HPV infection rates.⁵⁸ The authors state that, "As a rule,

directing prophylactic immunization at the sex with the highest pre-vaccine prevalence results in the largest reduction of the population prevalence".⁵⁸ The ACIP addressed the concerns about the cost-effectiveness of the vaccine in their 2011 routine recommendation for boys, noting that "a range of assumptions," including the vaccination rates for girls, can affect how much each prevented case of infection cost.⁵⁷ Nonetheless, the ACIP concluded HPV vaccination would be worthwhile for boys and men up to 21, as vaccinating boys also benefits female partners. Models demonstrated that vaccinating only men having sex with men (MSM) would have been more cost effective than vaccinating all boys, due to the difference in prevalence rates, but studies among providers revealed general uneasiness in making those determinations at the recommended vaccination age of 11-12 years old.⁵⁷

Current Recommendations

Both Cervarix and Gardasil are currently available on the market for use against HPV infection. Gardasil is licensed by the FDA for the prevention of vulvar, anal, cervical and vaginal cancers, as well as genital warts. It is approved for use in females ages 9 through 26 and for males between the same ages.⁵⁹ Cervarix is licensed for the prevention of cervical cancer, cervical intraepithelial neoplasia, and other precancerous lesions caused by oncogenic HPV types 16 and 18 in females aged 9 to 25 years.⁶⁰ Since clinical trials of both Gardasil and Cervarix have only explored their effectiveness against cervical cancer precursors and genital warts, they currently do not have FDA approval for protection against other types of HPV-associated cancers, including other anogenital cancers and oropharyngeal cancers.¹⁵

Currently, the ACIP recommends that girls and boys aged 11-12 years receive the HPV vaccine as part of their routine care, although vaccinations can begin as young as 9 years of age.¹⁵ Females can receive either Gardasil or Cervarix, while only Gardasil is recommended for males. Both vaccines are given as a three dose series of intramuscular injections over a period of six months. Current recommendations maintain that the second dose should be administered one to two months after the first dose, and the third dose six months after the first dose.¹⁵ However, there is no maximum interval between doses, and if the schedule is interrupted, the series does not need to be restarted.²⁰ The HPV vaccine may be administered at the same time as other vaccines recommended in the same age range, such as such as Tdap and quadrivalent meningococcal conjugate (MCV4) vaccines, as it is likely to improve schedule adherence.¹⁵ The HPV vaccine is considered to be most effective in 11 or 12 year olds because it is less likely that these individuals have had sexual intercourse, based on the average age of sexual debut in the United States.¹⁵ Additionally, data on HPV epidemiology, cost-effectiveness evaluations, and pre-marketing clinical trials, which demonstrated the highest post-vaccination antibody titers at age 11 or 12 compared to older age groups, is the basis for the routine vaccination recommendation at age 11 or 12 years.¹⁵

A "catch up" vaccination is recommended for females and males aged 13 to 26 years who have not either been previously vaccinated or completed the series.¹⁵ Full benefit would be received by those not yet sexually active. As a non-therapeutic treatment, neither vaccine can treat nor cure existing conditions caused by HPV, such as persistent infection, pre-neoplastic lesions, or genital warts. However, the vaccines would protect against genotypes not already acquired.¹⁵ Current evidence demonstrates that only

a small percentage of sexually active individuals in these recommended catch-up age groups have been infected with both HPV 16 and 18 or all four HPV types covered by the vaccines.¹⁵ There is currently no approval from the FDA for use in individuals greater than 26 years of age; however, if an individual initiates the series, but does not complete it prior to turning 26, the remaining doses can still be administered afterwards.²⁰ Other recommendations from the ACIP include giving the three dose series to (1) females under the age of 27 with abnormal Pap smears (2) females under the age of 27 with a positive HPV DNA test (3) females or males under the age of 27 with a history of genital warts (4) females or males under the age of 27 with immunosuppression, whether secondary to disease or medication and (5) females under the age of 27 who are breastfeeding.¹⁵

No studies have been done on the interchangeability of Gardasil and Cervarix, so currently, the ACIP recommends that the same HPV vaccine be used for the entire three dose series.¹⁵ One vaccine has not been endorsed over the other⁵⁵, but rather, the official recommendation allows for the administration of either vaccine.⁴² Currently, the only known difference between the two vaccines is the protection against genital warts offered by Gardasil.⁵⁵ There is no known difference in regard to immunogenicity, duration of immunity, or cross-protection, as well as no significant price difference. The ACIP has emphasized that the primary goal of vaccination is cervical cancer prevention, and the best way to reach this goal is to have both vaccines available to the public. If one vaccine was preferentially recommended over the other, the lesser-preferred vaccine might drop off the market, which could lead to frequent shortages in the supply of the recommended vaccine.⁵⁵ The ACIP's current recommendation of either vaccine has allowed for protection against supply disruptions, and has provided insurance if safety issues emerge

for one vaccine in the future.⁵⁵ However, since 2006, whether because of the earlier approval date or its unique coverage of the HPV strains that result in genital warts, most HPV vaccine administered in the U.S. has been Gardasil.¹⁵

Current National Policies

The United States, along with Australia, Canada, and the United Kingdom, were the first countries to include HPV vaccination in their national immunization programs.⁵⁶ Financing for HPV vaccination is not uniform in the U.S., but rather, is a mixture of public and private funding. It is estimated that in the U.S., about 56% of routine childhood vaccines are publicly funded, while the remainder are financed by the private sector.⁵⁴ Because they are recommended by the ACIP, both vaccines are covered under the CDC's Vaccines for Children (VFC) Programs.⁶¹ The VFC provides federally purchased vaccines to enrolled private and public healthcare providers for use among children who are Medicaid-dependent, underinsured (seen at Federally Qualified Health Centers), uninsured, or American Indian or Alaskan Native, through the age of 18.¹⁵ Under the VFC, about 32% of adolescents are eligible for HPV vaccination.⁵⁶ Those that did not qualify for the HPV vaccination series prior to the Patient Protection and Affordable Care Act of 2010, had to rely on privately financing, either through out-of-pocket expenses or private insurance. However, non-grandfathered private insurance plans must now cover HPV vaccination at no cost for those that fall into the ACIP's recommended age ranges.⁶² Children eligible for the State Children's Health Insurance Program (SCHIP) are also covered, as SCHIP programs must reimburse for vaccines recommended by the ACIP.⁶³ Additionally, a vaccine assistance program funded by

Merck is available to uninsured women between the ages of 19 and 26, and requires care be provided by a private physician who already distributes other Merck products.⁶³

In 2006, after Gardasil was approved by the FDA, the ACIP did not take a position on whether vaccination should be mandatory by law as such policy decisions are left up to the individual states.⁴³ In turn, some state legislatures granted their Health Departments the power to require vaccines.⁶⁴ To date, at least 25 states and territories have enacted legislation on HPV vaccinations: Colorado, District of Columbia, Illinois, Indiana, Iowa, Louisiana, Maine, Maryland, Michigan, Minnesota, Missouri, Nevada, New Mexico, New York, North Carolina, North Dakota, Oregon, Puerto Rico, Rhode Island, South Dakota, Texas, Utah, Virginia, Washington and Wisconsin.⁶⁴ School entry mandates have been effective in increasing uptake for other vaccines, so many of these states included a school mandate in their legislation, leading to much controversy.^{42,64} To date, only the District of Columbia and Virginia have mandated vaccination. In this state and district, girls must receive all three doses of the HPV vaccine, with compulsory series initiation prior to entry into sixth grade, unless religious, moral, or medical exemption is claimed.^{62,64}

Texas was the first state to attempt a vaccine mandate in 2007, when an executive order was issued by the governor requiring vaccination for all girls to enter middle school, but the order was quickly overturned by the state legislature.⁴⁸ New York and Kentucky currently have pending legislation that would make the vaccine mandatory for school entrance with an “opt-out” policy, which are both in various stages of committee review.⁶⁴ As of January 2015, three states (Hawaii, Indiana, and New York) have proposed HPV-related legislation for the 2014-2015 session.⁶⁴

More than twenty other states currently have laws in place that recommend HPV vaccination, provide funding for the vaccine, and/or support public education about HPV and its vaccine.⁶² A number of states, including New Hampshire and South Dakota, have laws that require providers to cover the cost of the HPV vaccine, as well as provide federal and state funding to deliver the vaccine for no cost through their health departments.^{63,64} Some states, such as North Carolina and Washington, have added the HPV vaccine to their universal vaccine programs.⁶³ In regards to education, several states have laws mandating that schools/health departments distribute educational information about the vaccine to parents. Indiana further requires that parents of girls entering middle school provide a statement of their HPV vaccination decision, which is then communicated to the state health department.⁶⁴

Uptake and Barriers

Despite its proven safety and efficacy, current HPV vaccine uptake in the United States is inadequate. Using data from the 2007-2013 National Immunization Survey-Teen (NIS-Teen), the CDC reported that 57.3% of females aged 13-17 had received at least one dose of the HPV vaccine in 2013, an increase from 25.1% in 2007 and 53.8% in 2012, but that only 37.6% had completed the series.¹⁵ Vaccination rates for boys in the same age range in 2013 were even lower, with only 34.6% having received at least one dose, still an increase from 20.8% in 2012¹⁵, while 13.9% had completed all three doses, which was an increase from 6.8% in 2012. These statistics are extremely low compared to administration rates of other vaccines.⁶⁵ The CDC estimates that if the vaccine had been administered to all adolescent girls born in 2000 during routine health care visits

when they received their other vaccines, vaccination coverage for at least one dose by age 13 years in this cohort would have been 91.3%.⁶⁶

The national immunization rates above mask significant variation among subpopulations. Coverage rates were higher for Hispanics than for Caucasians among girls who received any number of doses of the vaccine. The series completion rate was markedly lower among African American females, compared to White and Hispanic girls. Among boys who received any number of doses of the vaccine, coverage was greater among Hispanic and African American males compared to Caucasians.

Socioeconomic status also affected coverage rates: overall, coverage for 1 or 2 doses of the vaccine was higher for girls below the poverty level, compared to those living at or above the poverty level, with no difference seen in the series completion rate. Coverage for any number of doses of the vaccine was greater for boys below the poverty level.

Additionally, coverage varied widely between states. The percentage of girls between the ages of 13 and 17 who received at least one dose of the vaccine ranged from 39.9% in Kansas to 76.6% in Rhode Island. For boys, coverage ranged from 11.0% in Kansas to 69.3% in Rhode Island.⁶⁷

Various studies have identified age, race, education, and socioeconomic factors as major factors that affect vaccination rates. Those closer to the minimum age of 9 for vaccination have demonstrated lower uptake than older, high school aged adolescents, possibly because parents have an inaccurate perception of their children's sexual activity.⁶⁸ Providers are also often unaware or do not ask about adolescent sexual health, including age of sexual debut. This lack of awareness may reduce a physician's ability to recommend vaccination at the appropriate age.⁶⁹ A recent study done among 124 parents

and 37 providers, investigating missed opportunities for HPV vaccination in adolescent girls, found that providers who delayed recommending the HPV vaccine to girls perceived to be at low risk for early sexual activity reported the lowest vaccine coverage rates among their patients. The same study demonstrated that providers did not feel they were able to adequately predict age of sexual debut among their patients.⁷⁰ Vaccine coverage for 10-14 year old girls in the United States has been estimated to be as low as 14%.⁷¹

Ethnicity is also a critical factor in vaccine uptake, as African American and low-income young women, in particular, are far less likely than Latina, White, or higher-income young women to receive the HPV vaccine.⁷² Low-income and minority adolescents are equally or more likely to start the HPV vaccination series, but are less likely to complete the series. While 50% of African American females initiate the HPV vaccine series, compared to 51% of Caucasian females, only 29% complete the series, compared to 34% of Caucasian females. Latina females tend to do a bit better, with 63% receiving at least one dose, and 36% completing the series.⁷³ Several studies have noted that Hispanics are much more likely to take up the HPV vaccine than African Americans, but the reasons for this difference are not yet clear.⁷⁴⁻⁷⁹ It is likely that social networks and perceived social support play an important role in increasing uptake. Particularly in Hispanic or rural communities, researchers have found that if young women and/or parents feel that it is socially desirable to receive the HPV vaccine, then they will do so with greater frequency.^{80,81} Lack of information, concern about side-effects, lack of health insurance and logistical challenges to series completion have been cited as major barriers to vaccine uptake among African American populations.⁷³ African American

women have higher rates of HPV infections than do women of other ethnic groups.

Additionally, the 2011 Youth Risk Behavior report found that 14% of African American girls initiate sexual intercourse prior to the age of 13, compared to 7.1% of Latinas and 3.9% of whites, highlighting the need for early HPV vaccination in this ethnic group.⁷³

Knowledge, and resulting attitudes, regarding HPV and its vaccine also affect vaccination rates. Knowledge levels have generally been found to be poor across both genders. A cross-sectional study done in 2007 in women ages 18-75 demonstrated that only 40% of women had ever heard of HPV, and of those 40%, less than half knew it caused cervical cancer.⁸² Another study surveying over 1,500 college students enrolled at a large public university in the Northeast United States in 2009 established that 13.6% of participants were unclear about the prevalence of HPV infections, 51.5% did not know that HPV is transmitted by skin-to-skin contact, and 72% did not know that HPV cannot be transmitted via bodily fluids. Participants were also misinformed about the fact that most women with HPV infections do not develop cervical cancer.⁸³ A systemic review of studies looking at HPV-related beliefs and HPV vaccine acceptability has shown that vaccine acceptability is higher when people have a high level of knowledge regarding HPV infection, believe the vaccine is effective, and believe they are susceptible to HPV infection.⁸⁴ Parental knowledge and beliefs are also influential in acceptance of the vaccine. In the 2013 NIS-Teen, 23.0% and 37.4% of surveyed parents did not intend to vaccinate their daughters and sons, respectively, in the following year.⁶⁶ They were asked to identify the main reason why they did not want to vaccinate their child. The top four main reasons provided were a lack of knowledge, a belief that the vaccine was not needed, the vaccine not being recommended by their health care provider, and concerns

about vaccine safety and/or side effects. Lack of knowledge was cited by the parents of both girls and boys (15.5% each), as was the belief that the vaccine was not needed (girls: 14.7%; boys 17.9%).⁶⁶

Provider recommendation is one of the strongest facilitators of vaccine uptake and conversely, a lack of provider discussion and recommendation leads to lower uptake. A national computer-based survey conducted in 2010 revealed that individuals whose health-care providers “strongly recommended” vaccination as compared to those whose providers “recommended” vaccination were more likely to complete the 3-dose HPV series.⁸⁵ In the 2013 NIS-Teen, 22.8% of parents of boys cited a lack of provider recommendation as the main reason for not vaccinating their child, while among parents of girls, 13.8% cited this reason.⁶⁶

There is a connection between low coverage rates and a lack of insurance.⁵⁹ Numerous studies have shown that socioeconomic factors such as proximity to healthcare facilities, availability of insurance and cost of vaccine were factors that contributed to differential vaccine uptake.^{79,84,86-89} In the case of HPV, cost is the major barrier, given the steep pricing of both Gardasil and Cervarix. According to the CDC’s pediatric/VFC Vaccine price list, Merck’s HPV-Quadrivalent Gardasil® has a packaging CDC cost/dose of \$107.156, and a private sector cost/dose of \$141.38. GlaxoSmithKline’s HPV-Bivalent Cervarix® has a packaging CDC cost/dose of \$100.85, and a private sector cost/dose of \$128.75.⁹⁰ However, there are numerous free vaccine programs, including VFC and SCHIP, as described previously.

