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THE COST-EFFECTIVENESS AND FEMINIZATION OF THE HUMAN PAPILLOMAVIRUS VACCINE

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An Investigation into Parental Concerns and Popular Media Concerning Vaccination

By

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Abstract: Approved in 2006, the Human Papillomavirus (HPV) vaccine provided a medical breakthrough in combating cancer by inoculating first female and then male adolescents in 2010. In 2016, a new HPV vaccine was approved for all adolescents. However, it is the most expensive vaccine created in the United States and its female centered prescription led to debates regarding the vaccine's necessity and risks. For the STS portion of this paper, analysis of the language in the vaccine's prescriptions from 2006, 2010, and 2016 demonstrates two implicit assumptions regarding female health built into the vaccine's rollout. Comparison of the two assumptions to the popular media campaigns and parental responses over time shows that as male vaccination became more common and the list of HPV-related cancers grew, debates regarding its effect on sexual behaviors were dampened. However, distrust of the vaccine due to corporate marketing grew. The second part of the study uses the net-present value calculation to identify whether administering the vaccine is cost-effective by comparing the marginal benefit of the medical treatment and mortality costs foregone and the marginal cost of the two-dose vaccination per individual. The calculations demonstrate that vaccination at 2018 rates and full vaccination are not cost-effective at the current price and dose schedule. Overall, this study finds that there are still stereotyping effects on adolescent girls from the 2006 prescriptions and that funding for the vaccine's development is not cost-effective and could be used in other medical interventions.

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1. INTRODUCTION

The intersection between gender and medicine is a common topic of discussion among Science, Technology, Society (STS) scholars. The lenses of philosophy, history, and social science are important components of the STS field that enable scholars to better understand how gender shapes medical care. A key topic in healthcare economics is interpreting the cost-effectiveness of medical technologies, such as vaccinations. Both analyses can be applied to studying the Human Papillomavirus (HPV) vaccine, first approved in the United States in 2006 for female adolescents and in 2010 for male adolescents.[1] The present study indicates a relationship between the sexualization and feminization of the HPV vaccine and the public uptake rates, a pattern similar to what occurred when oral contraceptives came to the market, according to physician Ellen Daley.[2]

The aim of this paper is twofold: To use scientific documentation and popular media to better understand why prescriptions around the HPV vaccine administration changed in the U.S. and how the changes impacted uptake levels and gendered ideals in sexual health. This investigation argues that the debate surrounded more cultural than medical concerns regarding the vaccine and that these concerns from parents differ from the assumptions found in the prescription's language. An example of a cultural concern was that the vaccine could be introducing the idea of risky sexual practices at an earlier age versus a medical concern that the vaccine could reduce progressive cervical cancer cell development in women. The second aim of this study is to determine whether HPV inoculation is cost-effective as a cervical and oropharyngeal cancer prevention method at 2018 vaccination levels and 100% vaccination.

[1] "Human Papillomavirus (HPV) Vaccines," *National Cancer Institute*, last modified 2021. 1.
[2] Ellen M. Daley et al., "The feminization of HPV: How science, politics, economics, and gender norms shaped U.S. HPV vaccine implementation," *Papillomavirus Res.* 3, (2017): 143.

To investigate the first goal, the paper will apply a social studies lens to identify the assumptions within the vaccine's prescription recommendations. The second section will analyze the themes in medical studies and popular media and compare them to the concerns found in parental communities. Then a cost-effectiveness analysis will be applied using a net-present discounted value model to identify whether the vaccine is an effective use of government funding considering its high price tag. The second piece of the study finds that HPV inoculation is not cost-effective at current rates of oropharyngeal and cervical cancer rates in the United States, which lends some support to parental concerns surrounding its necessity.

1.1. Vaccine Timeline

As science and cultural ideals around medical care evolved, so did the HPV vaccine's administration prescriptions. This section offers history regarding HPV research and defines the three main turning points, as seen in Figure 1, for the vaccine's administration and how they altered the patient pool by changing the sex and age of the patients being given the vaccine.

Figure 1.

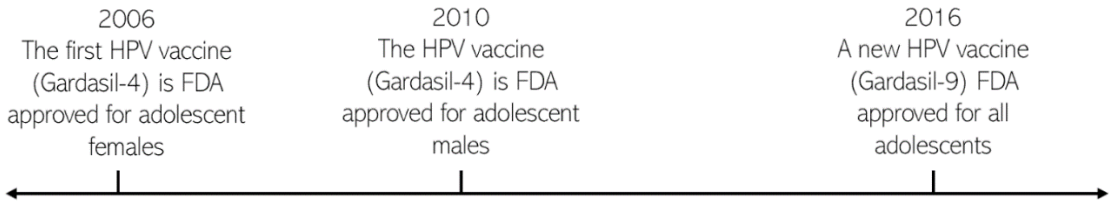

Figure 1. The figure shows the three years where the CDC/FDA revised the HPV vaccine prescriptions. *Source: CDC/FDA*

In 1979 epidemiologists began observing links between cervical cancer and sexually transmitted diseases, and in 1984, German researcher Harald zur Hausen isolated HPV 16 and 18

from squamous cell carcinomas of the cervix.[3] In 1990, scientist Joel Palefsky found that 50% of a sample of gay men with AIDS had HPV, linking the virus to higher incidences of anal cancer.[4]

After randomized control trials in 2006, the Food and Drug Administration (FDA) approved the use of the first HPV vaccine for female patients between the ages of 9 and 26 years old.[5] The 2006 HPV vaccine was a quadrivalent version that protected against the four most prevalent strains of the virus (types 6, 11, 16, 18).[6] It was the first vaccine aimed at combating cancer, particularly cervical cancer in women. Upon the 2006 FDA approval, the vaccine was only administered to females to offer inoculation against a sexually transmitted disease (STD) linked to 70% of cervical cancer cases.[7]

In late 2007, Merck & Co. launched a large, randomized control trial of the HPV vaccine in 4,000 healthy men aged 16 to 26 to expand its FDA labeling. The results of these trials were submitted to the FDA for male vaccine approval in December 2008 with the goal of indirectly increasing female protection from HPV.[8] In August 2009, the FDA approved the HPV vaccine for males between 10 and 25 years old due to anal cancer concerns and the evidence that vaccinated males could help reduce HPV cases in female partners.[9]

In 2015, a Gardasil 9-valent (9v) HPV vaccine was developed to protect against five additional strains linked to cervical and other cancers (types 31, 33, 45, 52, 58). The 9v vaccine was found to offer protection against nearly 90%, rather than 70%, of cervical cancers, because

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[3] Ellen M. Daley et al., "The feminization of HPV: How science, politics, economics, and gender norms shaped U.S. HPV vaccine implementation," *Papillomavirus Res.* 3, (2017): 143.
[4] Ibid.
[5] Department of Health and Human Services, "June 8, 2006 Approval Letter- Human Papillomavirus Quadrivalent Vaccine, Recombinant," *Food and Drug Administration*, June 8, 2006.
[6] David Yang, "Update on the new 9-valent vaccine for human papillomavirus prevention," *Can Fam Physician* 62, no. 5 (2016): 399.
[7] Partha Basu et al., "Efficacy and Safety of Human Papillomavirus Vaccine…," *South Asian J Cancer* 2, no. 4 (2013): 188.
[8] Keith Wailoo, *Three Shots at Prevention: The HPV Vaccine and the Politics of Medicine's Simple Solutions*. Baltimore: Johns Hopkins University Press, 2010. 42.
[9] Ibid.

the five additional strains the 9v vaccine protects against account for 17% of cancerous lesions linked to HPV.[10] The vaccine trials demonstrated increased protection from the vaccines for both male and female adolescents between the ages of 9 and 15 years old, which led the FDA to make universal recommendations for the 9vHPV vaccine. As of 2016, the recommendations for the 9vHPV vaccine are that it should be given to all individuals between the ages of 9 and 26, regardless of gender.[11] It should be noted, though, that scientists did not find that the addition of five strains greatly increased protection against HPV related cancers found in anatomically male bodies.[12] In addition, more recent clinical trials have found correlations between HPV incidence and oropharyngeal cancer rates in the United States, and rates have been steadily increasing over the past 20 years.[13]

2. AIM OF THIS PAPER

The background given thus far demonstrates that medical research had established the relationship between HPV and cancers, especially anal and cervical cancer, but the timeline of applying these results differed. Throughout history, women's health has been the target of controversy, notably when birth control pills gained increased marketing after more adolescent females became pregnant in the 1950s.[14] The HPV vaccine offers another example of medical testing, and analyzing its history, prescriptions, and marketing offers insight into cultural ideals over time. By targeting only females at first, the vaccine opened a debate around promiscuity and sexual transmission risks. Although the vaccine was pushed as a cancer risk reducing

[10] David Yang, "Update on the new 9-valent vaccine for human papillomavirus prevention," *Can Fam Physician* 62, no. 5 (2016): 400.
[11] Keith Wailoo, *Three Shots at Prevention: The HPV Vaccine and the Politics of Medicine's Simple Solutions.* Baltimore: Johns Hopkins University Press, 2010. 44.
[12] Ibid.
[13] "United States Cancer Statistics Data Visualizations: Oral Cavity and Pharynx Cancer in Males." *Centers for Disease Control and Prevention,* last modified 2018.
[14] Keith Wailoo, *Three Shots at Prevention: The HPV Vaccine and the Politics of Medicine's Simple Solutions*. Baltimore: Johns Hopkins University Press, 2010. 113.

technology, vaccine uptake has been slow and reached a high in 2018, where only 61% of females and 56% of males, between the ages of 13 and 17, had been fully vaccinated against HPV.[15] These rates are below the scientists' predicted rates of at least 70% vaccination by 2018 and the herd immunity goal of 85% vaccination.[16] There might be multiple reasons for this trend, including the individualized nature of the vaccine, the gendered roll out, and the need for parental consent for an adolescent to receive immunizations.