Due to the only recent recommendation for routine HPV vaccination in boys, there has not been as much research on uptake and barriers as there has been in girls. It is

known that vaccine uptake in boys is profoundly lower than in girls, as described previously. As in girls, racial and socioeconomic disparities have been seen with coverage. Caucasian males are less likely to initiate vaccination than Latino and African American males, 20.8% compared to 25.9% and 31.7% respectively. Those with a family income above the federal poverty line are also less likely to start the vaccination series (17.3%) than those below the poverty line (29.9%). Various surveys conducted among parents have demonstrated that low-income and minority parents are highly receptive to male HPV vaccination, as compared to higher-income and Caucasian parents.⁷³ Series completion is poor across the board, with only 4.6% of Caucasian boys, 5.4% of African American boys, and 12.9% of Latino boys completing the 3 dose series.⁷³ Results from the 2010-2011 NIS-Teen revealed that parents of boys were more likely to initiate vaccination if they had received a healthcare provider recommendation or if their child was eligible for the VFC program.³⁰ Parental concerns over the perceived potential for encouraging or increasing promiscuity have been cited in many studies as barriers to wider adoption of the HPV vaccine. Further complicating this association, the recommendation for boys has been linked to oral and anal sex, suggesting special risks for adolescents having male to male sex.

Studies have demonstrated a high prevalence of STIs and HPV among MSM. A 1-year prospective cohort study investigating the early sexual behaviors of MSM found a HPV prevalence of 69.6% over the course of 1 year, with an incidence rate of 38.5/1000 person-months. This report also indicated that while many had heard of the infection, very few could identify the virus as the cause of anal or oral cancers. Only 14% identified HPV as a serious problem.⁹¹ The coverage rate for this population is currently

unknown.

Health education

Given that prior research has shown that knowledge and attitudes regarding HPV and its vaccine greatly impact vaccination rates, this project aimed to educate participants through a didactic presentation. Health education is a critical tool in improving the health of a population, as it increases individuals' capacity to access and use health information to gain control of their health.

The World Health Organization defines health education as “consciously constructed opportunities for learning involving some form of communication, designed to improve health literacy, including improving knowledge, and developing life skills, which are conducive to individual and community health”.⁹² Health literacy, in turn, has been defined as “the capacity to obtain, process and understand basic health information and services required to make informed decisions that will allow health-enhancing actions at the individual, social, and environmental levels”.⁹³ Current evidence shows that the educational programs most likely to achieve positive, informed change incorporate a complete understanding of both targeted health behaviors and the environmental context in which they occur.⁹² The three basic categories of health education are primary, secondary, and tertiary. Primary education seeks to reinforce good health habits which may or may not already exist. This ideally leads to preventive health behavior, where an individual, who perceives himself to be in a state of good health, takes on an activity with the goal of preventing or detecting disease. Secondary education aims to either avoid a decline in health or restore good health if such a decline has already occurred. This ideally leads to illness behavior where an individual who perceives himself to be ill takes

on an activity to either define that illness or determine appropriate treatment. Finally, the goals of tertiary education are rehabilitation and adaptation, following some sort of deterioration in health. This should lead to sick-role behavior, which is when an individual receives treatment.^{94,95} Therefore, the continuum of health education covers preventive care and the promotion of optimal health to the detection of illness and treatment. In the case of this study, the goal was primary education, to lead to the prevention of HPV through accessing HPV vaccination.

Current evidence suggests that parental health literacy does not affect health care utilization among adolescents, despite the assumption that adults make health care decisions for their children.⁹³ One study investigating an adolescent population with asthma demonstrated no association between parental health knowledge and child health care use. Additionally, studies among first- and second-generation immigrant families show that parents often have limited interactions with the American health care system.⁹³ Therefore, it is hypothesized that adolescent health literacy plays a significant role in health care utilization in general and in the uptake of HPV specifically.

Several intervention planning models, based on health behavioral theories, were considered in developing the informational tools utilized in this project, that include: (1) intrapersonal, with a focus on individual capacity; (2) interpersonal, with a focus on support groups; or (3) environmental, with a focus on institutional, community, or public policy factors.⁹² The only theories that were considered for this study were those of an intrapersonal nature, which attempt to modify individuals' knowledge, beliefs, attitudes, and intentions. There are six theories that fall into this category. The first is the rational model, which, through the presentation of unbiased information, seeks to encourage

positive and prevent negative health behaviors among individuals to create positive behavioral change.⁹² The disadvantage to this model is that knowledge is usually not sufficient to create behavior change. The second theory is the health belief model, which reasons that the greater an individual's perceived severity of and susceptibility to a disease, the greater his willingness to take preventive measures.⁹² Additionally, this model argues that an individual is more likely to create positive behavioral change when the perceived benefits of that change are greater than the perceived barriers. The third theory is the extended parallel process model, which tries to create change with "fear tactics," presenting information that is biased and/or emotionally arousing.⁹² In this model, those individuals with a high perceived susceptibility to and severity of disease, as well as high perceived efficacy (i.e. confidence in one's own ability to prevent harm), will be the most likely to create positive change. The fourth theory is the transtheoretical model of change, which defines five stages of behavioral change: precontemplation, contemplation, preparation, action, and maintenance.⁹² The fifth theory is the theory of planned behavior, which argues that intent to create positive behavior change is necessary for both achieving and maintaining that change.⁹² This model assumes that attitudes of both the individual creating the change as well as members of their social group affect intent. Finally, the sixth theory is the activated health education model, which consists of three phases: the experiential phase, the awareness phase, and the responsibility phase. These phases respectively involve an individual assessing his own health, receiving information about the target positive behavior change, and then implementing that change.⁹²

Successful education occurs with an understanding of context, so communication barriers, including physiological, environmental, psychological, and cultural barriers, as well as demographic factors, such as age, sex, educational level, and employment, play a major role in determining the best method of dissemination.⁹⁶ Community-based health education, particularly, should rely on social relationships and organizations to reach large populations.⁹⁵ In this study, an effort was made to learn from adolescent participants, understanding the cultural and ecological context in which they exist, by collecting feedback on the educational intervention utilized in this project. These comments will be used to improve the effectiveness of future interventions.

Specific Aims

This study uses youth groups and physicians to investigate: (1) the knowledge of adolescents concerning HPV and the HPV vaccine, with a particular focus on perceptions regarding susceptibility to and severity of contracting HPV; (2) attitudes and beliefs regarding HPV and the HPV vaccine; (3) the main barriers and facilitators to vaccination in Hartford; (4) the role of education in shaping knowledge base, perceptions, and participation in vaccination; and (5) the effects of the opinions of peers, parents, media, and physicians on vaccination decisions.

Chapter 2: Setting

This project was conducted in Connecticut's capital city of Hartford, in collaboration with the City of Hartford Department of Health and Human Services. The 2010 Census placed Hartford's population at 124,775, 3.5% of Connecticut's total population of 3,574,097. More recently, in 2013, Hartford's population was estimated at 125,017, a 0.2% increase since 2010.⁹⁷ Of Hartford's total population in 2010, 25.8% were under the age of 18, while 51.7% were female. Hartford has a predominantly minority population: 29.8% white, 38.7% black or African American, 43.4% Hispanic or Latino, 0.6% American Indian or Alaska Native, and 2.8% Asian.⁹⁷ The large minority population is reflected in the demographic composition of Hartford's public schools; 90% of enrolled students in Hartford's district schools were students of color in 2012.⁹⁸

Connecticut is the most economically disparate state, with several of the richest and poorest cities in the United States. Hartford falls into the latter category, with an average family income of only \$42,775. Three out of ten families in Hartford live below the federal poverty line, which in 2011, was \$22,811 for a family of four.^{99,100} Moreover, there is a high poverty rate among children under the age of 18; according to the American Community Survey, the rate in 2012 was 47.9%.⁹⁹ However, Hartford's metropolitan region, which includes Hartford, Tolland, and Middlesex counties, is the 13th richest metropolitan area, as defined by the Census, with an average family income of \$99,597 in 2009. This is an income gap of approximately \$56,000 between the city of Hartford and its surrounding counties for an average family.¹⁰⁰ Statewide, poverty rates for African Americans and Hispanics are vastly higher, at 22.9% and 27.3%, respectively, in 2011, than those for non-Hispanic whites (6.2%).⁹⁹

With this striking level of poverty, it is important to know a population's insurance status, especially while investigating a health intervention that is as expensive as the HPV vaccine. The U.S. Census Bureau, using data from the American Community Survey, releases yearly estimates for health insurance coverage in each state. In 2011, approximately 8.8% of all individuals in Connecticut were uninsured, though a more recent estimate in 2013 placed the uninsured rate at 9.4%.^{99,101} Children under the age of 18 had an uninsured rate of 2.9% at the time of the 2011 survey. Rates ranged between cities from 10.5% in Waterbury to 23.3% in Bridgeport. Hartford's rate was mid-range, at 18.3%, with 6.9% of all children under the age of 18 years underinsured. As with poverty rates, statewide, uninsured rates for African Americans and Hispanics were significantly higher, at 12.1% and 20.4%, than that for non-Hispanic whites (5.9%).⁹⁹ These state and city uninsured rates seem low compared to the poverty rates discussed previously, likely because of recent state and federal health care reforms, which have expanded Medicaid eligibility for adults below the federal poverty line without children, allowed children to stay on their parents' insurance up until the age of 26, and expanded eligibility for parents and pregnant women in the state's HUSKY insurance program.⁹⁹

Perhaps related to the large economic disparities that exist between Hartford and the rest of the state, there is a significant achievement gap between the Hartford Public School District and most other school districts in Connecticut. Data released by the Connecticut State Department of Education for the 2008-2009 school year revealed that only 27.9% of students performed at "goal" level on standardized tests in Hartford, with a four-year high school graduation rate of 42%. Only 61% of adults in Hartford have a high school diploma.¹⁰² More recent data from the 2012-2013 school year revealed a stable

four-year high school graduate rate of 42.5%, with a dropout rate of 23.6%.¹⁰³ The 2008-2009 report also conveyed some demographic information about Hartford's public school students. Ninety-two percent of students in the Hartford Public Schools qualified for free or reduced lunch, reflecting the city's overall low per capita income. Forty-three percent of students lived in households where English was not the primary language, and 14% of students started school in 2008 without being fluent in English.¹⁰² These statistics reflect the unique characteristics of the city of Hartford and its population that needed to be taken into consideration while formulating this study's methodology.

HPV in Connecticut

In Connecticut, HPV is not a reportable disease, so there is little data on state incidence or prevalence rates. However, the Connecticut Department of Public Health (CT DPH) does track cervical precancerous lesions, which can be used as a surrogate marker for infection.¹⁰⁴ HPV-related cervical intraepithelial neoplasia grades 2 and 3 (CIN 2/3) and adenocarcinoma in situ (AIS) were added to the reportable diseases and laboratory reportable significant findings lists in Connecticut in 2008.¹⁰⁴ Pathology laboratories in the state reported 3,702 cases of CIN2/3 and AIS in 2008, representing 2,999 individual women.¹⁰⁴ The majority of cases had a diagnosis of CIN 2, while only 1% were diagnosed with AIS.¹⁰⁴ Data have also demonstrated an overall statewide incidence rate of CIN 2/3 and AIS of 212 cases per 100,000 females, aged 15 and over. The highest rate was found in New London County, of 292/100,000 females, while Windham and Tolland counties had the lowest rates of 161 and 162/100,000 females, respectively. Hartford County had a mid-range rate of 180 cases per 100,000 females.¹⁰⁴ State trends regarding age distribution of infection reflected national trends, with young

women being disproportionately affected. In 2008, females between the ages of 18 and 29 had the highest incidence rate of infection, with a rate of 706/100,000 and a total of 1,658 cases, while those older than 50 had the lowest incidence rate, of 36/100,000.¹⁰⁴

As part of the analysis for a report published in the Morbidity and Mortality Weekly Report (MMWR) on April 20, 2012, the CDC calculated rates and actual counts of HPV-associated cancers by state. Again, Connecticut state trends reflected national trends. Of all HPV-associated cancers, cervical carcinoma had the highest incidence rate (6.13/100,000).¹⁰⁵ Oropharyngeal SCC had a rate of 6.09 cases/100,000 in men, but only 1.30/100,000 in women. The rates of anal SCC were low for men and women, 1.14 and 1.64/100,000, respectively. Vulvar SCC, vaginal SCC, and penile SCC all had incidence rates of less than 2 per 100,000 individuals.¹⁰⁵

The National Immunization Survey estimates the rate of HPV vaccination coverage among adolescents aged 13-17, by sex and by state. Based on this survey, in 2013, the estimated vaccination coverage for girls in Connecticut was 56.0% for the first dose, 49.0% for the second dose, and 40.1% for the third dose. The percentage of females who received three doses among those who had at least one HPV dose was 78.4%. Regarding males, the coverage for the first dose was 52.3%, 36.4% for the second dose, and 23.4% for the third dose. The percentage of males who received three doses among those who had at least one HPV dose was 66.0%.¹⁰⁶ A literature search regarding HPV vaccine uptake in the city of Hartford did not reveal any public data, so a complete picture of vaccination status among Hartford's youth is not known. Secondary data were collected from Carol Steinke, RN, BSN, the Public Health Nursing Supervisor at the City of Hartford's Department Health and Human Services (DHHS) (email communication,

February 2014). She provided estimates regarding the HPV vaccination coverage rate among those attending the DHHS STD Clinic in Hartford. Data from the start of tracking in 2012 to 2014 revealed that the Gardasil vaccine series had been started on 234 individuals, of which 68%, or 158 individuals, were females, and 32%, or 76 individuals, were males. Of these 234 individuals, 56% completed 2 doses, while 29% completed the full series.

These low coverage rates likely reflect the fact that there is currently no HPV vaccine mandate in the state. In the 2006-2007 state legislative session, three bills were introduced regarding the HPV vaccine. HB 5485 proposed to cover the 3-dose vaccine series under the state's HUSKY plan for girls aged 11 to 18 years. This bill was sent to the Senate Appropriations Committee, where it was approved. HB 6085 proposed to add the HPV vaccine to the adolescent vaccine schedule, as well as create an outreach program to educate the public about cervical cancer and the vaccine. This bill was referred to the Joint Committee on Public Health, but did not leave the committee. Finally, HB 6977 would have implemented a HPV mandate for all girls in the state entering the 6th grade, but was also not approved. Since then, no other legislation has been introduced in the state regarding HPV.⁶⁴

As with HPV vaccine uptake, a literature search regarding the level of knowledge and attitudes about HPV and its vaccine among those residing in Hartford reveals very little public data. One study was conducted among Connecticut-licensed pediatricians in 2008 to investigate practitioner acceptability of the HPV vaccine, which found that pediatricians with greater self-reported knowledge about HPV were more likely to have discussions about sexually transmitted infections with their patients.¹⁰⁷ However, this

study was conducted prior to the routine recommendation of the vaccine for boys, and did not investigate attitudes among individuals actually receiving the vaccine. Additional epidemiological data are now coming from the Connecticut Emerging Infections Program, which is a joint project between the CT DPH and the Yale University School of Public Health. Enhanced surveillance for CIN 2/3 and AIS among women between 18 and 39 years old living in New Haven County is expected to continue for the next 10 years, and will hopefully allow for monitoring of the impact of the HPV vaccine.¹⁰⁴

Chapter 3: Methodology

The project from which the data in this thesis were drawn was conducted by a group of 12 students who participated in the required practicum course in the Winter/Spring semester of the University of Connecticut's Master in Public Health program. The project was conducted in collaboration with the City of Hartford's Department of Health and Human Services (DHHS).

Key Informant Interviews

This project was initiated with an informal meeting with the Executive Assistant to the Director of the DHHS who briefed the group about the organization and provided suggestions for contacts in Hartford to reach parents and adolescents. Subsequently, information was gathered from the Public Health Nursing Supervisor at the DHHS on the approximate vaccination coverage rate of Hartford's youth, as no formal data have been published to date. Data from the start of tracking were provided from the City of Hartford's DHHS STD clinic and are presented in *Chapter 4*. These secondary data provided the only data regarding vaccine uptake in Hartford that was acquired during the course of this project.

Contacts were made at the National Black HIV/AIDS Awareness Day Community Fair in Hartford on February 7, 2014. Individuals were approached at their respective booths, at which time the goals of this study were described. A brief presentation regarding HPV and the HPV vaccine, vaccine uptake, and suspected facilitators and barriers to vaccination was given to those who wanted more information. It was explained that one of the aims was to pilot test a didactic presentation with groups of parents and adolescents, after which the opportunity to participate was offered.

Physician Interviews

Semi-structured key informant interviews with physicians were also conducted (see physician interview protocol in Appendix I). These sessions were held to document the knowledge and attitudes of family physicians on HPV and the HPV vaccine, in addition to the factors that influence physicians' decisions to recommend the vaccine, who physicians recommend the vaccine to, and how physicians deal with negative responses from parent figures. An interview protocol was developed that contained questions covering the domains previously mentioned. The first section specifically addressed physicians' patient panels, asking such questions as "What percentage of your patients does not have health insurance?" and "If you had to estimate, what percentage of your patient panel are white, Black, Hispanic, or Asian?" The second section assessed physician practice, in an attempt to understand the opinions of HPV vaccination in their patients, as well as barriers to vaccination in their population. Physicians were asked if they offered the HPV vaccine to their patients. Open-ended questions followed, such as "Could you describe how you presented the vaccine to your last patient, and how you described it to the adolescent and/or parent?", "Could you give an example of a specific patient or parent that initially refused the vaccine and then changed their views when you discussed the reasons for the vaccine?", and "Do you think your input as a physician can change someone's mind from refusing the vaccine?" The final section assessed physician knowledge, and asked such questions as "Do you think that the HPV vaccine is effective?" and "Do you have any concerns with giving the vaccine to your patients?" A final question attempted to draw out recommendations to increase uptake, asking what could be implemented or changed to increase vaccination rates in Hartford.

A total of six physicians were interviewed, either by phone or in person. With assistance from other students and faculty members of the Master of Public Health program at the University of Connecticut, contact was initiated with various physicians throughout the greater Hartford area. Those contacted practiced in the Hartford area, or provided the majority of their services to Hartford residents. Purposive, non-random sampling of physicians was conducted: interview appointments were made with those that responded to the initial contact, based on mutual schedule availability. Other factors, including the racial, gender, and socioeconomic makeup of their patient populations, were not taken into account. Physicians were made aware of the project, contacted prior to the interview, and interviewed only with their consent.

Literature Review

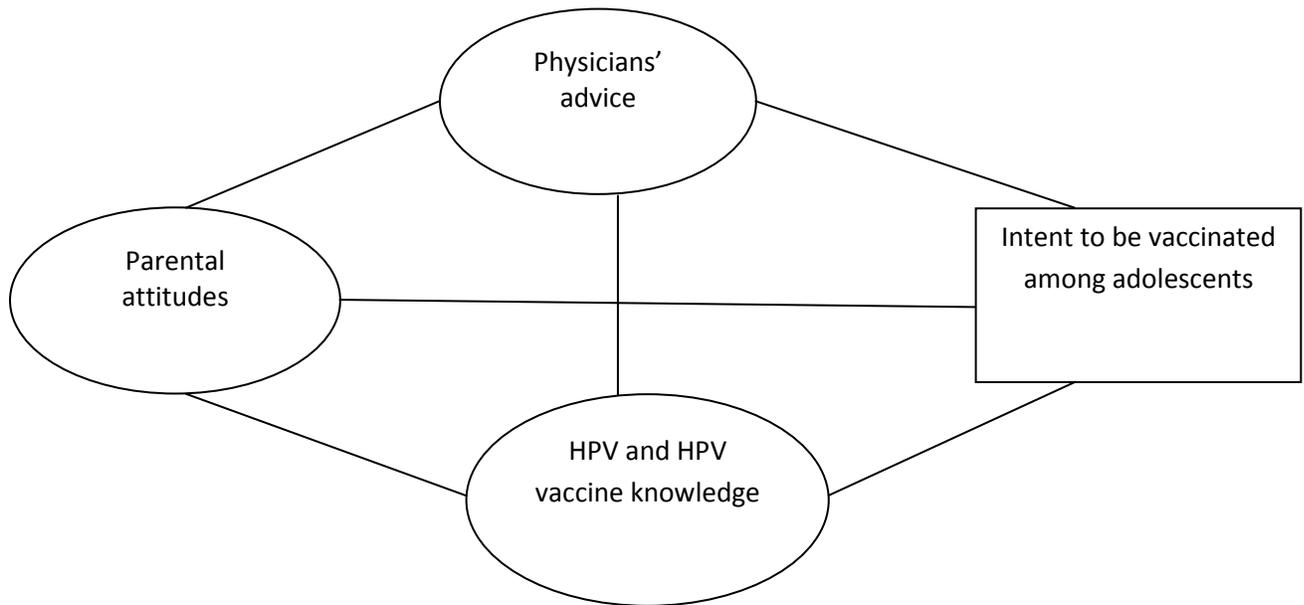
An extensive review of the existing literature was conducted. Four main topics were covered. First, the pathophysiology and biological mechanisms of HPV and the HPV vaccine were investigated. Specifically, information was gathered on the pathophysiology of HPV, focusing on the differences between the high-risk and low-risk strains; symptomatology; the mechanisms involved in the contribution to cervical and other kinds of cancer; the associated risk factors for this transition; and the mechanism of action of the two vaccines on the market. Epidemiological factors were examined as well, specifically looking at the incidence and prevalence of HPV in the United States, Connecticut, and Hartford; the distribution of infection by ethnicity and race; and the types/cases of cancer associated with HPV. Second, an in-depth exploration was done on the history of the HPV vaccine. The differences between Gardasil and Cervarix were examined, in addition to the process by which these vaccines were developed and tested,

the process of FDA approval, the evidence used to support efficacy and safety, the profits associated with vaccine uptake, and prior and current ACIP recommendations. The literature was thoroughly searched for any documented problems with vaccine safety or efficacy. Third, current HPV vaccine uptake was studied. The following questions were researched: What is the current uptake of the HPV vaccine? Are there any groups that have lower uptake than others? What are the barriers and facilitators that impact vaccine uptake among these groups? Is there any problem with people completing the series? Lastly, policies associated with the HPV vaccine were investigated. Specifically, information was gathered on how (and who) introduced the vaccine to the public, how public opinion on the vaccine was shaped, and the processes by which the vaccine was rolled out to both females and males. Financial issues were examined as well, including how the vaccine is funded, coverage under various insurance plans, and pricing of the vaccine. Finally, prior and current state mandates were investigated, specifically looking at the current situation in Hartford.

Research Model

Based on the key informant meetings and literature review, a hypothesized model was created that identified factors influencing the intent to be vaccinated among adolescents.

Figure 1—Research Model



Dependent Variable:

Intent to be vaccinated among adolescents

The dependent variable will assess intent to receive the HPV vaccine among Hartford adolescents with a close-ended survey question: “Do you plan on being vaccinated in the next year?” Only a “yes” answer will be considered confirmatory; failure to answer the question will be considered a lack of intent.

Independent Variables:

Parental attitudes

This domain will examine parental influence on vaccination intent. Specifically, through close-ended survey questions and open-ended discussion questions posed to adolescents, the role of parental consent as a facilitator of vaccination (and conversely, parental refusal as a barrier to vaccination) will be explored.

Physicians' advice

This domain will investigate physician influence on vaccination intent. Similar to the exploration of parental influence, close-ended survey questions and open-ended discussion questions posed to adolescents will target whether physician recommendation acts as a facilitator to vaccination. Additionally, key informant interviews conducted with physicians documented the knowledge and attitudes of family physicians on HPV and the HPV vaccine, the factors that influence physicians' decisions to recommend the vaccine, who physicians recommend the vaccine to, and how physicians deal with negative responses from parent figures. Physicians were asked what percentage of their patients accepts the HPV vaccine.

HPV and HPV vaccine knowledge

This domain will examine the knowledge base of Hartford adolescents concerning HPV and the HPV vaccine, with a particular focus on perceptions regarding susceptibility to and severity of contracting HPV. Additionally, attitudes and beliefs about the main barriers and facilitators to vaccination in Hartford will be explored. This will be done through close-ended survey questions addressing these issues. Answers to these survey questions will be coded as "1" for correct and "0" for incorrect, when compared to an investigator-created key. Correct answers will be added up into scales to create a final score to quantify knowledge. Overall scores will be compared both before and after the implementation of a didactic presentation. Additionally, open-ended discussion questions will be posed to expose potential misconceptions regarding HPV and the vaccine.

Hypotheses

Adolescents are at a stage in their life in which they are starting to gain independence from their parents and families, but still remain somewhat dependent on them to make critical decisions, such as those related to health. Therefore, it was hypothesized that:

- (1) The most significant influence on the intent to be vaccinated will be adolescent knowledge and beliefs. Knowledge will be positively correlated with the intent to be vaccinated.
- (2) Increased knowledge will be associated with the belief that HPV infection is serious, as well as that the HPV vaccine is effective.
- (3) Parental knowledge, beliefs, and guidance will significantly influence intent. Adolescents with parents and guardians with more negative attitudes regarding the vaccine will be less likely to want the vaccine.
- (4) A physician recommendation to be immunized for HPV will positively influence both parental and adolescent decision making.
- (5) The majority of adolescents will have heard of HPV and its vaccine prior to presentation and focus group discussions.
- (6) Prior to implementation of the educational intervention, adolescents will demonstrate a higher rate of misconceptions regarding HPV, than afterwards.
- (7) Belief that the HPV vaccine is effective will be most often identified as a facilitator for vaccination, while fear of side effects will be most often cited as a barrier.

Study Sample

This study was conducted with groups of adolescents drawn from various community-based organizations, which included Community Partners of Hartford, YWCA, Voices of Women of Color, and the DHHS' Hartford Teen Pregnancy Prevention Initiative. Through collaboration with the DHHS, as well as with assistance from other students and faculty members of the Master of Public Health program at the University of Connecticut, contact was initiated with various organizations throughout the greater Hartford area. Purposive, non-random sampling of groups of adolescents were selected by setting up appointments to present the informational tools discussed below, based only on the mutual schedule availability of the organization and the students.

Didactic Presentation

The first objective of this project was to educate adolescents through a brief informational session. A 15-20 minute PowerPoint presentation was prepared by the practicum team, utilizing topics gathered from the initial literature review and key informant interviews. The purpose of this didactic intervention was two-fold. First, it was presented to the groups of adolescents recruited from the various community-based organizations in Hartford specifically for this study. Second, it was used as a pilot test, and, once modified based on feedback from this study's participants, can be used to lay the groundwork for a future larger HPV awareness project in Hartford. Various students from the 2014 Spring semester practicum team, as well as one student from the 2014 Summer semester practicum course, conducted these presentations.

Principles from the rational model, the health belief model, the extended parallel process model, and the theory of planned behavior, as described in *Chapter 1*, were merged used to create the presentation utilized in this study. The presentation began with a brief anecdote about a teenager diagnosed with Stage 1A cervical cancer, adapted from a true story on a cancer support website (<https://www.fightlikeagirlclub.com>). This anecdote was followed by a description of HPV, covering transmission and potential consequences of infection, including the link to various malignancies. Images were displayed to illustrate the many ways HPV infection can present in the body. Previous studies have shown that HPV is often confused with herpes simplex virus (HSV) and human immunodeficiency virus (HIV), so the differences between these three viruses were described. Then, a description of the process by which HPV leads to cancer was provided. After addressing this basic information, the presentation attempted to rectify common misconceptions associated with HPV. It was explained that both males and females can be infected and that there is no cure for infection, though most infections are cleared by the immune system without intervention. Additionally, the seriousness of cervical cancer was emphasized.

The presentation then led into a description of the HPV vaccine, which included the differences between Gardasil and Cervarix, the dosing schedule, its mechanism of action, and its target population. As with HPV infection, common misconceptions associated with the vaccine were addressed and corrected. It was emphasized that an individual does not need to be sexually active to receive the vaccine, that the vaccine only prevents (and does not cure) infection, and that even if one remains abstinent until marriage, the vaccine is still important. It was explained that both males and females can

get the vaccine, and that the vaccine has been proven to be safe and effective, without known serious adverse reactions. This was followed by a brief note about the cost of the vaccine, and various options for financial assistance for those uninsured. The presentation ended with a suggestion for participants to talk to their physicians about receiving the vaccine.

Pre/Post-Surveys

To assess the impact of the presentation, a survey instrument was developed to be administered to adolescents both before and after the didactic presentation (see survey instrument in Appendix II). Questions were developed based on identified gaps in knowledge and common misconceptions gathered from the initial literature review and key informant interviews. The three-page survey instrument consisted of 25 primarily close-ended, multiple choice questions, addressing each of the factors identified in the initial research model.

The survey was distributed to a total of 75 adolescents twice, both before and after the PowerPoint presentation was administered, for a total of 145 responses. The student investigator of the study, or another student from the practicum team, delivered the survey instrument and explained the study goals, asking participants to answer each question to the best of their knowledge. However, the final sample involved multiple incomplete surveys. Additionally, while there were 75 pre-presentation surveys collected, there were only 70 post-presentation surveys returned.