The vaccine's recommendations were set by the FDA and the Centers for Disease Control and Prevention (CDC), which will be referred to as the health agencies in this paper. It is the agencies' research and approval processes that make the vaccine part of a technological system that can be studied from an STS point of view. This paper argues that the initial regulations and advice for the HPV vaccine embedded gender values and assumptions, creating a technical code for dispensing the vaccine. The paper will then analyze how the technical code changed from a female health centered approach to one more focused on universal societal health. This argument is made by comparing language in the CDC/FDA reports between 2006 and 2016 and interweaving that language with philosopher Andrew Feenberg's technical code (defined in section 2.1.1).

This paper's first assessment of the CDC guidelines shows that the language over time became more gender inclusive and less sexually focused, but it also fed into two assumptions surrounding women's health: That there was a greater concern for women's health, and that the burden of sexual health was placed more on women. Given that HPV cells do not differ between sexual anatomies, the vaccine itself is not built differently to cater to male vs. female anatomies,

[15] NIS-Teen Survey, "TeenVaxView Publications and Resources," *Center for Disease Control and Prevention*, last modified 2021.
[16] Keith Wailoo, *Three Shots at Prevention: The HPV Vaccine and the Politics of Medicine's Simple Solutions*. Baltimore: Johns Hopkins University Press, 2010. 46.

meaning that the chemical component of the vaccine is not gendered. The vaccine not being chemically gendered is useful in knowing how the vaccine's system was adapted to medical concerns of the health agencies. Following this, further analysis shows how different the focus of the media was to the changes in prescription language and how focused it was on countering points from parental debates. Put together, the analysis will show that the vaccine's prescription was rooted in stereotypes regarding women's health as being more crucial and sexually charged than men's health, stereotypes echoed in parental concerns regarding vaccinating their children. However, even as the prescription language became more gender neutral, parental concerns remained gendered, which led to a stagnating vaccination uptake rate.

2.1. STS Literature Review

The original 2006 vaccine was tailored towards directly protecting women from cervical cancer risks, placing women's health at the forefront of the recommendations. Recommendations for the vaccine's CDC/FDA prescriptions may reveal the social priorities of the vaccine. Philosopher Andrew Feenberg defined and applied the idea of the technical code, wherein "technology adapts to social change and responds to the set of societal values that inform mechanical design of technology."[17] The economic and social interests of society and scientists can constitute assumptions built into the technology.

When looking at important design elements of the vaccine's prescription, the analysis will consider the initial demographic recommendations and the reasons the health agencies gave for the vaccine's approval. The reasons are crucial parts of the technology as vaccines are social through the purpose they serve, and purposes are in the mind of the interpreter.[18] In this case study, the technological vaccine's network guides the allocation of vaccination in society. This

[17] Feenberg, Andrew. "Democratic Rationalization: Technology, Power, and Democracy." *Inquiry* 35 (1992): 705.
[18] Ibid., 708.

allocation information will be analyzed and broken down for each of the three main points of the vaccine's timeframe, and then used in the cultural analysis part of this paper. The scientists make the final choice among the principles guiding the technologically viable options for vaccination and then they define the solution that society uses to curb disease rates.[19] The HPV vaccine functions as a technological system, including its prescription and roll-out, so the vaccine's system can be analyzed as including the parameters on its administration set by the CDC, not just the contents of the vaccine. Feenberg's argument will be used to demonstrate the power technology has on its public perception.

Another idea of study stemming from Feenberg's argument is rationalization with appeal to efficiency. Feenberg argues that "a technological network can function in a way that is deemed efficient by a network of actors without being the best application of it for society."[20] This argument will be used to show that as the vaccine's prescription changed, parents' responses and thought processes changed, although perhaps not in the most efficient way. In this sense, the assumptions that were formed by society's debates and responses to the vaccine's prescriptions should be noted because they express which information regarding the technology was perceived by, and notable to the parents.

Feenberg's technical code theory demonstrates the power that public perception can have on a technology and helps to identify whether the perception can be impacted by technological revisions. The argument demonstrates that technology can adapt to social change, but also that social perceptions of medical technology can change in response to the technology changing. This argument will allow further exploration on what social factors influenced policy reactions and whether the reactions were addressed in the succeeding prescriptions. Overall, the technical

[19] Feenberg, Andrew. "Democratic Rationalization: Technology, Power, and Democracy." *Inquiry* 35 (1992): 708.
[20] Ibid., 711.

code argument outlines how to conduct the CDC/FDA source analysis and how research into the vaccine's cultural debates should be focused. The following analysis will extend past Feenberg's arguments that focus on artifacts and apply them to the HPV vaccine's system.

The first part of this paper will also utilize arguments from *Three Shots at Prevention*, edited by Keith Wailoo. This book offers a compilation of medical studies and commentary surrounding the HPV vaccine's medical and political effects in society. The chapters focused on in this book revolve around Wailoo's idea that "vaccines present a locus of controversy precisely because they offer future protection from present threats and because they depend on public fear to mobilize citizens."[21] Additionally, these chapters outline how the vaccine debate has emerged over time along with an unfolding controversy, with a focus on how the history of the HPV vaccine research demonstrates the moral and ethical ideals in sexual politics. Wailoo's analysis of societal attitudes towards the vaccine demonstrate that there are various understandings of the vaccine's potential benefits that depend on the patient's sex. The benefits differ for men versus women due to the vaccine's involvement with reproductive systems and sexual transmission.[22] Therefore, the vaccine's debate moves beyond the medical benefits of adolescent vaccination and includes debates on sexual education and sexuality which is affected by parental influence and individual morals. This paper follows arguments found in Wailoo's work by incorporating a parental audience response over time and comparing it to specific language from the health agencies regarding the vaccine. This paper uses primary sources to trace the vaccine's impact on society over time and understand what role gender played in parental decisions to vaccinate.

[21] Keith Wailoo, *Three Shots at Prevention: The HPV Vaccine and the Politics of Medicine's Simple Solutions*. Baltimore: Johns Hopkins University Press, 2010. 41.
[22] Ibid., 49.

3. METHODOLOGY OF CDC/FDA ANALYSIS

Breaking down the technical code and assumptions built into the HPV vaccine requires an analysis of the primary source language that point to the health agencies' prescriptions. This analysis will demonstrate the language scientists felt should be highlighted when the public learned about the vaccine and when doctors explained the vaccination to parents of adolescents. Analysis and comparison of the language in the 2006, 2010, and 2016 HPV vaccine approval press releases from the CDC and FDA offer a more in-depth view of the underlying assumptions present from the researchers developing the recommendations and how they changed over time. The analysis finds two main assumptions that stand out as societal ideals scientists built their recommendations from: That the prescriptions demonstrate a greater concern for female health and the belief that women were primarily responsible for reducing health risks of sexual activity.

4. HOW THE PRESCRIPTIONS CHANGE OVER TIME

4.1. The Assumption of a Greater Concern for Female Health

4.1.1. 2006 CDC Press Release Analysis

The 2006 CDC press release states that the vaccine is recommended explicitly for adolescent females to protect against cervical cancer and places stress on the relationship between HPV and cervical cancer. Cervical cancer affects solely people with cervixes (part of the female reproductive system), and therefore this press release outlines that the HPV vaccine is tailored specifically to the female sex. The press release states that the vaccine "is the first developed to prevent cervical cancer due to HPV", and that the recommendations "address a major health problem for women and represent a significant advance in women's health."[23] This creates an association between the virus and cervical cancer, but it almost closes the door to

[23] Department of Health and Human Services, & Roberts, J., "Clinical Review of Biologics License Application Supplement – male indication for GARDASIL," 6 (2009). Rockville. 14.

associations between HPV and other cancers. This is a notable exclusion, because research in the 1990s connected HPV and anal sex. This is a key part of how the focus of the vaccine became centered around female cancer prevention, even though the press release does state "that more than 20 million men and women in the U.S. are currently infected with HPV."[24] This highlighting creates the assumption that any potential association between HPV and other ailments are inferior to the connection between HPV and cervical cancer.

The emphasis on the effects of HPV in women signals a silence of HPV's effects on men. The FDA's 2006 prescription indirectly states that having evidence of the vaccine's protections of women's reproductive health is enough to support the vaccine's administration, but its impact on male health is not. With a causal relationship being established between HPV and both cervical and anal cancer, but only the link between HPV and cervical cancer addressed in the recommendations, there is a greater focus on using this vaccine to protect women's health. This is evidenced by the fact that despite a causal link being established for both sexes, the vaccine trials were initially conducted only on females. This idea provides evidence of the assumption that female health was intended to be the center of vaccination against HPV.