The survey was initiated with questions addressing one of the three dependent variables in the initial research model, HPV and HPV vaccine knowledge. Three single-answer, multiple choice questions were first asked to establish the level of pre-existing

knowledge about HPV. Namely, respondents were asked whether they had ever heard of HPV, what they thought HPV is, and what they thought the most common STD is. This was followed by a multiple-choice question, asking respondents to circle any condition they thought HPV could cause. Answer choices included correct choices such as cancers of the reproductive system for women and genital warts, as well as incorrect choices such as AIDS and breast cancer. The presence of common misconceptions was then tested through true or false questions. Examples of question stems were, “You would always know if you had an HPV infection,” “Antibiotics can cure HPV,” and “If you wait to have sex until after marriage, you cannot get HPV.” More specific questions testing knowledge were also asked, including a fill-in question asking respondents to fill in the age at which HPV vaccination can start, and a question inquiring about the number of vaccine doses needed to complete the series. A key was created with the correct answers, and compared to participants’ responses. Correct answers were added up into scales to create a final score to quantify knowledge for each participant; overall performance was compared before and after the presentation.

Two questions focused on attitudes towards HPV and its vaccine, and were not counted towards the final “knowledge score.” These were true or false questions, with the statements “HPV infection is serious” and “The HPV vaccine is effective in preventing HPV infection.” The relationship between the intent to be vaccinated and these question responses was tested. Two other questions (multi-answer, multiple choice) attempted to gain a better understanding of barriers and facilitators to vaccination. These addressed the independent variables of parental attitudes and physicians’ advice in the initial research model. The first question asked respondents to identify why a teenager would decide to

get vaccinated, assessing potential facilitators. Choices addressed both parental input (“His/her parents told him/her to”) and physician input (“His/her doctor told him/her to”), as well as personal beliefs (“To prevent HPV infection” and “To prevent cervical cancer”). The second asked respondents to identify reasons a teenager would decide *not* to be vaccinated, assessing potential barriers. Choices again included parental input (“His/her parents did not tell him/her to” and “His/her parents did not want him/her to”) as well as personal beliefs (“Thinking that the vaccine is unsafe,” “Fear that the vaccine will cause pain,” and “Cost of the vaccine”). For both of these questions, respondents were encouraged to circle all choices that applied. Again, the relationship between the intent to be vaccinated and responses to these questions was tested.

Finally, the dependent variable of the initial research model, vaccination intent among adolescents, was addressed with a yes/no question, which inquired, “Do you plan on being vaccinated in the next year?”

Focus Group Discussions

Following each informational presentation and administration of the post-presentation survey instrument, brief, semi-structured discussions were conducted with those adolescents in attendance (see question guide in Appendix III). The purpose of this activity was twofold. First, it was an opportunity for those in attendance to offer suggestions, recommendations, and cautions regarding the content and style of the didactic presentation. Second, it allowed the student investigator to gather more in-depth information on misconceptions and ideas about HPV, attitudes about vaccination, and perceived barriers and facilitators to vaccination.

Each session was initiated by a description of the purpose of the focus group, as well as instructions for how to answer the posed questions (e.g. “The group is *not* trying to reach an agreement; you may disagree with others as long as you do it in a respectful manner”). Reassurance was provided that participants could leave the discussion at any time, and that all dialogue would remain confidential, without being linked to names or other personal information. Questions regarding the presentation itself inquired about ways to improve the presentation and examples of content that could be added, revised, or removed. Questions about HPV and its vaccine addressed: (1) barriers to vaccination, (2) motivating factors for vaccination, (3) series completion, (4) vaccination in males, and (5) sources of information about HPV and its vaccine.

Statistical Methods

Quantitative data analysis was performed using SPSS 22.0. Descriptive statistics including frequencies, percentages, means, medians, and modes were analyzed for each question in the survey instrument. Frequencies were generated for the adolescent study sample, sorted by pre-presentation (n=75) and post-presentation (n=70) responses for each question. Answers to all knowledge questions were coded as “1” for correct and “0” for incorrect, as compared to an investigator-created key. Correct answers for the questions assessing knowledge were added up into scales to create a final score summarizing knowledge for each participant. Overall performance among participants was compared before and after the presentation. Relationships between bivariate categorical variables were tested using Chi-Square, while T-tests and one-way ANOVA were utilized for associations between categorical and continuous variables. Results were considered significant with a *p*-value less than or equal to a significance level of 0.05.

Qualitative data analysis of the adolescent focus group discussions and the physician interviews were performed using Atlas.ti, a computer based analytical tool designed to identify primary themes in qualitative textual data.¹⁰⁸ Five primary codes were created for the adolescent group discussions surrounding major themes and included: knowledge; barriers; misconceptions; facilitators; and presentation improvements. Discussions were then systematically reviewed and codes were assigned to quotations and dialogues covering each of the five codes. Atlas.ti was then used to generate query reports surrounding each of the major codes. Query reports were reviewed and major themes were extracted. The same was done for the physician interviews. In this case, eight primary codes were created, which included: physician characteristics/patient demographics; estimated HPV coverage rates; HPV vaccine acceptance and physician practice; physician knowledge; insurance/cost issues; patient barriers; physician barriers; and recommendation.

IRB Exemption

This project received exemption status through the University of Connecticut Health Center Institutional Review Board (UCHC IRB). No identifying or personal information, such as names, past medical history, or vaccine status, were gathered from study participants.

Notes from the focus group sessions were recorded either by a scribe in a Word document, or by tape recorder when allowed. The scribe anonymously documented the participants' responses and input in the discussion. No names or other personal identifying information were included; individual responses were labeled P1, P2, etc. (i.e. Participant 1, Participant 2). The group members were asked not to use his or her own or

anyone else's name in the discussions. If names were used, they were not recorded in the Word document, or were removed from the record post-discussion.

Physician interview sessions were also recorded, and later transcribed into a Word document. Practitioners' responses were anonymously documented, labeled as P1, P2, etc. (i.e. Practitioner 1, Practitioner 2). The practitioners were asked not to use their, or anyone else's, name in the discussion. No names or other personal identifiable information were included in the transcripts. If names were used, they were not recorded in the Word document.

Chapter 4: Results

Key Informant Interviews

Discussions were held with representatives from various organizations at the National Black HIV/AIDS Awareness Day Community Fair in Hartford on February 7, 2014. Attending the Fair provided a sense of how key stakeholders in the community felt about HPV and the vaccine at the onset of the study. Most individuals approached during the fair, including a service coordinator for Community Health Services, the mentoring program director from True Colors: Sexual Minority Youth and Family Services, and volunteers from Hands On Hartford, agreed that infection with HPV is a serious issue, and that the vaccine is an effective preventive strategy. The general consensus was also that the vaccine is under-utilized, particularly among the youth of Hartford, often due to parent distrust/refusal of the vaccine. An epidemiologist from the STD Control Program at the Department of Public Health expressed his belief that poor HPV vaccine uptake among adolescents is one of the biggest unresolved public health issues in Hartford.

Every group represented at the fair was approached, at which time the goals of this study were described and the opportunity to participate was offered. Most groups, including Community Health Services, True Colors, and Planned Parenthood, were highly interested in the project, providing their contact information for further communication. One religious-based program expressed reluctance to support this study's goals by setting up presentation groups with adolescents and parents, citing an abstinence-only educational policy.

Key informant interviews were also conducted with six physicians from the Hartford area.

Physician Characteristics / Patient Demographics

Two physicians were pediatricians, whose patient panels were entirely made up of children under the age of 18 years. Another physician was an obstetrician/gynecologist, whose patient panel consisted of females over the age of 13 years. Twenty to thirty percent of this doctor's patients were reported to be under the age of 18 years. Three family medicine physicians were also interviewed, who reported that children under the age of 18 years made up 10% to 45% of their patient panels.

These healthcare providers had racially diverse patient panels, consisting of large proportions of racial minorities. Overall, patient panels consisted of ranges of 10% to 30% Caucasians, 10% to 40% Hispanics, and 20% to 80% African Americans. Asian patients represented a small minority, ranging from 5% to 10% of total patient populations. Most of these patients were reported to be Hartford residents. Hartford residents made up a majority of the patient panels of four physicians, ranging from 80% to 90%. Another physician reported that half of his patients were from Hartford, while the last related that approximately one-third of his patients were from the Hartford area.

Estimated HPV Coverage Rates

Physicians were asked to estimate the rates of vaccine coverage in the United States ("If you had to guess, in the United States, what percentage of adolescent females have received one shot of the vaccine? And what percentage has received the complete three-shot series?"). Responses were fairly accurate based on current female vaccination rates in the United States. Physicians estimated that 30% to 60% of patients received one vaccine, and that 15% to 40% have received the full three-dose vaccine series. In 2013,

the CDC reported that 57.3% of females aged 13-17 had received at least one dose of the HPV vaccine and 37.6% had completed the 3-dose series.⁶⁶

HPV Vaccine Acceptance and Physician Practice

Most physicians said that if offered the vaccine during a visit, the majority of patients accept. One physician stated that approximately half of his patients accept the vaccine, while four others responded that 80% to 90% of their patients accept it. The final physician approximated an acceptance rate of 65%, reporting that many of his patients and their parents wanted to wait until they were older to start the series. When asked, “What percentage of patients offered the vaccine accept the vaccine?” he responded:

They accept. More and more, they have accepted more. The majority of patients accept it. But I think that about 25-35% refuse. I have a lot of them, like 30-35% that say, “I won’t do it today, how about you do it next time?”

All six physicians said that they offer the vaccine to their patients as part of routine health maintenance. The five physicians whose patient panels consisted of both female and male patients said that they offered the vaccine to both genders between the ages of 9 and 26. However, most reported that vaccination was most heavily promoted around the age of 11 years:

In our clinic, we start telling parents about the vaccine at the age of 9. Starting when they reach adolescence, that’s when we start asking them to get the vaccine, usually around the age of 11 or 12.

When offering the vaccine, most reported that they emphasized the efficacy of the vaccine, highlighting the protection it offers against cervical cancer and genital warts. Those that see male patients also reported talking about its efficacy against penile cancer and genital warts in boys.

Well I always tell people that this vaccine is available for protecting them against the HPV virus, it's a series of three shots, HPV can be a precursor to cervical cancer later on, and even if they have been exposed to HPV in the past, this can protect them from the strains that they have not been exposed to. And then, I tell them anyone who is sexually active could have been exposed to any of the HPV viruses.

The obstetrician/gynecologist responded that most of her younger patients are pregnant and have to wait until after pregnancy to receive the vaccine. This physician also mentioned that she does not try to change a patient's mind if the vaccine is refused.

If a patient says, 'No, I do not want it,' it's not just that they don't like it, they just don't want it. I do not argue with them.

Another physician reported that an opt-out system was utilized in her office, where the standard practice is to routinely offer patients the vaccine, but allow them (or their parents) to decide to refuse the vaccine:

We usually default to the patient. We kind of tell them that they are going to get the vaccine and they would have to choose to refuse it. [They would have to opt out?] Yes, they would have to opt out of it. [Is that standard for the entire practice?] Yes, that is standard for the entire practice.

Physician Knowledge of the HPV Vaccine

Four out of the six physicians who participated believed in the efficacy of the HPV vaccine. One mentioned concerns that it has not been proven to be effective against cervical cancer or genital warts, and only offers it because it is recommended. This physician also reported that only one third of her patients have received the HPV vaccine.

I don't fully believe that it's been proven to be effective, so I have a hard time being 100% behind it. I offer it because I am supposed to... I don't believe that it has been in existence long enough to know whether it is effective or not. [Do you think it's effective against genital warts?] No, the purpose of it is to help prevent the high-risk HPV's, the ones that can lead to cancer.

The sixth physician expressed concern that the vaccine is relatively new. One of the four that expressed confidence in the vaccine stated that he felt more time is necessary to see decreased rates of genital warts and cervical cancer. When asked, “Do you think that the HPV vaccine is effective?” he responded:

I think so. I think we do not fully know yet but we will see in another one to two decades. We will see if the incidence of cervical cancer and genital warts decreases in one to two decades.

Insurance / Cost Issues

The percentage of uninsured patients among the physicians’ patient panels was low, with all six reporting a percentage less than 10%. As a result, cost did not seem to be a major barrier to vaccination, as it is covered under most private and public insurances. Five out of six physicians agreed that cost was not an issue, and one reported that it was an issue only for self-pay patients. One physician described how the Vaccines for Children (VFC) Program covers the costs for those uninsured. When asked, “Is cost a barrier to vaccination in your patients?” she responded,

Not usually because almost all of our patients get their vaccines through the VFC program... It’s now covered actually even for the commercially insured under the VFC program, but I’m not 100% sure on that. So initially there might have been some wariness about that but it has not been a big factor for us.

Two physicians reported the breakdown of insurance types for their patients, both stating that around 60% to 80% are covered on Medicare or Medicaid, with the rest on private insurance. One mentioned the availability of Husky Health insurance (the State of Connecticut’s public health coverage program providing free or low-cost health care for Connecticut kids and teens) for children whose parents are uninsured:

I have a large percentage of people, I would say around 60%, who are covered on Medicare or Medicaid. For kids, they're covered with Husky insurance, which is like Medicaid.

Patient Barriers

When questioned about barriers to vaccination, common themes emerged. When the physicians were asked, “What are some other reasons that patients or their parents have refused the vaccine?” most stated that teenagers do not like receiving needles. Some indicated that a small percentage of their patients are completely anti-vaccine. The majority cited a fear of side effects as a major barrier. As one physician reported:

Some people do not believe in vaccines, but I do not have many of these. Some people already had the vaccine, but some people have heard stories. It could be hearsay, but they do not want to get vaccinated because of those reasons.

Some stated that it was difficult to recommend the vaccine without a school entrance mandate. One physician noted that parents of his patients easily accept a vaccine that is necessary to enter school, but are wary of any additional vaccines.

Sure, we do tell them [parents] that it's not one of the required vaccines for school so that differentiates it from the rest. That gives them an option to refuse it and still send their children to school.

All six physicians reported deflecting concerns that vaccinating against HPV may increase sexual activity or lower the age of the initiation of sexual activity. As one stated:

Sometimes I get parents who just don't want to give the vaccine to their kids. Lots of parents are scared that they're giving a vaccine that might make their kids more sexually active, or have sex at an earlier age, but I think that it's a good idea to give the vaccine before they're sexually active and before they're really aware of what sex is. Like, the Hepatitis B shot in children. We give that to every kid after they're born, and it prevents a blood-borne infection. I don't think that it makes people more likely to use IV drugs, and I really don't think that giving an HPV shot will make people more likely to have sex at a younger age.

Many parents refuse the vaccine because their children are not sexually active. However, as the physician above stated, vaccination is best started at an age before sexual activity, as it is a preventive tool. One physician replied that at the age of 9 or 10 years, it may be hard to convince a parent to accept the vaccine. When their children are in the early adolescent stage, around 11 or 12 years, they become more open to vaccinating their children.

If you start offering it at 11, 12, 13, 14, I think their parents are already scared of sexual activity, so they're more used to the idea, and they're like "Yes, please give it to them!" [Yes, there's a big difference between a 9 and 12 year old]. Yes. Exactly.

One physician provided an example of a specific patient:

I had one parent who refused the vaccine because she thought that we should wait until her daughter was older. For some parents, it's hard to see their little girl and think about giving them a vaccine that prevents against a sexually transmitted disease... For some parents, it's really hard to accept that their kid may choose to have premarital sex, especially for traditional families. So I basically told her that it's best to get it at this age, so that whatever age she chooses to become sexually active, she'll be protected, and mom seemed to think that was reasonable.

It appears that some patients do not believe that they need the vaccine. One physician reported a case where a patient, who refused the vaccine every year since the age of 10, developed genital warts at the age of 17, and then asked for the vaccine. The patient apparently asked for the vaccine in the hopes of curing her genital warts. The physician described the situation:

I do have one kid that comes to me who at 17 came in with genital warts for the first time, and every visit from her ten year old visit on, had been offered the vaccine, initially her guardian refusing on her part and then she refusing. 'Til she came in with genital warts, and then she said 'I'll take the vaccine now.' And we gave it to her because there are different serotypes, but they just couldn't believe

before that they would really need it.

Misconceptions such as these among patients appeared to be common. One physician expressed a belief that the number one reason for low vaccination rates is a lack of information, and not understanding the importance of the vaccine:

The number one reason is lack of knowledge because they do not understand the importance of the vaccine or the reason to have it at all. They do not understand that HPV can lead to cancer. So I would say the number one reason is lack of information.

Those treating males described gender-specific barriers as well. The HPV vaccine is often described as the “Cervical Cancer Vaccine,” leading parents to believe that there are no perceived benefits from vaccinating boys. One physician described the trouble in convincing parents of boys to accept the vaccine:

I think it's because a lot of parents think that it's an exclusively female disease. I tell them about penile and anal cancers that can develop in men. However, I have to admit that penile cancers are pretty rare. And most men who develop anal cancer are gay, so that's a tough sell to parents to talk about the chances that their kid might be gay, so we should protect them from anal cancer as well.

However, many physicians reported talking about the benefits for female partners:

[H]onestly, if I had to vaccinate my sons, I would give it to them just to protect their sexual partners. I think that by giving it to boys, you can prevent the boys from giving it to more girls, and it would make the vaccine much more effective than just giving it to half of the population.

Physician Barriers

Most physicians reported that they did not have any specific concerns administering the HPV vaccine. They reported warning their patients about the routine side effects associated with any vaccination, including pain on injection and bleeding.

However, one physician reported that the reports of neurological side effects made her wary, despite the lack of evidence of severe adverse effects in the literature:

I personally heard of stories where girls have had neurological difficulties after receiving the HPV vaccination, so I have a hard time being 100% behind it. I don't want to cause more problems than I am healing.

One physician reported concerns that her patients were not receiving all three doses within the recommended time frame, and therefore not receiving optimal protection from the vaccine.

Yes, my concern is that the most effective way to give the vaccine is to get all three shots in one year. If you lose patients to follow up, I'm worried that they won't get the full course of the vaccine or they won't get it in time and therefore the vaccine would not work as well as it should.

Recommendations

Three out of the six physicians expressed their belief in the importance of an education program for their patients to increase knowledge of HPV and its vaccine. One indicated that the education program should target both teens and parents, and stated:

I think that we need more education. Some people have heard of it [HPV vaccine] but don't know what it's for or what the purpose is and what the health outcomes are. So I think that we need a lot more education.

Two physicians said that a school mandate was needed to increase vaccination rates. The schedule for the vaccine, with three shots given over a six month period, can be difficult in pediatric patients, especially since they may have to miss school for their appointments. Additionally, since pediatric patients are used to seeing their pediatricians only annually or biennially for well-child check-ups, many miss their follow-up

appointments for the second and third shots. One physician argued that if the vaccine was made mandatory to enter school, rates of vaccination would increase. When asked, “What do you think can be implemented or changed to increase the rates of HPV vaccination in Hartford?” she replied,

School. If schools make it mandatory then they [teens] cannot get into school without it. That helps a lot, because parents would come in to get the vaccine, and the nurses at school would remind them.

Another physician believed that the vaccine should be administered at school for easier follow-up:

If it were offered in school, it would be a lot easier because they don't have to miss a day, or the parent doesn't have to remember to take off from work, or whatever to come back for the other vaccines.

Another possible solution proposed was an automatic letter sent to the patient as a reminder to come in for the follow-up doses of the vaccine. Two physicians specifically reported that in their clinics, this was not done. One speculated on a solution for his own clinic:

The other thing would be, I don't know, maybe for a system to remind them in six months to come back to get their third vaccine. I don't know if we should send out a letter or an automatic notification. The ideal thing is that the doctor will send out a letter saying, “You are missing the third vaccine, come back to get it done.”

A final recommendation was made regarding the current ACIP-recommended vaccination schedule of three doses, given within 6 months. One physician stated that the three dose schedule is difficult to keep in young, healthy adolescents who only rarely see their physicians. Therefore, he recommended that more research be done to determine if

one vaccine is effective enough, or if the vaccine can be given yearly with the same efficacy to make administration easier:

I know it's now being looked at to see if one shot actually might actually be enough... the studies done to determine whether it is effective is only based on a specific schedule that they decided to try. Other dosing schedules could make some scientific sense.

Quantitative Analysis: Pre/Post-Surveys

General Information

Adolescent respondents were drawn from community organizations in the city of Hartford: Community Partners of Hartford, YWCA, Voices of Women of Color, and the DHHS' Hartford Teen Pregnancy Prevention Initiative.

Table 1—Participants by Session

Session Number	Pre-Presentation Surveys # (%)	Post-Presentation Surveys # (%)
1	8 (10.7)	8 (11.4)
2	8 (10.7)	8 (11.4)
3	10 (13.3)	13 (18.6)
4	32 (42.7)	25 (35.7)
5	6 (8.0)	8 (11.4)
6	11 (14.7)	8 (11.4)
Total Sample	75	70

Vaccination Intent

The dependent variable in the initial research model, the intent to be vaccinated among Hartford adolescents, was assessed with a close-ended survey question, “*Do you plan on being vaccinated in the next year?*” At baseline, prior to the presentation, 58 out

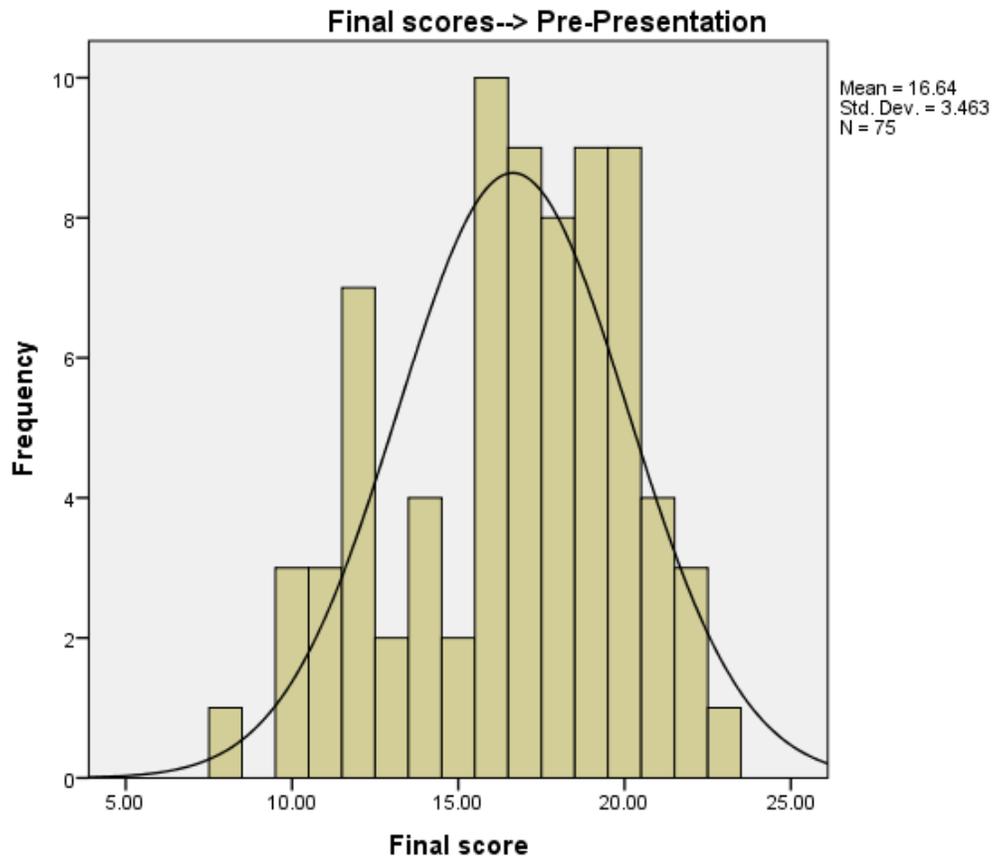
of 75 adolescents (63.8%) answered in the affirmative. No statistically significant association was found between time of administration of the survey (pre-presentation versus post-presentation) and vaccination intent, suggesting that the presentation had no effect on intent.

HPV and HPV vaccine knowledge

As hypothesized, a majority of adolescents, 73.3% (55) of participants, had heard of HPV prior to administration of the survey. There was a statistically significant difference from pre-presentation to post-presentation ($p=0.010$), understandably so, as this topic was the focus of the didactic presentation.

Answers to the survey questions specifically designed to assess knowledge were coded as “1” for correct and “0” for incorrect and then added up to create a final score to quantify knowledge. The maximum score an individual could receive was 26. Prior to the presentation, at baseline, scores ranged from 8 to 23, with a mean of 16.6 and a standard deviation of 3.46. Distribution of scores can be seen in the histogram below:

Figure 2—Distribution of Knowledge Scores among Pre-Presentation Survey Responses

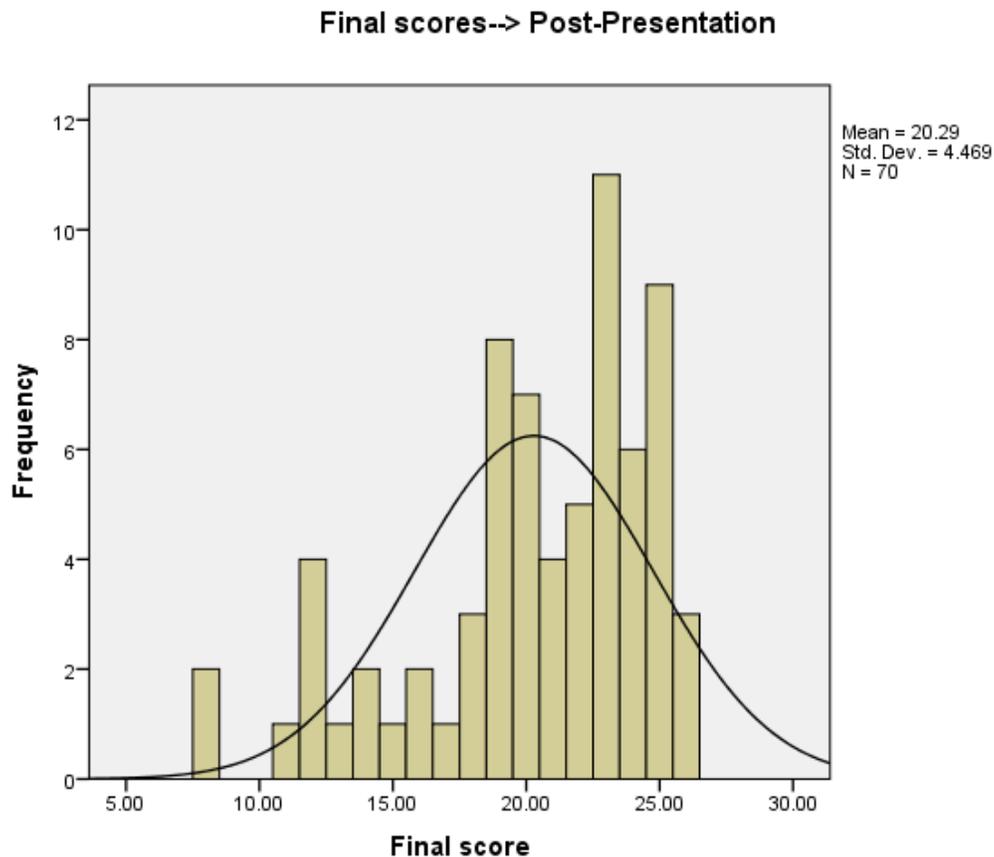


A logistic regression was conducted to determine if knowledge, as quantified by this final score, affected the dependent variable, or the intent to be vaccinated. It had been hypothesized that the most significant influence on intent would be adolescent knowledge. While the direction of change was consistent with the hypothesis, the association was not statistically significant either before or after the presentation.

There was a statistically significant difference in mean performance between the pre-presentation and post-presentation responses ($p = <0.001$), providing evidence that the presentation was at least effective in increasing knowledge in the short term. Post-

presentation, scores ranged from 8 to 26, with a mean of 20.3 and a standard deviation of 4.47. Distribution of scores can be seen in the histogram below:

Figure 3—Distribution of Knowledge Scores among Post-Presentation Survey Responses



Correct response rates to specific survey questions illustrate the improvement in knowledge from before to after the presentation. Participants were first asked “*What do you think HPV is?*” and given five possible answer choices: (1) A common cold (2) A skin rash (3) A sexually transmitted disease (4) An infection patients get from hospitals, and (5) I don’t know what HPV is. Out of 74 pre-presentation responses, 77.0% answered with the correct choice of “*A sexually transmitted disease.*” There was a statistically significant difference between pre-presentation and post-presentation responses

($p=0.018$), with the percentage answering correctly increasing to 91.4%. A similar question inquired, “*What is the most common STD?*” The frequency of each possible response to this question by pre-presentation and post-presentation responses, are provided in the table below:

Table 2—Most Common STD

Question	Pre-Presentation % (#)	Post-Presentation % (#)	P value
Most common STD			
- <i>HPV</i>	17.8 (13)	50.0 (34)	<0.001
- <i>Chlamydia</i>	34.2 (25)	5.9 (4)	<0.001
- <i>Gonorrhea</i>	5.5 (4)	33.8 (23)	<0.001
- <i>Herpes</i>	13.7 (10)	2.9 (2)	0.022
- <i>HIV</i>	28.8 (21)	7.4 (5)	0.001
Total Responses (#)	73	68	

As predicted, there was a statistically significant increase in the correct response, HPV, after the presentation. There was a significant decrease in all incorrect responses, except for gonorrhea. For unknown reasons, more individuals selected this incorrect choice after the presentation than before.