4.1.2. 2009-2014 FDA Report Analysis

For the purpose of this analysis, the 2006 CDC press release is equivalent to 2009 FDA Report on the research of the vaccine. This document will be compared to the language of the scientists and researchers from the 2006 and 2016 CDC press releases to identify the technical code focused on prioritizing women's health. The report discusses the proposal to expand the HPV vaccine eligibility to men aged 9 to 26-years-old. The first ideas mentioned are that the current vaccine licensed by the FDA is for prevention of "cervical, vulvar, and vaginal cancers",

[24] Department of Health and Human Services, & Roberts, J., "Clinical Review of Biologics License Application Supplement – male indication for GARDASIL," 6 (2009). Rockville. 14.

specifically related to women's health and that this expansion would "protect men from HPV causing genital warts."[25] This juxtaposition of the two makes it seem as if the protection from cervical cancer offered for females and the protection against genital warts offered for males are equivalent. This is also not mentioning the research tying HPV in males and the increased incidence of anal cancer. Even though the CDC lists that 90% of anal cancers and 91% of cervical cancers are caused by HPV infections, only the tie to cervical cancer was addressed in these 2006 recommendations.[26] There is an attempt to include males in the research and recommendations but the language of equating cancer to genital wart rates is still creating an imbalance of burden of the vaccine for one sex over the other. This is because the diseases the report associates with female HPV infection (cancers) have greater long-term consequences than what they identify as consequences of male HPV infection. With this written in the principles of administration, it is placing HPV vaccination as more important for long-term health of women than that of men, even though there is evidence to support as strong an association between HPV and male cancers.

This brings up a burden of proof question raised by the political nature of the technology; evidence for male vaccination after clinical trials is still not enough to place it on the same recommendation level as there was for females. Therefore, the evidence needed to recommend the vaccine is set lower for women even though there is similar association between HPV and both cervical and male anal cancers. In addition, the 2010 mortality rate of cervical cancer was 25% and for male oropharyngeal cancer was 23%, demonstrating similar mortality risks between

[25] Department of Health and Human Services, & Roberts, J., "Clinical Review of Biologics License Application Supplement – male indication for GARDASIL," 6 (2009). Rockville. 13.
[26] "How many Cancers Are Linked with HPV Each Year?" *Centers for Disease Control and Prevention*, last modified 2021.

these two cancers.[27] The vaccine was approved for use in men in 2010, but it is interesting to analyze that the evidence was enough to state that the HPV vaccine was immediately approved and recommended for females but not immediately approved and recommended for males, even though they can also suffer from anal cancer.[28]

In 2014, the CDC published a Human Papillomavirus Vaccination Recommendation update to describe the vaccines available and provide data on current research. The only section where the gendered language enters is in the discussion of other modes of HPV prevention, where pap smears are highlighted as a necessary means of cervical cancer prevention, even when inoculated.[29] The other sections regarding the clinical trial research for the vaccine is split between male and female trial groups of various ages, and both are addressed as "reaping benefit from the vaccine in order to prevent certain types of cancer."[30] However, there is prioritization of women's health in testing of the vaccine even when testing occurred in men. The evidence was not enough to place it on the same recommendation level as was present for females, leading to a burden of proof difference in the health agencies' recommendations.

4.1.3. 2016 CDC Press Release Analysis

The gendered language in the 2016 CDC press release is completely removed, with the CDC recommending "that 11 to 12-year-olds receive two doses of HPV vaccine…"[31] There is no longer the reference between needing the HPV vaccine to prevent cervical cancer, instead the vaccine is deemed as "safe, effective, and long-lasting protection against HPV cancers."[32] The

[27] "United States Cancer Statistics Data Visualizations: Cervical Cancer in Females and Oral Cavity and Pharynx Cancer in Males," *Centers for Disease Control and Prevention,* last modified 2018.
[28] Department of Health and Human Services, & Roberts, J., "Clinical Review of Biologics License Application Supplement – male indication for GARDASIL," 6 (2009). Rockville. 14.
[29] Ibid., 10.
[30] Ibid., 11.
[31] Center for Disease Control and Prevention, "CDC's Advisory Committee Recommends Human Papillomavirus Virus Vaccination," (2016). Atlanta.
[32] Ibid.

first paragraph is more age focused than the previous press releases, where the recommendation is stricter to 11 and 12-year-olds, with 15 to 26 year-olds needing an extra dose to catch up on protection.[33] There is once again this implicit assumption that receiving the vaccine at a certain age is young people contributing to society's future health, but the burden is no longer just on women. There is also mention that the vaccine research was done on different age groups, putting the focus of study of the impact of the vaccine on different age groups rather than sexes.

4.1.4. Overall Trends

Something to consider after analyzing the three primary sources is that in 2016 the gendered language is removed from the CDC's recommendations, but the HPV affiliated cancers are still gendered and focused on reproductive anatomy. The main HPV-related cancers that vaccination is outlined to prevent in males are anal and oropharyngeal cancer, both of which can also be found in females. Although cervical cancer prevention was the initial reason given for vaccination, over time, the emphasis on protecting women's health over men's lessened.

However, even as approval encapsulated all genders, the recommended guidelines for vaccination remained different due to a less pressing causal relationship established between HPV-related cancers in males.[34] By having the causes of some HPV-related cancers tied to sex organs, it points to a key idea in the HPV vaccine debate regarding whether vaccination is necessary for adolescents. This is a key point of contention for parents, but it is important to note that the press releases do not define why receiving the vaccine young is necessary.

[33] Center for Disease Control and Prevention, "CDC's Advisory Committee Recommends Human Papillomavirus Virus Vaccination," (2016). Atlanta.
[34] Center for Disease Control and Prevention, "Fewer Shots Offer More Incentive to Prevent HPV Cancers," (2016). Atlanta.

4.2. The Assumption of Female Responsibility for Sexual Health

4.2.1. 2006 CDC Press Release Analysis

The linguistic association in this report also begins to place responsibility of limiting the spread of STDs onto females, even though offering the vaccine to their male partners would also help females. This begins to place an assumption in society that women are responsible for the sexual health of all and ought to take the preventive measures available to maintain health.

In the third paragraph, the CDC states that "the vaccine should be administered before onset of sexual activity (i.e. before women are exposed to the virus), but females who are sexually active should still be vaccinated."[35] This seems to place fault on the females for not being vaccinated early enough when in reality, many adolescents do not have control over their vaccination status or may not understand what they are being vaccinated against as they are minors. As parents in most states take control of their children's vaccination status, it is interesting to consider how the language is catering towards the parents rather than the adolescents. The emphasis on sexual activity points to a need for parents to take control of their daughter's sexual health before the children can.

The language in the next couple of paragraphs links vaccination to the need to take sexual protection practices. The paragraphs discuss the implications of the vaccine in curbing cervical cancer rates for women in the United States, including that the vaccine protects against 70% of cervical cancer cases. Once again, the focus is on preventing cervical cancer, rather than HPV. It seems that the causes of cervical cancer are entangled between sexual behavior and HPV infection. Scientifically, HPV infections can lead to cervical cancer, but the language poses female sexual behavior as the causal factor and therefore that the risks associated with sexual

[35] Center for Disease Control and Prevention, "CDC's Advisory Committee Recommends Human Papillomavirus Virus Vaccination," (2016). Atlanta.

behavior need to be curbed before the onset of activity. This entanglement could be leading to misbeliefs that parents had regarding how the vaccine would impact their daughters, such as it potentially increasing promiscuity, a myth that is still linked to the vaccine today. The vaccine's clinical trials were also centered around finding a link between the vaccine and preventing an anatomically female cancer, cervical. This focus on females and sexual behavior places the burden of sexual protection on females, even though male partners could be passing HPV onto females. The possibility of offering the vaccine to males to protect females is not addressed.

Another interesting part of the press release is that it holds the implicit assumption that after the age of 26, women are sexually active and therefore too exposed to the virus for the vaccine to be beneficial. This will be important to consider in the analysis of parental arguments questioning the necessity of vaccination at a young age. The report states that "the vaccine should be administered before onset of sexual activity (i.e., before women are exposed to the virus)" which explicitly equates sexual activity to HPV exposure. The vaccine was said to not be as effective after one was sexually active and potentially exposed to the virus, but placing a limit assumes that one will have been sexually active by at least the age of 26. This points to the immediacy of getting the vaccine before sexual activity but assumes that protection after the age of 26 is not effective, arbitrarily setting the maximum age of beginning sexual activity.[36] It is also important to note that this paragraph makes it seem as if vaccination would protect one against HPV, but it makes no mention of needing to institute other safe sex practices. The vaccine would not prevent one from getting the virus, it would reduce the risk of someone getting the infection that can develop into cervical cancer. Therefore, additional safe sex

[36] Center for Disease Control and Prevention, "CDC's Advisory Committee Recommends Human Papillomavirus Virus Vaccination," (2016). Atlanta.

practices should be used in conjunction with vaccination for women, which the article does not spell out for adolescents it is looking to attract.

This interpretation of vaccination is a crucial part of the vaccine's technical code because it presents the assumption that vaccination will enable women to protect their sexual health but does not address how men can help contribute to this. The mechanism of protection is centered around protecting women directly by inoculating them and does not address the impact of not addressing men.

In addition to focusing on the importance of protecting female sexual health through inoculation, the link between HPV and sexual activity is established. The paper states that HPV is "a sexually transmitted disease and affects more than 20 million men AND women in the United States."[37] Both sexes being affected is explicitly mentioned, but one being singled out as more important for the regulations shifts the burden of protection onto women by stating that "by age 50, at least 80% of women will have acquired HPV infection" with no mention of similar statistics for men.[38] This indirectly implies that women are responsible for protecting both sexes. This assumption would produce the outcome that by having women take greater control over sexual health, their partners benefit as well. Therefore, women are also protecting male partners from HPV related diseases even though the latter are not stated as directly benefiting from the vaccine. However, the reverse effect of inoculating men which would help reduce HPV rates in women is not discussed, reinforcing the burden of sexual health protection on women.

Inoculation is not the only recommended course of action women should take to protect their sexual health. The report also mentions that "women should continue to get pap tests as a

[37] Center for Disease Control and Prevention, "CDC's Advisory Committee Recommends Human Papillomavirus Virus Vaccination," (2016). Atlanta.
[38] Ibid.

safeguard against cervical cancer" after vaccination.[39] Therefore, the vaccine is an additional step in women's health that is recommended, increasing the timeline during which women need to start taking on responsibility of their sexual health. Women no longer need to start medical care of their reproductive health at 21 (for pap smears) but now around age nine (for vaccination). This is key to understand as it points to the entrance of parents in sexual health decision making.

4.2.2. 2009-2014 FDA Report Analysis

Mainly, both men and women are listed as needing the vaccine and the gender differentiated cancers are mentioned as associations with HPV. This report was updated as additional research trials on the risk of HPV and cancer rates in male adolescents were conducted and the links between female sex cancers and HPV were strengthened. The recommendations from the 2006 and 2010 reports are repeated in the 2014 report, but the latter report also offered more in-depth information on how HPV manifests into cancer and its immunology.[40] The descriptions of the testing and the immunology of the vaccine itself are non-gendered. In the HPV Prevalence and Incidence section, it is mentioned that research has been done equally on men and women to analyze the vaccines seroprevalence and efficiency in specific age groups. The descriptions of the viral transmission do address the virus being an STD and places the burden of sexual health on both genders.

This amendment can signal a change in medical assumptions underlying the recommendations for HPV vaccination. This change was instigated by additional medical research being conducted, which in turn increased societal awareness surrounding the risks of HPV as an STD. This change demonstrates that because vaccination increased over time, the

[39] Center for Disease Control and Prevention, "CDC's Advisory Committee Recommends Human Papillomavirus Virus Vaccination," (2016). Atlanta.
[40] L. Markowitz et al., "Human Papillomavirus Vaccination: Recommendations of the Advisory Committee on Immunization Practices (ACIP)," (2014). Rockville. 6.

profile of it as an STD did as well, which propelled society to want to learn more about the vaccine's effects and benefits. In the first few years of the vaccine's approval for male adolescents, vaccination rates increased dramatically compared to that of the initial years where it was approved for females. In 2008 and 2009, 21% and 27% of females were fully vaccinated against HPV, and in 2011 and 2012 (the first two years males could be vaccinated) 42% and 45% of males were vaccinated. Therefore, societal action of increasing the rate of vaccination for males and the idea that males too needed to be protected from STDs, moved some of the burden that had been placed on females for sexual protection onto males as well.

4.2.3. 2016 CDC Press Release Analysis

Another piece that has been wiped from the report is that HPV cancer producing strains are sexually transmitted, transmission of the virus or its classification as an STD is not directly addressed in this release. Although, the risks of sexual activity and HPV are, the classification of HPV as an STD is not. This is important to consider because when the vaccine was available to only females, the idea of sexual protection was emphasized, but once the gendered division in reception is removed, so is the direct emphasis on sexual protection. Therefore, the assumption that sexual health is the prime reason for getting this vaccine is not as prevalent, it is more focused on protecting overall health of society. This language is also detangling the relationship between cervical/anal cancers and sexual activity.

Instead of simply listing the ages, the necessity of the HPV vaccine is compared to other required vaccines for children, including meningitis and whooping cough.[41] By doing this, the CDC is implicitly saying that the HPV vaccine meets a similar threshold of importance as the other vaccinations that almost 90% of American children receive before adulthood. This is an

[41] L. Markowitz et al., "Human Papillomavirus Vaccination: Recommendations of the Advisory Committee on Immunization Practices (ACIP)," (2014). Rockville. 6.

effort to increase the importance of the vaccine and potentially boost its profile to increase uptake. This attempt to further engrain the HPV vaccination into a routine societal move is connected to the idea that a technology eventually becomes so engrained in the needs of society that it becomes a part of society's identity. This is an effort to change parental behavior standards by stating that these vaccinations are crucial for proper medical factors of society.

4.2.4. Overall Trends

The less gendered recommendation over time attempts to remove the burden of sexual health from being solely on women, but historical work in female medicine displays that this is a difficult idea to eliminate. Physicians Ellen Daley et al. argue that feminization of medicine has its association with contraceptive technologies where the focus of procreative responsibility is placed on females.[42] This indirectly excludes males and other stakeholders by creating a strong societal perception of contraception as feminine. Daley's argument provides some support for the claim that the CDC literature and prescription guidelines fostered a feminine view of the HPV vaccine by the public, even though it is not itself contraception but linked to safe-sex practices. What is interesting is that as the female centered language was removed from the recommendations, the link between sexual intercourse and HPV transmission disappeared. This is consistent with the assumption that sexual health should be outlined primarily when women's health is involved, but it is less relevant when addressing male health. This is further tying the burden of sexual health to females.

4.3. Main points

The two assumptions outlined the cultural ideas that were then projected onto the public for consumption and embedded in the vaccine's rollout procedures even after the prescription

[42] Ellen M. Daley et al., "The feminization of HPV: How science, politics, economics, and gender norms shaped U.S. HPV vaccine implementation," *Papillomavirus Res.* 3, (2017): 143.

changes. The ideas and trends in thinking pulled from this language will be analyzed with media from society (parental blogs and magazines) to see how the changes were interpreted. It will also be interesting to see if the social conversations from parents and media impacted the CDC language over the years, especially as the connection between HPV and sexual activity is removed from the CDC language over time.

5. METHODOLOGY OF MEDIA AND PARENTAL ANALYSIS

To analyze how the rhetoric has changed in the media throughout the vaccine's progression, this paper explores studies and magazine articles targeted to both parental and teenage audiences. Magazine articles and advertisements for the vaccine were found by searching through Proquest Historical Newspapers from the Claremont Colleges Library databases. The goal was to find sources that were catered to adolescent and adult audiences, such as *The New York Times* and *The LA Times.* The keywords used in the search for articles included "HPV" and "vaccine" and the search date range was restricted to between January 1, 2006, and December 31, 2021. The goal was to find articles from consistent newspaper sources in response to the 2006 vaccine, the 2010 prescription amendments, and the 2016 vaccine change.

To explore parental concerns regarding the vaccine, articles and parental studies were explored and compared between 2006 to 2010, 2010 to 2016, and 2016 to onward. This is important because the HPV vaccination requires surrogate decision making from the parents, but contrary to other child immunizations, it concerns immunizing teens that are old enough to have views and opinions of their own. The 2006 parental decisions were found in a chapter from Wailoo's book, and the 2010 and 2016 parental decisions were found by searching to identify studies conducted by medical associations.

6. PUBLIC MEDIA TRENDS

This section will outline media perception of the HPV vaccine between 2006 to present and analyze the content using the ideas pulled from the language of the CDC and FDA reports. The goal is to analyze how the vaccine was portrayed to the public in newspapers and magazines and how the rhetoric changed over time. This analysis will be used in comparison to the parental and prescription analysis over time to identify common cultural trends that could have pushed the prescription changes along. There are three ideas that will be focused on in the analysis: the emphasis on the vaccine preventing cancer vs. preventing HPV, the necessity of the vaccine for adolescents at a young age, and the vaccine's effect on participating in risky sexual behavior.

6.1. Vaccine Preventing Cancer Vs. Preventing HPV

Over time, articles started to pivot from offering information on HPV and more towards the focus of preventing cervical cancer. In a May 11, 2006, *Los Angeles Times* article, reporter Jonathan Bor published the findings of the Merck &. Co drug trial that showed promise for the vaccine to be approved by the FDA in the following months. The article provides numerical evidence of the vaccine's effectiveness in protecting against HPV and includes quotes from experts in the field that echo the original Gardasil advertisement message that vaccination is needed for one to be a reasonable member of society.[43] For example, gynecologist, Dr. Gene Rudd, states that the vaccine is important because "where there are diseases, the only reasonable way you can protect individuals and society is to be immunized."[44] This echoes the idea that getting the vaccine would make one a reasonable member of society, similar to the language used in the 2016 CDC report where getting the HPV vaccine was compared to getting other commonly accepted vaccines such as Tdap.