The next question was a multiple-choice question that asked respondents to select conditions caused by HPV infection. Answer choices included correct selections such as cancers of the reproductive system for women and genital warts, as well as incorrect choices such as AIDS and breast cancer. The frequency of each possible response to this question was sorted by pre-presentation and post-presentation responses, provided in Table 3:

Table 3—Sequelae of HPV Infection

Question	Pre-Presentation % (#)	Post-Presentation % (#)	P value
What can HPV lead to			
- <i>Cancers of the reproductive system for women</i>	56.8 (42)	85.7 (60)	<0.001
- <i>Cancers of the reproductive system for men</i>	41.9 (31)	57.1 (40)	0.067
- <i>Mouth/throat cancer</i>	24.3 (18)	48.6 (34)	0.002
- <i>AIDS</i>	29.7 (22)	14.3 (10)	0.026
- <i>Genital warts</i>	35.1 (26)	71.4 (50)	<0.001
- <i>Breast Cancer</i>	9.5 (7)	5.7 (4)	0.398
Total Responses (#)	74	70	

There was a statistically significant increase in the correct responses from pre- to post-presentation of “*Cancers of the reproductive system for women,*” “*Mouth/throat cancer,*” and “*Genital warts.*” Although there was a slight increase in the response rate for the correct answer of “*Cancers of the reproductive system for men,*” from 41.9% to 57.1%, it was not significant at the 0.05 level. In future educational interventions, then, a greater emphasis is needed on the sequelae of HPV infection in men. There was also a statistically significant decrease in the incorrect answer choice of “*AIDS*” and though the response rate for “*Breast cancer*” slightly decreased as well, it was not significant.

The concept that both genders can be affected by HPV and can receive the HPV vaccine was also tested. Prior to the presentation, 86.7% of adolescents answered correctly that HPV can affect both females and males, which increased to 100% after the survey (p=0.002). Though an increase was also seen in the percentage that correctly

answered that both males and females can receive the vaccine (87.8% to 94.3%), it was not a statistically significant change.

Two survey questions assessed knowledge regarding the dosing schedule for the HPV vaccine. Pre-presentation, 46.5% correctly stated that 3 doses are required to complete the vaccine series. There was a statistically significant improvement from pre-presentation to post-presentation ($p = <0.001$), with 80% delivering the correct response afterwards. The second question asked respondents to fill in the age at which HPV vaccination can start. The mean shifted from 13.8 pre-presentation, to 11.0 post-presentation, into the correct range of 9-13.

Misconceptions

Many of the questions used to determine the final knowledge score served another purpose: revealing the presence of common misconceptions regarding HPV and the HPV vaccine through true or false questions. The prevalence of misconceptions both before and after the didactic presentation was high. The frequency of the correct response to each of these questions by pre-presentation and post-presentation responses is provided in the table below.

Table 4—Misconceptions Surrounding HPV and the HPV Vaccine

Question	Pre-Presentation % (# Correct /Total Responses)	Post-Presentation % (# Correct /Total Responses)	P value
Men can get HPV from homosexual or heterosexual sex	83.6 (61/73)	89.7 (61/68)	0.286
HPV is preventable	87.5 (63/72)	87.1 (61/70)	0.949

The HPV vaccine can prevent genital warts	32.9 (24/73)	63.2 (43/68)	<0.001
The HPV vaccine can prevent cervical cancer	47.9 (35/73)	80.3 (53/66)	<0.001
You would always know if you had an HPV infection	86.7 (65/75)	84.2 (59/70)	0.684
You can get HPV by not keeping yourself clean	50.7 (37/73)	44.3 (31/70)	0.444
Antibiotics can cure HPV	50.7 (34/67)	75.0 (51/68)	0.004
If you wait to have sex until after marriage, you cannot get HPV	86.7 (65/75)	87.1 (61/70)	0.932
The HPV vaccine is only for adults	89.2 (66/74)	90.0 (63/70)	0.874
Only sexually active people should get the vaccine	78.4 (58/74)	88.4 (61/69)	0.109
If you get the HPV vaccine, you don't need to use condoms because you're protected from STDs	86.5 (64/74)	85.3 (58/68)	0.838
If a teenage gets the HPV vaccine, he or she will be more likely to have sex	75.0 (54/72)	66.2 (43/65)	0.255

It was hypothesized that adolescents would demonstrate a higher rate of misconceptions regarding HPV and its vaccine prior to implementation of the educational intervention than afterwards. With the exception of the statistically significant improvements seen in the correct response rates to *“The HPV vaccine can prevent genital*

warts,” “*The HPV vaccine can prevent cervical cancer,*” and “*Antibiotics can cure HPV,*” this hypothesis was not supported. After the presentation, 63.2% of adolescents correctly answered that the HPV vaccine can prevent genital warts, compared to 32.9% beforehand. The percentage that correctly answered that the HPV vaccine can prevent cervical cancer also increased from 47.9% to 80.3%. Finally, three-quarters of adolescents correctly responded that antibiotics cannot cure HPV post-presentation, compared to 50.7% of adolescents pre-presentation.

The percentage of adolescents responding correctly to the other questions either remained static or trended downwards. For some of these questions, it is likely that the high pre-presentation correct response rate led to a lack of significant improvement; for example, 86.7% and 87.1% of adolescents responded correctly to the statement “*If you wait to have sex until after marriage, you cannot get HPV,*” and 83.6% and 89.7% of adolescents correctly answered that men can get HPV from homosexual or heterosexual sex, pre-presentation and post-presentation respectively. However, a significant percentage of adolescents continued to endorse common misconceptions post-presentation—55.7% continued to believe that one can acquire HPV with poor hygiene, 33.8% believed that the HPV vaccine promotes promiscuity, and 14.7% believed that one does not need to use condoms for protection against sexually transmitted diseases after HPV vaccination. It is not understood whether this was due to question wording or a deficiency in the presentation itself. These are the key areas that should be targeted for increased education.

Attitudes and Beliefs

It was hypothesized that adolescent attitudes and beliefs, along with knowledge, would positively influence the intent to be vaccinated. Specifically, it was believed that adolescents who believe HPV infection is serious would be more likely to desire vaccination, as would adolescents who believe the HPV vaccine is effective in preventing infection. Two questions in the survey instrument addressed this hypothesis. These were true or false questions, with the statements “*HPV infection is serious*” and “*The HPV vaccine is effective in preventing HPV infection.*” At baseline, prior to the presentation, 94.7% agreed that HPV infection is serious. There was no significant change in this percentage from pre-presentation to post-presentation. Out of 71 pre-presentation responses, 80.3% believed that the HPV vaccine is effective in preventing HPV infection. The change from pre-presentation to post-presentation indicated an upward trend to 91.0% ($p=0.073$).

Statistically significant associations were not found between belief that HPV infection is serious and vaccination intent, or belief in the efficacy of the HPV vaccine and vaccination intent, either before or after the presentation. However, logistic regressions were conducted to determine if knowledge, as quantified by this final score, affected these beliefs. At baseline, prior to the presentation, for every one unit change in the final knowledge score, the log odds of believing the HPV vaccine is effective significantly increased by 0.387 ($p=0.001$). While the direction of change was consistent, increased knowledge was not significantly associated with the belief that HPV infection is serious. After the presentation, for every one unit change in the final knowledge score, the log odds of believing the HPV vaccine is effective significantly increased by 0.437

($p=0.003$), while the log odds of believing HPV infection is serious significantly increased by 1.099 ($p=0.032$).

Barriers and Facilitators

Two survey questions attempted to gain a better understanding of barriers to and facilitators of vaccination. The first question asked respondents to identify why a teenager would decide to get vaccinated, assessing potential facilitators. The second asked respondents to identify reasons a teenager would decide *not* to be vaccinated, assessing potential barriers. For both of these questions, respondents were encouraged to circle all choices that applied. It was hypothesized that belief in the efficacy of the HPV vaccine would be identified as the major facilitator for vaccination, while fear of side effects would be cited as the major barrier. The frequency of each possible response to these questions by pre-presentation and post-presentation responses is provided in Tables 5 and 6:

Table 5—Facilitators of HPV Vaccination

Question	Pre-Presentation % (#)	Post-Presentation % (#)	P value
What are some reasons a teenager would decide to get vaccinated?			
- <i>His/her parents told him/her to</i>	61.3 (46)	65.7 (46)	0.584
- <i>His/her doctor told him/her to</i>	64.0 (48)	62.9 (44)	0.886
- <i>To prevent HPV infection</i>	70.7 (53)	67.1 (47)	0.647
- <i>To prevent cervical cancer</i>	50.7 (38)	58.6 (41)	0.340

- <i>Because his/her friends all received the vaccine</i>	32.0 (24)	34.3 (24)	0.770
Total Responses (#)	75	70	

Table 6—Barriers to HPV Vaccination

Question	Pre-Presentation % (#)	Post-Presentation % (#)	P value
What are some reasons a teenager would decide NOT to get vaccinated?			
- <i>Not knowing where to get the vaccine</i>	53.3 (40)	58.6 (41)	0.526
- <i>Thinking the vaccine is not necessary</i>	57.3 (43)	61.4 (43)	0.616
- <i>Thinking the vaccine is unsafe</i>	37.3 (28)	42.9 (30)	0.497
- <i>Fear that the vaccine will cause pain</i>	49.3 (37)	58.6 (41)	0.265
- <i>Cost of the vaccine</i>	50.7 (38)	60.0 (42)	0.259
- <i>His/her parents did not tell him/her to</i>	44.0 (33)	48.6 (34)	0.581
- <i>His/her parents did not want him/her to</i>	33.3 (25)	37.1 (26)	0.631
Total Responses (#)	75	70	

As can be seen from Table 5, the most common response to why an adolescent would receive the HPV vaccine was “*To prevent HPV infection,*” both before and after the presentation (70.7% and 67.1%, respectively). The least common reason cited was “*Because his/her friends all received the vaccine*” (32.0% pre-presentation and 34.3% post-presentation). There were no significant changes seen in response rates from before

to after the presentation. The most common barrier cited was “*Thinking the vaccine is not necessary*” (57.3% pre-presentation and 61.4% post-presentation), followed closely by “*Not knowing where to get the vaccine*” (53.3% and 58.6%) and “*Cost of the vaccine*” (50.7% and 60.0%). Though it was hypothesized that fear of adverse reactions would be cited as the major barrier, adolescents did not choose “*Fear that the vaccine will cause pain*” and “*Thinking the vaccine is unsafe*” so often. Again, there were no significant changes seen between pre-presentation and post-presentation responses.

For these two questions, a blank space was also provided to allow for fill-in answers. Written responses given for “*What are some reasons a teenager would decide to get vaccinated?*” were: “Incentives at PCP office and at school by nurse,” “Be safe,” and “Want to be safe.” Fill-in responses provided for “*What are some reasons a teenager would decide NOT to get vaccinated*” were: “Not aware of the vaccine,” “Don’t know about HPV,” “Not sure what it is,” “Danger,” “Against religious beliefs,” and “Scared.”

One of the independent variables in the initial research model was parental attitudes. It was hypothesized that adolescents with parents and guardians with more negative attitudes regarding the vaccine would be less likely to want the vaccine. However, there was no significant association found between citing parental encouragement to receive the vaccine, a lack of parental encouragement, or parental refusal and vaccination intent. Another independent variable in the research model was physicians’ advice. It was hypothesized that a physician recommendation to be immunized for HPV would positively influence adolescent decision making. However, once again, there was no significant association between citing physician recommendation as a facilitator and vaccination intent.

Qualitative Analysis: Focus Group Discussions

Five major codes were identified for qualitative analysis of the focus group discussions including: knowledge; misconceptions; barriers; facilitators, and presentation improvements.

Knowledge

The majority of adolescents had heard about HPV previously from a variety of sources. The most common response to, “Where have you heard about HPV before today?” was school (for example as one participant stated, “*My high school gave us some information about it*”), followed by the doctor’s office (“*My doctor told me about it, and there were brochures in the doctor’s office*”). Other sources included their parents and the media (“*I heard about it while watching TV*”). However, two adolescents did express uncertainty about where to receive information about HPV. As one individual from Focus Group #4 responded, “*How are you supposed to find out about it?*”

Although the majority of adolescents answered positively when asked if they had heard of HPV and the vaccine, a major recurring theme throughout discussions was an unawareness of cervical cancer and the existence of the Papanicolaou test, more commonly known as the Pap smear, as a preventive measure. Five out of the six focus groups had questions regarding these topics. For example, an adolescent from Focus Group #1 inquired, “*What is cervical cancer?*” and another from Focus Group #4 asked, “*I had a question, what’s a Pap smear?*” Both “Pap smear” and “cervical cancer” were used in the didactic presentation without much explanation, assuming that participants had prior knowledge.

Misconceptions

Questions asked by participants during the course of each focus group discussion demonstrated a wide variety of misconceptions. Focus group discussions were held following administration of the didactic presentation, meaning that these erroneous beliefs remained despite the attempted educational intervention. A major recurring theme focused on the false notion that only sexually active individuals can receive the vaccine. When asked, “Why do you think the majority of youth have not been vaccinated?” an adolescent from Focus Group #1 responded, “*Because they are not sexually active,*” while another from Focus Group #4 stated, “*They are not having sex.*”

Other questions focused on the method of transmission of HPV, providing ideas for additional details to add to the didactic presentation. Questions asked include:

“It says you can get it from skin to skin contact, so what if I touch someone on their hair or back or put lotion on them?”

“Here's a question- can you get it from smoking?”

“If a guy has it on the lips and the girl kisses him, will the girl get it?”

“Is it something that can run in your family?”

Finally, when asked, “Do you have any other questions about HPV that we didn't answer in the presentation?” a few adolescents asked questions indicating some underlying confusion about the differences between HPV and herpes simplex virus (HSV), and HPV and human immunodeficiency virus (HIV). One adolescent from Focus Group #6 asked about disclosing a positive HPV status to a partner: “*Is it illegal to have sex with someone if you have HPV and you know that, but you don't tell the other person?*” Another adolescent asked about the presence of “sores” with HPV infection,

while a third inquired, *“If you have HPV, don’t you have to take lots of medication all the time?”*

Barriers

The adolescents were posed this question: “Only 40% of eligible youth have received the HPV vaccine. Why do you think the majority of youth have not been vaccinated?” In response, participants mentioned a variety of potential reasons. One recurring theme was the fear of adverse reactions. The majority cited this barrier as the reason for the low uptake rate, as well as the low series completion rate, in Connecticut.

Responses by adolescents included:

“Maybe because they don't like needles; I am scared of needles.”

“Because they may be scared of what the results are going to be, or something from it. They might find out something that they don't want to find out. Like side effects from the vaccine.”

“It probably hurts so they don't want it.”

Another recurring theme was a lack of education, and therefore, knowledge. As one adolescent succinctly stated, *“People don’t know about the complications from the virus, so they don’t think it’s [the vaccine] important.”* Another responded *“There is a lack of information about the virus.”*

When asked what information they learned from the presentation that they didn’t know before, adolescents mentioned a variety of key facts related to infection and the vaccine:

“I didn’t know HPV could cause cancer.”

“I learned that HPV could actually be really bad.”

“I didn’t know that HPV can have no symptoms.”

“I didn’t know it was a common sexually transmitted infection.”

“I learned that men can get HPV as well.”

A lack of knowledge among parents was mentioned as a barrier as well. As one adolescent in Focus Group #1 stated, *“Parents are not talking about it. Some parents don't like to talk to their child openly about sex. Parents think that you only need the vaccine if you are having sex.”*

Barriers to series completion were also covered. Adolescents were asked, *“Among girls who receive the first dose, many do not return for the two follow up doses – why do you think this is?”* The majority of responses addressed the notion that only one dose of the vaccine is needed:

“They think that one vaccination is enough for them.”

“Maybe because they got one, they think they're OK.”