[43] Jonathan Bor, "Young Girls could be in line for Vaccine to Stop Cervical Cancer," *Los Angeles Times* A.10 (2006).
[44] Ibid.

After this article was published, *Vogue* magazine started including page-long Gardasil advertisements in December 2006 that offered educational information and pushed for parents and daughters to ask their doctors for the vaccine. The first issue included scientific information connecting cervical cancer prevention to Gardasil and pushed girls to talk to their doctors about receiving protection, but did not offer information on how to protect themselves from HPV through sexual transmission.[45] The advertisements were different in each Vogue edition, but most stated a version of the following message: "the HPV vaccine can protect against cervical cancer in the future" without offering a description of HPV transmission or offering other resources to get information surrounding protection against STDs.[46] An example of a Vogue advertisement is seen in Figure 2.[47]

Figure 2.

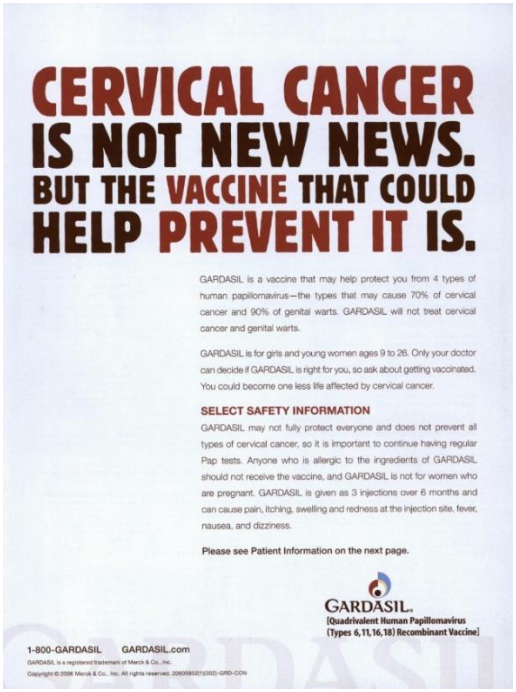

Figure 2. This shows an advertisement for the vaccine in a 2006 edition of *Vogue*.
Source: "Advertisement: Gardasil," Vogue 196, no. 12 (2006). New York.

[45] "Advertisement: Gardasil," *Vogue* 196, no. 12 (2006). New York.
[46] Ibid.
[47] Ibid.

On February 28, 2007, reporter Denise Gellene from the *Los Angeles Times* followed up on Johnathan Bor's article that offers even more statistical information pertaining to the lowered risks of cervical cancer for women between the ages of 14 and 29 years old. The article also offers information on where women could get more educated on the disease and the vaccine, particularly because of how common the infection was and how fast it was becoming a political rather than medical debate following the FDA approval.[48] From this article, the focus of the vaccine was to prevent future cancer cases, not in reducing HPV cases. This jump from not including information regarding sexual transmission and information on what HPV is, is similar to that found in the 2010 and 2016 prescription languages. In addition, mention of the vaccine protecting against a sexually transmitted disease decreased over time. By having increasing cervical cancer rates as the vaccine's focal point for the vaccination campaign, there was an unbalanced burden on women to protect sexual health, as seen in the language analysis above.

6.2. Necessity of the Vaccine

Another common theme in popular media between 2006-2016, is proving the necessity of the vaccine, especially for women to be socially responsible individuals and protect society's future health. As stated above, obstetrician-gynecologist quoted in the 2006 *Los Angeles Times* article, Dr. Gene Rudd, expresses that "the only reasonable way to protect individuals and society from diseases out there is to be immunized."[49] This article details that societally responsible individuals are vaccinated and demonstrates how doctors advertised the necessity of the vaccine to parents. The articles show that over time the reasons for offering men the vaccine extended past protecting women, but also protecting themselves and future partners.

[48] Denise Gellene, "Millions of Women Carry HPV strains that Vaccine can Block," *Los Angeles Times* A.12 (2007).
[49] Jonathan Bor, "Young Girls could be in line for Vaccine to Stop Cervical Cancer," *Los Angeles Times* A.10 (2006).

One concern regarding the necessity of the vaccine was that parents were unsure as to what the vaccine would accomplish, considering that yearly pap smears were still recommended for women. The articles were working to make sure that parents taught their daughters that pap smears were still the best method of preventing progressive cervical cancer cases. In an article from *The Women's Health Activist,* Dr. Fugh-Bergman and Dr. Massion described that the vaccine lowers the risk of getting HPV and abnormal pap smear results which means that women would be less likely to need a procedure to remove the abnormal cells.[50] This procedure could increase the risk of a woman having a premature birth later on, echoing Merck's advertisement message that getting the vaccine makes women societally responsible individuals for current and future generations. Therefore, the pap smear does still offer the best detection of progressive cervical cancer, but the vaccine helps to reduce needing cancerous cell removal procedures.

As more discussion occurred, more articles regarding male vaccination were being published. In 2009, the topic of male vaccination became more mainstream because Merck & Co. started conducting randomized control vaccination trials to gain approval for Gardasil use in adolescent males. A 2009 article from *Seventeen* magazine echoes this call for educating girls about potential risks of not getting vaccinated due to the possibility of getting the virus from any kind of sexual relations. Without using lots of numbers or complicated scientific language, the article offers educational resources for readers and encourages them to share them with their parents, tying in the surrogate decision-making idea.[51] The push for male vaccination became a topic of women's health as well, and a Winter 2010 edition of *Ms.* magazine echoes calls for HPV vaccination to be in effect for men as the virus can travel between partners through skin

[50] Adriane Fugh-Berman and Charlea Massion, "Preventing Cervical Cancer: Pap Tests, HPV Vaccines & Common Sense," *The Women's Health Activist: Washington* 34, no. 1 (2009).
[51] Megan Cahn, "Protect Yourself From Cancer," *Seventeen* (2009).

contact and can be transmitted through all kinds of sexual contact; circumstances and the sex of the partner did not matter.[52]

Following the male HPV vaccine's FDA approval, the rhetoric surrounding the vaccine's benefits for both genders did not change much. On October 26, 2011, *Los Angeles Times* reporter Shari Roan wrote that the vaccine has been shown to protect against HPV strains leading to anal cancer and that this 2011 change serves to equalize the burden of vaccination to both sexes.[53] A November 1, 2011, *Los Angeles Times* article offered more of an educational report. Here the FDA approval is defined, and the idea of HPV causing genital warts in both genders is mentioned.[54] Therefore over time the articles demonstrate that necessity of the vaccine became extended past the need for women protecting themselves and their future families and included men protecting themselves and their potential partners.

The link between HPV and other types of cancers started to get increased media attention over the next few months, as shown in a November 2011 *USA Today, Farmingdale* article. The reporter tries to extend the discussion of HPV to other kinds of cancers, including anal and oral cancers that predominantly affect men. Pushing for greater vaccination from parents and children by demonstrating an increased benefit from receiving the vaccine, increasing its necessity.[55] Reporter Karen Kaplan from the *Los Angeles Times* on February 10, 2015 echoed this same rhetoric surrounding the importance of vaccinating both genders because of the evidence connecting HPV to cancers that can afflict all bodies. She admits that HPV can lead to more than

[52] Adina Nack, "Why Men's Health Is a Feminist Issue," *Ms.: Arlington* 20, no. 1 (2010).
[53] Shari Roan, "Routine HPV vaccination is recommended for boys," *Los Angeles Times* A.1 (2011).
[54] "HPV Vaccine for Boys? Yes," *Los Angeles Times* A.16 (2011).
[55] "HPV goes Beyond Cervical Cancer," *USA Today: Farmingdale* 140, no. 2798 (2011).

just cervical cancer, but penile, anal, and oropharyngeal cancers, which is then followed up with the emphasis on helping both boys and girls.[56]

Following this discussion, 2016 media demonstrates when necessity of the vaccine for men started to take off. For example, a July 13, 2016 article from *TeenVogue* targets adolescent boys and is raising awareness on campaigns pushing males to get the vaccine, assuring them that it does pertain to their health, not just female health.[57] This article is also pushing the idea that teens should take control of their health, and not assume that if the vaccine was necessary, their doctors would have already given the shot.

Another way necessity was advertised after 2016, was by catering specifically to adolescents and pushing them to have a more overall health benefit approach to evaluating vaccination. An April 2017 edition of *Girl's Life* offers a couple accounts of young girls that contracted STDs through unprotected sexual interactions, not just intercourse.[58] The goal is to push girls to talk to doctors and parents about getting tested and having a healthy conversation with partners before having intimate contact with them. This article offers an increased pool of risk in getting HPV, increasing its potential causes and telling adolescents that this vaccine can help in more unprotected situations. A similar article was published in the October 2016 issue of *Men's Health* that calls for parents to get their children vaccinated early to protect their future health, much like one recommends their children not to smoke or drink too much. It uses parental logic to draw comparisons between situations: it is something else one can do to better their health now for a better future, like not partaking in certain risky activities.[59] This article wraps up

[56] Karen Kaplan, "HPV Vaccines don't lead to risky sex, study says," *Los Angeles Times* A.6 (2015).
[57] Brittney McNamara, "Why Boys Aren't Getting the HPV Shot," *TeenVogue*, (2016).
[58] Sarah Wassner Flynn, "The #1 Teen Health Risk no one wants to Talk about," *Girls' Life: Baltimore* 23, no. 5 (2017).
[59] Ron Geraci, "Safe or Screwed," *Men's Health: New York* 31, no. 8 (2016).

the connection between increased necessity of the vaccine, the idea that vaccination is a benefit to society, and that vaccination represents rationality of the individual.