“They might think that it's already done and they don't need any more shots.”

“Many people think they are all set, or cured, after the first dose.”

One adolescent expressed confusion over the three-shot dosing schedule, inquiring, *“Why can't you just combine all three shots into one big needle? Why do you need three shots?”* On the other hand, a number of participants mentioned that a reminder from a physician would be helpful in increasing the series completion rate:

“If someone is in a transition period, like moving, they may not have a PCP to remind them to get all the vaccine doses.”

“People are lazy and forget to go back for the second and third time.”

A major recurring theme throughout the discussion of barriers focused on vaccination in males. Participants were asked why they thought the rate of vaccine uptake

is so low for boys, especially when compared with the rate among girls. One adolescent in Focus Group #6 mentioned the lack of vaccine promotion for males:

“When I was at the doctor the vaccine was described to me as a way to protect my partner, so it made it seem like this whole HPV vaccine is geared towards girls and not really for guys. The guys are just helping, so they don’t feel like they really need it for themselves.”

Another individual from Focus Group #1 expressed a similar sentiment, stating,

“Because they [boys] really don’t know about it, and haven’t heard of HPV,” while a female from Focus Group #4 mentioned, *“They [boys] don’t think they have a high risk of getting it [HPV].”* Additionally, many adolescents believed that males simply see their physicians less often, making statements such as *“Girls go to the doctor more often,”* *“Guys are embarrassed to go to the doctor,”* and *“There are no ‘annuals’ for guys.”*

Other gender stereotypes and misconceptions also came into play. For example, a female from Focus Group #4 stated, *“Because they don’t have a vagina and we do,”* mistakenly alluding to the view that males cannot get HPV.

Two adolescents brought up the fact that there is currently no school mandate in place. The HPV vaccine is not a mandatory prerequisite for entrance into school, as many other vaccines are. As one stated, *“It [the HPV vaccine] is not required, so when it’s an option, people don’t do it.”* The relatively high cost of the vaccine was also mentioned twice, both during Focus Group #4:

“Some people, they don’t have insurance, and they don’t have enough money to get tested.”

“Isn’t it sometimes because of the money? They might have to pay every single time that they come in for it with three doses.”

Finally, believing that the vaccine is not necessary and not caring also were mentioned as obstacles.

Facilitators

Many of the expressed barriers to vaccination were also brought up in the discussion of facilitators. When asked what they thought would motivate children and adolescents to get vaccinated, participants provided a variety of responses that reflected what they felt would be their main barrier(s) to vaccination. Many adolescents expressed concern over the cost of the vaccine. Therefore, it was mentioned multiple times that the availability of a free vaccine would be a motivator in accepting the vaccine. One adolescent inquired, *“If I don’t have insurance, can I get it here [school] for free?”* A school administrator who participated in Focus Group #5 contributed to this topic:

“If there was no cost to the vaccine, people would be motivated to get it. My deductible will end up having me pay a lot of money for the vaccine, so if it were me, I would have declined getting it before seeing this presentation and knowing all the information.”

A few adolescents also mentioned that they would be more likely to get the vaccine if it was required for school entry. As one stated, *“If it was required, it would be urgent to people, it’s just a suggestion.”*

A major recurring theme focused on education, particularly a need to better educate adolescents about HPV and the availability of the vaccine. A few adolescents mentioned that they were more receptive to receiving the vaccine after the presentation, as they understood its importance. One adolescent from Focus Group #6 emphasized, *“Knowing the seriousness of the virus would motivate people to get vaccinated.”* Other adolescents stated that they were unaware that the vaccine was an option, with a couple

specifically mentioning that their physicians had never spoken to them about it. One adolescent stated, *“Sometimes, like, when they want to have sex, they might not know about this [the vaccine], so people should be educated about it a little better.”* Finally, knowing about the availability of the vaccine itself was cited as a facilitator. *“Knowing that they can get it anytime”* was one response when Focus Group #1 was asked about motivating factors.

Presentation Improvements

Generally, adolescents were extremely receptive to the didactic presentation. When asked what they thought about the presentation, the majority of adolescents responded with statements such as, *“Great,” “Very helpful,”* and *“We liked it.”* Every focus group discussion lasted at least 30 minutes, as participants were eager to provide suggestions and clarify lingering questions regarding HPV and the vaccine.

When asked how to improve the presentation, many helpful suggestions were provided. A majority of the participants communicated that more graphic visuals were needed to effectively reach adolescents. As one adolescent from Focus Group #4 stated, *“If you don’t have a visual of what it [HPV infection] looks like, then how are we going to know?”* Another adolescent from Focus Group #1 expressed a similar sentiment, stating, *“Yes, we like the pictures, and we would like more graphic ones.”* Along the same lines, other participants suggested bringing in tangible items that they could interact with, such as the needles used to administer the vaccine or the instruments used to perform a Pap smear. One adolescent stated *“Bring us some of the stuff. Like bring us some of the medicines and tools so that we can actually see what it’s like. To see how it actually looks in real life.”*

Another recommended improvement was placing a greater emphasis on the seriousness of HPV infection. Many questions were asked during the course of the discussions about vaccine side effects, efficacy, dosing schedule, and HPV genotypes, topics that were covered by the preceding presentation. For example, an adolescent from Focus Group #4 inquired, “*There’s different types of HPV?*” This suggests that greater emphasis, or more time, is needed on these particular topics in future educational interventions.

Chapter 5: Discussion and Conclusion

Key Results

This thesis sought to shed light on the knowledge and attitudes concerning HPV and the HPV vaccine, as well as the role of education in shaping knowledge, perceptions, and participation in vaccination, in the Hartford, CT adolescent population. The initial research model identified three factors hypothesized to influence the intent to be vaccinated among adolescents: HPV and HPV vaccine knowledge, physicians' advice, and parental attitudes. Several conclusions can be drawn from the qualitative and quantitative data generated in the course of this study.

Knowledge and Misconceptions

The majority of adolescents had heard of HPV prior to study participation. School, physicians' offices, the media, and parents were listed as sources of information during the focus group discussions. However, there were significant gaps in understanding of the nature and consequences of HPV infection, as well as availability of the HPV vaccine. For example, prior to the didactic presentation, 33% of participants were unaware that HPV is a sexually transmitted disease, while approximately half did not know that the HPV vaccine is administered in a 3-dose series. During the focus group sessions, when asked what information they learned from the presentation that they did not know beforehand, adolescents mentioned a variety of key facts related to infection and the vaccine, such as *"I didn't know HPV could cause cancer," "I didn't know that HPV can have no symptoms,"* and *"I learned that men can get HPV as well."* Questions were also posed that indicated confusion about the modes of transmission, methods of prevention, and the prevalence of HPV infections.

Certain misconceptions were particularly common, including the view that one can acquire HPV with poor hygiene, HPV can cause AIDS, antibiotics can cure HPV, and one does not need to use condoms for protection against sexually transmitted diseases after HPV vaccination.

The association of HPV with adolescent sexuality resulted in misapprehensions concerning the vaccine. A recurrent theme through both survey and focus group data was the idea that only sexually active individuals should receive the HPV vaccine. Prior to the presentation, more than one-fifth of participants endorsed this belief, while responses during the focus group sessions reinforced the pervasiveness of this idea. A quarter of adolescents also endorsed the idea that the HPV vaccine promotes promiscuity in the pre-presentation survey. All six physicians interviewed reported cases of parental refusal of the vaccine because their children were not sexually active. Physicians also reported deflecting parental concerns that vaccinating against HPV may increase sexual activity or lower the age of the initiation of sexual activity.

The literature review demonstrated a dearth of research on male vaccination. The media and even the medical community have often referred to HPV vaccine as the “Cervical Cancer Vaccine,” downplaying the additional protection afforded for men. This gap was reflected in this study by a lack of knowledge among participants concerning HPV in men. Prior to the presentation, 58% of adolescents did not believe that HPV can lead to cancers of the reproductive system in men, while 13% did not know that both males and females can get HPV or that both can receive the vaccine. Close to one-fifth of all adolescents surveyed were not aware that men can get HPV from homosexual or heterosexual sex before the presentation. During the focus group discussions, adolescents

reported that there was a lack of emphasis on male vaccination, from their parents, physicians, and the media. This view was supported by the physician interviews, in which physicians noted difficulties in recommending the vaccine for boys, citing the female-oriented advertising of the vaccine, the rarity of sequelae in men, and the association of infection with homosexual sex as barriers. Those who were successful in getting male patients to accept the vaccine focused discussions with patients on its efficacy against penile cancer and genital warts, as well as the benefits for female partners.

A major goal of this study was to understand how knowledge influences attitudes regarding HPV and the HPV vaccine. Prior to the presentation, HPV knowledge and belief in the effectiveness of the HPV vaccine was found to be significantly associated. Post-presentation, significant associations were found between knowledge and belief in both the effectiveness of the vaccine and the seriousness of HPV infection. These associations were supported by discussions during the focus groups, in which adolescents felt that many of their peers had not received the vaccine because they were not aware of the virus's consequences, and therefore did not believe the vaccine was important. Qualitative data from the physician interviews also reinforced this idea. One physician stressed that not knowing that HPV can cause cancer was causing his patients to underestimate the importance of the vaccine. These attitudes highlight the need to educate parents and adolescents about the importance of HPV vaccine.

Barriers and Facilitators of Vaccination

Several barriers to vaccination were identified. Most had been observed in previous studies, but not specifically in the Hartford, Connecticut adolescent population. While fear of adverse reactions was postulated to be the major barrier to vaccination

intent, quantitative data did not support this hypothesis. Post-presentation, adolescents cited believing the vaccine is unsafe (43%) and that the vaccine will cause pain (59%) as barriers to vaccination.

A majority of adolescents cited cost as a barrier, as well as the belief that the vaccine is not necessary. Many adolescents noted that the availability of a free vaccine would be a motivator in accepting the vaccine, even though the majority of physicians agreed that cost was not an issue among their patients. All doctors mentioned that very few of their patients were uninsured, likely due to the availability of Husky Health insurance in the state of Connecticut. Additionally, the Vaccines for Children (VFC) Program covers the cost of the HPV vaccine for the uninsured, making the high cost of the vaccine a non-issue among Hartford teens.

Focus group discussion responses supported the idea that fear of adverse reactions was a major reason why many adolescents avoid vaccination. Adolescents responded that they were “scared of needles,” stating that the vaccine “probably hurts.” This view was echoed in physicians’ responses in which a fear of side effects, reinforced by anti-vaccine media coverage, was cited as a major barrier to vaccination among their patients. One physician even reported that she herself believed in the reports of neurological side effects associated with the vaccine, stating that she could not full endorse it to her patients.

Much of the controversy related to the initial rollout of the HPV vaccine centered on the idea of mandatory vaccination. However, in this study, both adolescents and physicians mentioned that the lack of a school entrance mandate made it easier for

parents and children to refuse or avoid the vaccine, with two physicians suggesting the need for a school mandate to increase vaccination rates in Hartford.

The three-dose regimen was also blamed numerous times for the low vaccination uptake. During the focus group discussions, many adolescents stated that they believed their peers were not completing the series because they believed one dose was adequate. It was mentioned that a physician reminder to come back for the other two doses would be helpful, an idea that physicians also seemed to support. One physician specifically recommended that more research be done to determine if one dose of the vaccine would be sufficient, or if the vaccine could be given annually, during routine well-child visits, with the same efficacy to make administration easier.

A major goal of this study was to understand the effects of parental attitudes and physicians' advice on vaccination intent. Previous studies have identified the importance of provider recommendation and parental support to vaccination initiation.⁸⁵ This study found no significant association between citing parental encouragement to receive the vaccine, a lack of parental encouragement, or parental refusal, or citing physician recommendation to receive the vaccine, and vaccination intent. Regardless, the surveys and focus group discussions did provide some evidence that provider and parental attitudes are important for vaccine uptake. Prior to the presentation, 61% of adolescent participants cited parental encouragement as a reason to get vaccinated, while 44% cited a lack of parental encouragement and parental refusal (33%) as barriers to vaccination. During the focus groups, some adolescents mentioned that their parents refused to talk about the vaccine, due to its link to sexual activity. Prior to the presentation, 64% of adolescents also stated that they believed physician recommendation would encourage a

teenager to get vaccinated. Discussions during focus group sessions and physician interviews supported the importance of physician advice. Adolescents discussed the fact that they would particularly rely on physicians for introduction to the vaccine, series completion, and vaccine promotion for males. Most physicians interviewed said that if offered the vaccine during a visit, the majority of patients accept. They suggested that offering the vaccine as part of routine health maintenance would increase vaccination rates. One physician interviewed mentioned concerns that the vaccine has not been proven to be effective against cervical cancer or genital warts, and only offers it because it is recommended. Additionally, she stated that she does not try to change a patient's mind if the vaccine is refused. This physician reported that only one-third of her patients have received the HPV vaccine, providing some evidence that provider attitudes are important for vaccine uptake.

Intent

Before the presentation, approximately 64% of adolescents responded that they intended to receive the HPV vaccine in the next year. Given that prior evidence has shown that knowledge and attitudes regarding HPV and its vaccine greatly impact vaccination rates, this project aimed to educate participants through a didactic presentation. However, there was no statistically significant association found between intent to get vaccinated on the post-presentation survey as compared to the pre-presentation survey, suggesting that the presentation had no effect on intent. Additionally, no statistically significant association was found between knowledge and intent, though the direction of change was in the direction expected. Belief that HPV infection is serious

and belief in the efficacy of the HPV vaccine were also not found to be associated with intent.

Impact of the Educational Intervention

A major recurring theme during focus groups and physician interviews was the importance of education, particularly the need to better educate adolescents about HPV and the availability of the vaccine. A few adolescents mentioned that they were more receptive to receiving the vaccine after the presentation, as they understood its importance. Additionally, there was a significant increase in mean knowledge from the pre-presentation to the post-presentation survey responses, providing evidence that the presentation was effective in increasing knowledge. Physicians also expressed their belief in the importance of an education program for their patients to increase knowledge of HPV and its vaccine, emphasizing that it should ideally target both teens and parents.

Areas for improvement were identified through the focus group discussions. Questions asked by participants during each discussion session continued to demonstrate a wide variety of misconceptions, meaning that many erroneous beliefs remained despite the attempted educational intervention. Although topics such as the modes of transmission, methods of prevention, and the prevalence of HPV infections were addressed in the presentation, adolescents were left with many questions regarding these issues. There was particular confusion about the differences between HPV, HSV, and HIV. Finally, some adolescents seemed to be unaware of the Pap smear as a preventive measure against cervical cancer, suggesting the need for more extensive explanations on these topics in future interventions.

Generally, adolescents were extremely receptive to the didactic presentation and participated enthusiastically in the post-presentation focus group sessions. Suggestions for improvement focused on the need for more graphic visuals and items for participants to look at, such as the needles used to administer the vaccine or the instruments used to perform a Pap smear. Many adolescents wanted a greater emphasis on the seriousness of HPV infection as encouragement to get the vaccine.