6.3. The Vaccine and Risky Sexual Behavior

Another common thread throughout popular media regarding the HPV vaccine was an effort to dispel rumors that the vaccine led to an increase in risky or "taboo" sexual behaviors. In the April 24, 2007, edition of *The Advocate*, reporter Morgan Kroll addresses the importance of vaccinating boys, "not only to protect women but to protect them from anal cancer risks."[60] It also acknowledges that Merck was in favor of pushing for this approval, but primarily because it would get them increased revenue, even though approving it for pre-sexual boys who were at risk of contracting it through anal sex would be "more controversial than the female approval is already."[61] This article demonstrates how the discussion surrounding male vaccination and sexuality was a topic of concern for parents at the time and that it was a reason given for why boys may not have been approved for vaccination early on.

Another common idea found across HPV vaccine articles in 2007 surrounding sexual behavior is debunking the myth for parents that the vaccine increases sexual promiscuity. An October 2007 article of *USA Today*, *Farmingdale* explains a study that debunks misinformation that getting the HPV vaccine causes girls to engage in more sex than unvaccinated females. This follows studies that 10% of parents were concerned that vaccinating their young daughters would encourage them to have more sex.[62] The goal here is to present scientific information catered to parents to put them at ease and prove that science does not support the idea that vaccination increases sexual risky behavior of the patients.

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[60] Morgan Kroll, "HPV: No boys allowed," *The Advocate: Los Angeles*, 16 (2007).
[61] Ibid.
[62] "Will Teenage Girls Have More Sex?" *USA Today: Farmingdale* 136, no. 2749 (2007).

In a March 2016 *Cosmopolitan* magazine article, reporter Katherine Schreiber pushed for women to not be ashamed to discuss STD protection with their partners, although the article is focused on heterosexual relationships. This article is framing women as needing to be vaccinated to protect against infection from any kind of sexual activity, stating that "strains of HPV can easily pass on the infection to pretty much anyone they go down on, make out with, or decide to have sex with sans condom."[63] This flips the concern around by stating that sexual practices are less risky with the vaccine, but the vaccine itself does not implicitly drive an increase in risky sexual behavior. In fact, the article discusses that the vaccine should be given to men and pushes women to talk to their partners about being vaccinated, both of which could lead to safer sexual relations. This connects to the idea of the necessity of the vaccine but also points to sexual behavior being considered risky if unvaccinated, whereas the vaccine itself would not increase sexual behavior, just make current relations safer. Therefore, the article demonstrates that over time all genders were pushed to get the vaccine to protect themselves and others from the risk of HPV from any kind of sexual interaction.

6.4. Trends Over Time

After 2017, there were a couple more teen magazine articles published but as time went by, media regarding the vaccine has been more concentrated in educational campaigns from medical associations or international organizations that aimed to bring a more international scope to HPV vaccination. This was due to the decreasing rate of cervical cancer cases in the United States compared to less wealthy countries.

The article research also pointed to the discussions regarding the HPV vaccine in teenage magazines increasing after 2016, while its discussion to more adult audiences plateaued. This

[63] Katherine Schreiber, "The Super-Important Reason You Need to Talk to Your Guy About HPV," *Cosmopolitan*, (2016).

could be due to many factors, including the rapid increase in social media influence. However, it does point to a shift in the audience for HPV vaccination campaigns and educational pamphlets because now periodicals were focused on giving the information to the patients rather than convincing the parents to accept it for their children. This shift in audience is also mirrored by a shift in the information presented, because the more recent articles focus more on the importance of safe sexual practices, although still heterosexually focused. However, the scientific facts and previous studies were more expanded upon when the parents were the main audience and periodicals and women's magazines were the medium. Overall, the three themes detailed above offer a picture of how popular media framed the vaccine to the public and expresses what media believed was most important to note in response to the vaccine's prescriptions over time. These trends will be important to consider when looking at parental concerns to see if the concerns over time mirrored the common threads found in the government language and popular media.

7. HOW DID THE PARENTAL RESPONSE CHANGE?

Analyzing the parental response to the HPV vaccine throughout time is important because adolescent vaccinations require surrogate decision-making and the parental ideals feed into the opinions of their children. There are three main common concerns from parental blogs and clinical studies within the studied time frame: questions of the vaccine's necessity, the relationship between HPV and sexual behavior, and distrust in science.

7.1. Questions of Necessity

Similar to how media tackled the question of necessity of the vaccine, this was a main parental concern that lessened over time as men became accepted into the vaccination pool. A study of parent's vaccine decisions was conducted by scientists Karen Noakes et al. in late 2006 that included in-depth interviews of 20 American mothers and one father who all expressed

interest in modifying existing compulsory vaccination schedules for their children.[64] As the vaccine protects against strains of HPV that are primarily transmitted through sexual contact, these parents expressed that they do not see the necessity of such a vaccine for young adolescents. One mother was described in the study as "wanting to seek out the vaccine for her 11-year-old daughter eventually but felt that it was currently unnecessary since her daughter was not yet interested in sex."[65] Parents in this study demonstrate the assumption that the vaccine is needed only right before sex starts, not years before, but possibly even that the vaccine would not offer much of a difference to an adolescent's health. Some of these parents also expressed concern that by giving their daughters the vaccine, it removes a potential tool for teaching responsibility which as parents, they believe is their job.[66] This created a tension between vaccination campaigns and parents as it raised concern that parental duties were being encroached upon.

In the midst of this study's result, there have also been some pro-vaccine conservative family groups like Focus on the Family who endorse teaching abstinence until marriage as the best practice against STDs but also acknowledge the risks of getting HPV from nonconsensual relations. The group stated in 2006 that "HPV infection can result from sexual abuse or assault and that a person may marry someone still carrying the virus. This provides strong reasons why someone practicing abstinence may benefit from the vaccine."[67] Even some groups that found the vaccine at odds with their spiritual beliefs had found necessity of the vaccine, which added to the controversy among parental communities.

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[64] Karen Noakes et al., "Parental Response to the Introduction of a Vaccine against Human Papillomavirus," *Human Vaccines* 2, (2006): 243.
[65] Karen Noakes et al., "Parental Response to the Introduction of a Vaccine against Human Papillomavirus," *Human Vaccines* 2, (2006): 243.
[66] Ibid.
[67] Moira Gaul, "Family Research Council Statement Regarding HPV Vaccines," *Family Research Council,* Feb. 21, 2006.

Merck & Co. was the initial producer of the HPV vaccine, Gardasil-4, in 2006. The Merck & Co. television advertisement published in response to the 2006 FDA approval had three parts: One Less, Make the Connection, and Tell Someone. Since girls were the only ones approved to receive the original vaccine, the advertisement focused only on girl's bodies being at risk of HPV. Funded by Merck & Co., this advertisement framed Gardasil as a cancer risk reducing vaccine, not as one preventing an STD that could manifest into cancerous cells. This was potentially to reduce the skepticism and assumptions surrounding STDs. The third part of the advertisement campaign is "Tell Someone" where the goal is to pay the information forward and to arm individuals with the moral, political, and public health leverage that could increase protection against cervical cancer in society.[68] In some versions of the print advertisement, the taglines include "Ideal girls make the right choices" and "The Power to Help Prevent Cervical Cancer is in Your Hands and on Your Daughter's Arm."[69] This last piece of the campaign includes mothers and the idea of surrogate decision making in the public discussion and also makes assumptions that to be an ideal member of society, girls should get the vaccine and mothers should push their daughters to make "the right choice." This ties to the talking point that to be vaccinated is to societally responsible.

Past debates regarding other contraception technologies, such as condoms and Plan B pills have had similar arguments regarding the idea that increasing access can lead to an increase in sexual behavior.[70] This is especially important in the HPV vaccine debate, where parents did not see the link between HPV and cervical cancer prevention as pressing in adolescence. The impact of HPV and sexual behavior was more glaring, leading parents to thinking about teaching

[68] "HPV – Tell Someone," *Merck & Co., Inc,* last modified 2006.
[69] Keith Wailoo, *Three Shots at Prevention: The HPV Vaccine and the Politics of Medicine's Simple Solutions*. Baltimore: Johns Hopkins University Press, 2010. 140.
[70] Karen Noakes et al., "Parental Response to the Introduction of a Vaccine against Human Papillomavirus," *Human Vaccines* 2, (2006): 246.

abstinence rather than vaccination for protection. In a 2014 study, researchers surveyed a sample of 1,504 parents of adolescents between the ages of 11 and 17 years old and 776 physicians to identify what kind of messaging would persuade parents to push for their children's vaccination and what information physicians would prefer offering their patients' parents. The result found that the most popular message was "this vaccine can prevent cancer in the said child."[71] 65% of parents were receptive to the message and 69% of physicians found it the most persuasive to offer parents and this was not affected by the parents' race, education, or child's sex.[72] Shorter messages that identified the link of HPV and cancer, especially cervical cancer, had the greatest beneficial results in pushing parents to vaccinate their children, whereas mentioning sexual behavior and transmission risks did not reap as favorable results.[73] The strength of the language was also important in pushing for vaccination because it demonstrated greater confidence the doctor had in the results of the vaccine. These results are reflected in the changed prescription language between 2006-2016. The study also showed that emphasizing the direct link between cervical cancer and HPV prevention and pointing out that the vaccine could yield fewer future abnormal pap smears best translated the necessity of the vaccine.

It should be noted that parental concerns surrounding the necessity of the vaccine at a young age was not addressed beyond the FDA statements that "vaccination should occur before the onset of sexual activity."[74] This continues to be a parental concern now as health agency language and popular media have not given more reasons for the proposed age of inoculation.

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[71] Karen Noakes et al., "Parental Response to the Introduction of a Vaccine against Human Papillomavirus," *Human Vaccines* 2, (2006): 246.
[72] Teri Malo et al., "Messages to Motivate Human Papillomavirus Vaccination: National Studies of Parents and Physicians," *Cancer Epidemiol Biomarkers Prev.* 25, no. 10 (2016): 1385.
[73] Ibid., 1389.
[74] Department of Health and Human Services, "June 8, 2006 Approval Letter- Human Papillomavirus Quadrivalent Vaccine, Recombinant," *Food and Drug Administration,* June 8, 2006.

7.2. Relationship between HPV and Sexual Behavior

Concerns regarding the potential for the vaccine to increase sexual promiscuity in young females was another prominent theme among parents. As demonstrated in section 6.3., much of popular media aimed to demonstrate the importance of taking sexual precautions even if one was not partaking in sexual practices and towards disproving the myth that the vaccine would lead to an increase in risky sexual behavior. In Karen Noakes et al.'s study, the parents believed that their daughters were better off learning responsibility from safe sex or abstinence practices instilled upon them from their families and that sexual health is tied to morals that parents should instill.[75] If their daughters were to get the vaccine, parental power to teach sexual protections could decrease, which parents felt could increase sexual behaviors that could lead to "unwanted consequences." This risk pushed parents to doubt the vaccine, especially if pap smears could detect cancerous cells and the fact that cervical cancer would not develop for decades.[76]

In 2016, the National HPV Vaccination Roundtable and Vaccinate Adolescents Against Cancers program convened two national meetings at the American Cancer Society. The goal of these meetings was to identify how to communicate to parents about the HPV vaccine to increase vaccination uptake through catered messaging online and through physicians. A main worry was that the disease it was protecting against was sexually transmitted, whereas abstinence could have a similar protection effect without requiring inoculation.[77] The study shows that main concerns in the parental community have stayed constant since 2006, but vaccine safety has increased in influence compared to the previous common concerns between the vaccine and the

[75] Karen Noakes et al., "Parental Response to the Introduction of a Vaccine against Human Papillomavirus," *Human Vaccines* 2, (2006): 245.
[76] Ibid., 246.
[77] Rebecca Perkins, "Engaging parents around vaccine confidence: proceedings from the National HPV Vaccination Roundtable meetings," *Hum Vaccin Immunother*, no. 15 (2018): 1639.

risk of increasing sexual promiscuity. The study ties this increase to the rise of anti-vaccination rhetoric through social media, creating increased skepticism in parental communities.

This study outlined changes that were made to parental communication, such as the need for doctors to adopt gender neutral language when recommending HPV vaccination to parents to lower the connection between the vaccine and sexuality or promiscuity.[78] This is similar to how the FDA changed the language between the 2010 and 2016 prescriptions. This is especially important considering that cervical and anal cancers are two of the most prevalent cancers stemming from HPV infections which have been linked in the media to sexual promiscuity for females and sexual relations between men. A topic that has gained prevalence in parental concerns over time is the rise in government vaccination mandates to attend public school, an idea that continues in court battles today and has increased concerns over parental autonomy.

7.3. Distrust of Science

Another common theme among these parents is that they see the HPV vaccine campaign as a large marketing push, and therefore lowering the medical value of the vaccine. This concern stems from the fact that the vaccine was heavily marketed by its producer at the onset of its FDA approval.

As mentioned above, in 2006 Merck & Co. created a three-part television campaign focused on framing Gardasil as a risk reducing vaccine from cancer, not as one preventing an STD that could manifest into cancerous cells. This was potentially to reduce the skepticism and assumptions surrounding STDs.

The “One Less” campaign starts by clearly outlining that by taking Gardasil, girls would be “one less” person at great risk of developing cervical cancer and that it is their responsibility as individuals to take on this vaccine to protect themselves and society. The advertisement

[78] Ibid., 1640.

presented adolescents from diverse backgrounds saying the tagline and pushing the vaccine as the right tool for protection from cervical cancer, rather than from consequences of unprotected sex.[79] The film advertisement presents the vaccine as empowering for women as it protects them from future risks of cervical cancer and their future families, because it pushes them to take care of their reproductive systems young. They are therefore making their bodies "less risky" by empowering themselves with both knowledge and biological protection.[80] One key piece of this campaign is that it does not mention HPV as the main target of the vaccine, but cervical cancer, which brushes over the idea of protection against an STD, like how popular media did in 2006.[81] This advertisement also emphasized the binding of a mother and daughter by showing images of the girls getting vaccinated in a family unit, but does not allow for sexuality to be explored.

The second part of the TV Public Service Announcement and Advertisement campaign from Merck & Co. was titled "Make a Connection." The goal here was to tell stories of survivors of cervical cancer and connect women together through their risks of developing the disease due to their reproductive bodily similarities.[82] These campaigns also used celebrities, such as Eva Longoria, to get a stronger connection between women across all races, as all women had equal risk of getting HPV. The goal of this advertisement was to open conversations of vaccines and to make the risks of HPV more widely known so that the vaccine could be seen as pertinent to women's lives. However, one noted idea parental communities noticed from the first two pieces of this advertisement was that Merck & Co. attempted to demonstrate an idea of unity amidst all women to get the vaccine but not all women had the same resources to access the vaccine.

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[79] "Gardasil - One Less 1," *Merck & Co., Inc,* last modified 2006.
[80] "Gardasil - One Less 1," *Merck & Co., Inc,* last modified 2006.
[81] Keith Wailoo, *Three Shots at Prevention: The HPV Vaccine and the Politics of Medicine's Simple Solutions.* Baltimore: Johns Hopkins University Press, 2010. 131.
[82] Malika Redmond, "A Critical Discourse Analysis of the Marketing of Merck & Co.'s Human Papillomavirus Vaccine Gardasil," *Georgia State University*, (2011).

Therefore, parents felt that the marketing brushed over the financial impediments to getting all doses of the vaccine, making the vaccine seem profit driven instead of focused on protecting girls.[83] The conversation was now to reduce the risk of cervical cancer by way of HPV, and that cervical cancer risk is what connects women together, not the risk of HPV.

This marketing push feeds into the third common concern among these parents: that the review and development process of the vaccine was more profit than medically driven, causing a distrust of science. One mother compared the HPV vaccine as if she would be "putting birth control in [her] child's orange juice, just in case."[84] Another parent expressed "[she felt] things are rushed through so fast to get on the market without due diligence done in safety testing."[85]

These campaigns made up the first Gardasil advertisement and increased public awareness of its availability, and its taglines became associated with the vaccine in the future as well as became infused with perceptions of the illnesses the vaccine protects against. However, the campaign did not address sexual protection or the possibility that males can use the HPV vaccine to not only protect women from risks of cervical cancer but also themselves from other cancers, similar to what the FDA language lacked in 2006. By focusing on females, the advertisement is placing the burden of health care protection on females, similar to how the FDA language in the 2006 report did. Sexuality is also not mentioned in this campaign; by excluding other members of the population, it is insinuating that women are the only ones at great risk of catching cancer-causing HPV. This countered articles at the time that were pointing to males benefiting from HPV vaccination, causing confusion among parents and adding a layer of distrust of the information that was being put forth.

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[83] Ibid.
[84] Keith Wailoo, *Three Shots at Prevention: The HPV Vaccine and the Politics of Medicine's Simple Solutions*. Baltimore: Johns Hopkins University Press, 2010. 245.
[85] Ibid.

Another important absence from the advertisement, notably in the "Make a Connection" piece, is the differing accessibility to the vaccine depending on one's race or income levels. The advertisement pushed for all women to get the vaccine and showing that all women have the same risk of getting HPV but did not mention that access is not the same across all women. The advertisement also did not offer resources women can use to find a provider and did not address that not all women have equal abilities to get the vaccine, especially given its 3-dose schedule (at the time) and high price tag. This focus on just pushing the vaccine, and not offering resources for differing communities demonstrated a lack of awareness from the company regarding accessibility. This advertisement feeds into the large marketing campaign that surrounded the HPV vaccine, and since they were pushed by the manufacturers, parents took to seeing the vaccine as more of a marketing stunt. This fed into their concerns around distrusting science because it was coming from a source who would be making a profit from vaccination.