Limitations of Current Study

A major limitation surrounded the narrow scope of adolescents sampled. All of the adolescents recruited for this study were involved with community groups focusing on service, leadership, and/or education. Thus, the population sampled was a convenience sample and not necessarily representative of the overall adolescent population in Hartford. Adolescents enrolled in community programs are likely to have greater access to health information compared to those who are not. Those less educated or less likely to utilize the health care system may not have been included in the sample. This factor could affect the generalizability of the results.

Additionally, due to the exemption status received through the University of Connecticut Health Center Institutional Review Board, no identifying or personal information were gathered from study participants. Therefore, factors that have been shown to affect HPV vaccination rates in other populations, such as race/ethnicity, gender, and socioeconomic status, were not accounted for in the implementation of the study. Information on current vaccination status was not collected: it may have been the case that adolescents who already been immunized had different attitudes and perceptions from those who had not had the immunization. The survey question regarding the main

outcome measure of vaccination intent assumed that adolescents had not already received the vaccine, and therefore was not worded well for those who had already been vaccinated at the time of survey administration. Thus, analyses using this measure for this population may not have been reliable. Future research should address this issue by comparing the opinions of those vaccinated with the unvaccinated.

Other limitations involved the pre- and post-presentation surveys. All information gathered in the survey was self-reported. Health behaviors that are self-reported can be biased, which can affect validity. Additionally, knowledge was mostly assessed using closed-ended questions. A recent systematic review indicated that HPV knowledge can be best measured with open-ended questions as close-ended questions lead to guessing.¹⁰⁹ Future studies should use open-ended questions, to see if similar results are found. A major limitation involved the short follow-up time between the presentation and the post-presentation survey. The intervention did have a positive effect on knowledge, but it is possible that this improvement could have dissipated over time. The post-presentation survey was consistently administered within ten to fifteen minutes of the conclusion of the presentation. Additionally, no immediate impact was seen with intent, but perhaps there was a long-term effect that could not be assessed with the short-term nature of this study.

The final sample involved multiple incomplete surveys, and while there were 75 pre-presentation surveys collected, only 70 post-presentation surveys were returned. It is not understood whether this was because of a lack of interest in the topic, the length of the survey, the fact that the survey had to be taken twice, or other demotivating factors. Missing answers to all questions counted towards the final knowledge score were counted

as incorrect answers, as it could not really be determined if participants did not know the answer or just skipped the question. This resulted in low statistical power, and statistically significant results related to the outcome measure of vaccination intent were not found.

This project should be viewed as a pilot study, laying the groundwork for a more systematic HPV awareness project in Hartford.

Future Directions and Possible Interventions

Using a variety of qualitative and quantitative methods, this thesis aimed to investigate the knowledge and attitudes of Hartford adolescents concerning HPV and the HPV vaccine. This study meant to highlight key areas for intervention that will increase knowledge regarding and access to the HPV vaccine, and ultimately, increase vaccination rates among Hartford's youth. Although this study looked into a large number of variables related to the main outcome measure of vaccination intent, more work is needed. First, this study should be applied to a larger and more diverse population, with participants drawn from the entirety of the Hartford community, rather than select community groups. Next, the lack of significant findings between the variables tested in this thesis and vaccination intent indicate that there is likely a complex range of variables that have both direct and indirect relationships with HPV vaccination decisions. Previous studies have demonstrated the importance of age, race/ethnicity, gender, socioeconomic factors, and education to vaccination uptake, all of which were not accounted for in this thesis' research model. Future studies should incorporate these variables. This study also investigated the impact of an educational intervention using unlinked cohort data. It would be interesting to evaluate future interventions using linked data, to assess

individual change. Finally, a comparison study of vaccinated versus non-vaccinated individuals would be beneficial to further determine the needs of future educational interventions. Improved understanding of the reasons for non-vaccination among the vaccine-naïve, as well as barriers to vaccine completion among those who have already started the series may increase the impact of future educational interventions.

Potential interventions to increase vaccine uptake among this study's population can be separated into four types, based on the level of implementation: policy, provider, family, and individual. Since the HPV vaccine first became available in 2006, an increasing number of countries have introduced it into their national programs. It has been found that countries with mandatory vaccination and school-based delivery have higher vaccine coverage than those with clinic-based, opportunistic programs, such as that that currently exists in the United States.⁵⁶ To date, in the U.S., only the District of Columbia, Virginia, and Puerto Rico have mandated vaccination. Connecticut currently covers the 3-dose vaccine series under the state's HUSKY plan for adolescents aged 11 to 18 years, but no bill concerning a HPV vaccine school mandate has been approved.⁶⁴ The idea of mandatory HPV vaccination has been a controversial one, in part due to its assumed link to sexual activity. It is hard to justify these objections from a public health standpoint. A school mandate would likely be an effective policy-level intervention to increase uptake among Hartford's youth. Requiring HPV vaccination by law (perhaps with an opt-out) would result in more widespread coverage than the current policies that rely just on education and encouragement. Qualitative data supported the idea of a mandate as a facilitator to vaccination among this study's population. Adolescents mentioned that they would be more likely to receive the vaccine if it was required for

school entry, while physicians stated that it was difficult to recommend the vaccine to patients without a school mandate. One physician suggested a school-based delivery program to improve follow-up and series completion.

In prior studies, provider recommendation has been found to be one of the strongest facilitators of vaccine uptake and conversely, a lack of provider discussion and recommendation leads to lower uptake. Qualitative data showed that adolescents seemed to particularly rely on physicians for introduction to the vaccine, series completion, and vaccine promotion for males. Most physicians interviewed said that if offered the vaccine during a visit, the majority of patients accept, emphasizing the need for the vaccine to be offered as part of routine health maintenance. According to the CDC, if all missed opportunities for vaccination were eliminated, vaccination coverage with at least one dose of the HPV vaccine for adolescents would be approximately 93%.⁷³ Therefore, an educational intervention targeting providers, perhaps through face-to-face discussions, an online program, or through printed educational materials, would likely greatly improve vaccination rates in the Hartford area. Further research is needed to assess which method would be most effective. Reminder systems or standing orders for nurses or physician assistants to vaccinate at routine appointments might also be successful.

This study attempted to intervene at the individual level, by pilot testing a didactic intervention to dispel some of the misconceptions surrounding the HPV vaccination, allowing adolescents to have the knowledge to gain control of their health and make vaccine-related decisions. The presentation was effective at increasing knowledge, but was not significantly associated with vaccination intent. Previous studies, however, have demonstrated that knowledge and attitudes regarding HPV and its vaccine do affect

vaccination rates. The current study has provided some experiences in developing appropriate future educational interventions, targeting both adolescents and their parents and guardians. Extensive efforts must be made to educate young men and women about the pervasiveness and seriousness of HPV, as well as the advantages of vaccination. There is a particular need to focus on the importance of vaccination in males given the general lack of knowledge on this topic seen in this study. Ties between the UConn Public Health Program, the Hartford Health Department, and the Hartford community were forged during this study, laying the groundwork for a future, larger HPV awareness project in Hartford.

As discussed in the introductory chapter, HPV is the most common sexually transmitted infection and is an infection with a significant public health impact. The HPV vaccine has been proven to be a highly efficacious tool for prevention, but is being underutilized, especially among Hartford's youth and other comparable populations. Progress will not be made towards easing the national and statewide HPV-related cancer and genital warts burden unless further research is conducted on uptake, attitudes, and barriers. Adolescents should be able to make vaccination decisions in a knowledgeable manner, with full support from their families, peers, and physicians.

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Appendix I: Physician Interview Protocol

Hello, we are _____, and we are working on a project with the Hartford Health Department to increase the rates of HPV vaccination in Hartford youth. As a healthcare provider in Hartford, your feedback can give us a valuable perspective of healthcare providers regarding HPV vaccination, and barriers to HPV vaccination in our target population. Your participation is voluntary and your participation will remain confidential. To facilitate transcription, your responses will be recorded and then typed into a Microsoft Word document. Your name will not be linked to the original recording, which will be deleted after transcription and your name will not be connected to the final typed notes. This interview should take about 15-20 minutes.

Thank you for your participation.

(Assessing patient panels) We believe that it's important to understand the demographics of the population that you take care of, so that we can gear our interviews based on your responses. We understand that exact percentages may be difficult to assess, but rough estimates will suffice.

1. *Do you take care of adults, pediatric patients, or both?
(If both) What percentage of your patients are adults? And what percentage of your patients are under the age of 18?*
2. *What percent of your patients are Hartford residents?*
3. *What percentage of your patients do not have health insurance?*
4. *If you had to estimate, what percentage of your patient panel are white, Black, Hispanic, or Asian?*

(Assessing physician practice) We also think it's important to understand your opinions of the HPV vaccination in your patients, and barriers to vaccination in your population.

1. *Do you offer the HPV vaccine to your patients?
(If yes) Do you offer the HPV vaccine as a regular component of your pediatric visits?
(If yes) To what age ranges do you offer the HPV vaccine? And do you offer the HPV vaccine to both males and females?*
2. *Could you describe how you presented the vaccine to your last patient, and how you described it to the adolescent and/or parent? Did they accept or reject the vaccination?*
3. *What percentage of patients offered the vaccine accept the vaccine?*
4. *Do you encounter any difficulties in giving or recommending the HPV vaccine?*
5. *Can you give an example of a specific patient or parent that initially refused the vaccine and then changed their views when you discussed the reasons for the vaccine? What was the reason for refusal? And was it possible for you to change their opinion?*
6. *What are some other reasons that patients or their parents have refused the vaccine?*
7. *Is cost a barrier to vaccination in your patients?*

8. *Do you think that your input as a physician can change someone's mind from refusing the vaccine?*

(Assessing physician knowledge) The last few questions are regarding your perceptions of the HPV vaccine.

1. *Do you think that the HPV vaccine is effective?*
2. *Do you have any concerns with giving the vaccine to your patients?*
3. *Do you think the HPV vaccine is effective in preventing cervical cancer?*
4. *Do you think that the HPV vaccine is effective in preventing genital warts?*
5. *If you had to guess, in the United States, what percentage of adolescent females have received one shot of the vaccine? And what percentage have received the complete three-shot series?*
6. *What do you think can be implemented or changed to increase the rates of HPV vaccination in Hartford?*

Thanks for your time. Your responses will be typed into a Microsoft Word document, and this information will help us target resources to increase HPV vaccination in Hartford youth.

Appendix II: Survey Instrument

Unless otherwise specified, please mark one answer per question. It's important to answer each question to the best of your knowledge:

1. Have you ever heard of HPV (Human Papillomavirus)?
 - a. Yes
 - b. No

2. What do you think HPV is?
 - a. A common cold
 - b. A skin rash
 - c. A sexually transmitted disease
 - d. An infection patients get from hospitals
 - e. I don't know what HPV is

3. What is the most common STD? (Circle only one)
 - a. HPV
 - b. Chlamydia
 - c. Gonorrhea
 - d. Herpes
 - e. HIV

4. What can HPV lead to? (Circle all that apply)
 - Cancers of the reproductive system for women (for example, cervical cancer, vaginal cancer)
 - Cancers of the reproductive system for men (for example, penile cancer)
 - Mouth/throat cancer
 - AIDS
 - Genital warts
 - Breast cancer
 - None of the above

5. Who does HPV affect?
 - a. Female
 - b. Male
 - c. Both

6. Men can get HPV from homosexual or heterosexual sex.
 - a. True
 - b. False

7. You would always know if you had an HPV infection.
 - a. True
 - b. False

8. You can get HPV by not keeping yourself clean.
 - a. True
 - b. False

9. Antibiotics can cure HPV.
 - a. True
 - b. False

10. If you wait to have sex until after marriage, you cannot get HPV.
 - a. True
 - b. False

11. HPV is preventable
 - a. True
 - b. False

12. At what age can HPV vaccination start? (Pick an age) _____

13. How many doses are there of the HPV vaccine?
 - a. 1
 - b. 2
 - c. 3

14. Who can get the HPV vaccine?
 - d. Female
 - e. Male
 - f. Both

15. The HPV vaccine is only for adults
 - a. True
 - b. False

16. Only sexually active people should get the vaccine
 - a. True
 - b. False

17. If you get the HPV vaccine, you don't need to use condoms because you're protected from sexually transmitted diseases.
 - a. True
 - b. False

18. HPV infection is serious.
 - a. True
 - b. False

19. The HPV vaccine is effective in preventing HPV infection.
- True
 - False
20. The HPV vaccine can prevent cervical cancer.
- True
 - False
21. The HPV vaccine can prevent genital warts.
- True
 - False
22. If a teenage gets the HPV vaccine, he or she will be more likely to have sex.
- True
 - False
23. What are some reasons a teenager would decide to get vaccinated? (Circle all that apply)
- His/her parents told him/her to
 - His/her doctor told him/her to
 - To prevent HPV infection
 - To prevent cervical cancer
 - Because his/her friends all received the vaccine
 - Other (fill in): _____
24. What are some reasons a teenager would decide NOT to get vaccinated? (Circle all that apply)
- Not knowing where to get the vaccine
 - Thinking the vaccine is not necessary
 - Thinking the vaccine is unsafe
 - Fear that the vaccine will cause pain
 - Cost of the vaccine
 - His/her parents did not tell him/her to
 - His/her parents did not want him/her to
 - Other (fill in): _____
25. Do you plan on being vaccinated in the next year?
- Yes
 - No

Appendix III: Focus Group Question Guide

First, the discussion group facilitator will introduce himself or herself and convey the following information:

There are two reasons for conducting the discussion group. First, we want to find out how we can improve the presentation we just shared with you. Second, we want to find out more about what you think about the HPV vaccine, including what might factors influence the decision to get vaccinated.

You do not need to answer any questions you don't feel comfortable answering and you can leave the discussion at any time if you would like.

There are no right or wrong answers.

The group is *not* trying to reach an agreement; you may disagree with others as long as you do it in a respectful manner.

If it is OK with the group, we were hoping to audio recorded the session so that we can refer back to it and ensure we did not miss what has been said. While we will not be recording or writing down names, to further protect your privacy, we ask that you do not say your name or others names during this discussion.

During the session, please make sure you speak one at a time, so that when we listen to the tape we can understand what people said.

We ask that you do not repeat outside of this group what the others have said during the group discussion.

Please be honest and free in what you say. We are here to understand the barriers of getting the HPV vaccine and understand that there are many reasons affecting this decision. Whatever we talk about here today will *not* be told to anyone in the community. Only the UConn students working on this project will know what was said in the form of anonymous information.

1. How could we improve the presentation?
2. Is there any content we could add, revise, or remove?
3. Where have you heard about HPV before today?
4. What new information did you learn from this presentation that you did not know before?
5. Do you have any other questions about HPV that we didn't answer in the presentation?
6. Only 40% of eligible youth have received the HPV vaccine. Why do you think the majority of youth have not been vaccinated?
7. What do you think would motivate children and adolescents to get vaccinated?
8. Among girls who receive the first dose, many do not return for the two follow up doses – why do you think this is?
9. As we discussed, vaccination rates are low among boys. Only 20% of boys receive the 1st dose, and only 7% of boys receive all 3 doses.
 - a. Why do you think the vaccination rate is so low for boys?
 - b. Why do you think it is higher among girls compared to boys?