7.4. Overall Trends

Overall, some parental concerns change slightly over time, especially towards the necessity of the vaccine, but others such as distrust of science and the link between vaccination and increased promiscuity have continued from 2006-onwards. These trends are like those found in the analysis on CDC/FDA language and the focus of the vaccine in popular media. This demonstrates that over time, especially with the acceptance of male vaccination, the vaccine has been shown to offer adolescents greater long-term benefits than risks.

However, the intersection between HPV's transmission and some parental concerns regarding sexuality have continued to permeate, even as CDC/FDA language has moved away from designating HPV as an STD and towards it being just a pre-cursor to cancers. These concerns regarding the possibility of the vaccine instigating promiscuity are centered around

daughters, which fits the themes pulled out from the CDC/FDA language that sexual health is centered around females, even if a larger proportion of males carry the virus. With the HPV vaccine being approved in 2006 for females only, this centered the arguments for and against the vaccine around female health, to a point where even when male vaccination came to fruition, it was mainly to protect women.

8. STS DISCUSSION

Overall, analysis regarding the HPV vaccine over the last 15 years demonstrates two main assumptions within the vaccine's recommendations. The assumptions that women's health requires a lower burden of proof than men's and that women need to take responsibility for the sexual health of society are embedded within the regulations, forming the technical code. Although the burden of women's sexual health changed in 2016, the former underlying assumption impacting the importance of women's and men's sexual health still presents itself, both in public media focus and in parental concerns. This study does not conclude why parental concerns were focused on what they were and whether these ideas are causing lower than expected vaccination rates, but they do point to dissonance in communication between scientists and parents.

The ideas pulled out from popular media and medical reports line up to concerns stemming from questions due to the CDC/FDA language, but parental concerns do not. The connection between vaccination and promiscuity is not addressed in the original language, even the relationship between HPV and sexual transmission is limited and removed over time. However, it has been a main parental concern surrounding the vaccine over time, especially revolving around female promiscuity. This points to a key cultural effect between the vaccine's initial focus on women and how it was translated to parents.

One key part not addressed by the debate is how transgender patients are viewed in this discussion. The earlier CDC and FDA prescriptions state gender as a binary construct, whereas the 2016 update solely states adolescents as a communal group. The impact that this cervical cancer focused discussion had on transgender individuals with cervixes is not addressed and is a topic to analyze in future research.

9. INTRODUCTION TO COST-EFFECTIVENESS

As pointed out in section seven, distrust of the vaccine due to its marketing was prevalent, especially with the vaccine being sold at a record high price for an immunization. To best understand parental concerns, this section analyzes whether obtaining the vaccine is cost-effective in reducing cancer cases and their associated costs. This section of the paper will explore the economic effectiveness of vaccinating adolescents against HPV at the 2018 rate, as well as the effectiveness of fully vaccinating individuals using a present discounted value model. I will analyze if the marginal cost of every full set of the vaccine (two-dose) administered to adolescents outweighs the marginal benefit it offers to those receiving it. The marginal cost will be defined by the sum of average market price of full vaccination and the marginal benefit will be defined by future health care and mortality costs prevented.

The above values will be defined using established literature and publicly available data regarding rates of vaccination, the average age associated with the onset of cancer, and the rate of return provided by vaccination. Calculations will be conducted for both men and women, as they have different associated illnesses from HPV, and will be estimated for vaccine administration ages ranging from 13 to 17 years of age. The model will use the HPV vaccination rate data from the CDC's annual teen immunization surveys between 2008 and 2018, and the current literature in section 10 will define the other pieces of information that will be calculated.

Present discounted value calculates how much the cost of medical expenses or mortality a certain period in the future is worth in today's dollars. To define the cost of loss of life due to an HPV associated cancer, this model will use the income approach.[86] This approach will be detailed further in section 11, with the goal of quantifying a human life using the estimated value

[86] J. Steven Landefeld and Eugene P. Seskin, "The Economic Value of Life: Linking Theory to Practice," *AJPH* 72, no. 6 (1982): 561.

of labor income that the deceased would have earned over their remaining lifetime had their untimely death not occurred. Economically, this model allows for analysis of whether the campaign to offer every adolescent a two-dose HPV vaccine is cost-effective in preventing associated cancer cases and fatalities. The analysis aims to answer the policy question of whether funding should be geared towards the administering this vaccine or other health care measures, such as providing payment for cancer treatments or different safe sex education programs.

This question is important to analyze for two reasons: the decreasing trends in United States associated cancer rates and the vaccine's high price. In other words, is the high price of inoculation justified if cancer rates are falling before the vaccine's effects have kicked in?

A. **Falling Cervical and Oropharyngeal Cancer Rates:** Over the past two decades, cervical cancer case and death rates have decreased, with the rate of new cases falling from 8.0 per 100,000 women in 2007 down to 7.0 per 100,000 women in 2018.[87] In parallel, the cervical cancer death rate fell from 2.6 per 100,000 women in 2007 down to 2.2 per 100,000 women in 2018.[88] Thus, despite the vaccinated population being too young to have received the vaccine's benefits, cervical cancer rates and fatalities have decreased. As rates have decreased before the vaccinated population has reached the average age (mid-forties) at which women are diagnosed with cervical cancer, the question of whether the campaign is cost-effective, and whether this campaign is the best way to continue this downward trend, becomes pertinent. Oropharyngeal cancer rates in men have gone from 17 cases per 100,000 men in 2007 to 18 cases per 100,000 men in

[87] "United States Cancer Statistics Changes Over Time: Cervix," *Centers for Disease Control and Prevention,* last modified 2018.
[88] Ibid.

2018.[89] Oropharyngeal cancer death rates in men have stayed stable at 4 deaths per 100,000 men between 2007 and 2018.[90] Thus, it may be the case that the HPV vaccine would fail a cost benefit analysis for one sex (female) but pass for the other (male).

B. **Substantial Vaccination Cost:** The vaccine's average price tag of $192.61 (with either private health insurance or Medicaid) per dose, even though prevention screening is still recommended with inoculation, potentially makes the vaccine inaccessible to lower income individuals. This begs the question of whether funds should be steered towards different uses, such as different sexual education, birth control alternatives, or research towards treatment of other fatal diseases.

The cost-effective analysis will continue like so: I will summarize the current literature on economic costs and benefits of the HPV vaccine to society. I will then provide background on the vaccine's protection rates, explaining how the research fits in with current literature while offering a new perspective on the issue and describing the method and data used to explore the research question. I then demonstrate the calculations and results of the analysis, provide a conclusion on the findings, and offer potential avenues for future research.

10. COST-EFFECTIVENESS LITERATURE REVIEW

The established literature this paper examines is categorized into five different subsections: Studies informing how to utilize the present discounted value model, studies on calculations of the value of a human life, studies analyzing cost-effectiveness of different policies for HPV vaccination in the United States, studies analyzing the cost-effectiveness of HPV vaccination for men, and studies analyzing the HPV vaccine's cost-effectiveness outside

[89] "United States Cancer Statistics Data Visualizations: Oral Cavity and Pharynx Cancer in Males." *Centers for Disease Control and Prevention,* last modified 2018.
[90] Ibid.

the United States. The papers in each of these categories will help provide and calculate assumptions for missing information in the model.

10.1. Present Discounted Value

In their article, Baudouin Standaert et al. outline how to assess the economic value of vaccinations based on the different stakeholders involved in policy decision making. Traditionally, cost-effectiveness analysis has been used to calculate the incremental cost-effectiveness ratio (ICER) to assess whether extra payment for a health benefit obtained is good value for the price from the perspective of the payer.[91] Previously, vaccines have been evaluated in terms of whether they reduce risk for losing quality-adjusted life-years (QALY). In earlier studies of vaccines, price erosion (consistent loss of price over time) occurred in a short period of time. However, this has not been observed in newer vaccines, particularly for HPV, because modern vaccines feature more complex research and development processes. Thus, a more dynamic model of cost-effectiveness should be used for modern vaccines.[92] The fiscal health model of present discounted value used in Standaert's study analyzes the economic value of a vaccine that does not produce benefits for a delayed period.

10.2. Statistical Value of a Human Life

Calculating the statistical value of a human life is necessary for analyzing whether the cost of inoculation is lower than the costs of loss of life from cancers the vaccine would increase protection against. In their paper, Steven Landefeld and Eugene Seskin, detail two methods of

[91] Baudouin Standaert, "How to Access for the Full Economic Value of Vaccines? From past to present, drawing lessons for the future," *Journal of Market Access & Health Policy* 8, no. 1 (2020).
[92] Ibid., 4.

calculating the value of a human life, the human capital and adjusted willingness-to-pay approaches.[93]

The human capital approach assumes that an individual's life is measured by future production potential at present discounted value, where the net loss to society of an individual's death is the difference between one's earnings and consumption expenditure. This approach contains two limitations: There is strong sensitivity to different discount rates and reliance on income to determine one's value, which gives unemployed and retired individuals a zero value.[94]

The willingness-to-pay approach attempts to rectify some of these limitations by using principles similar to the potential Pareto improvement principles.[95] This model determines what a population at risk is willing to pay for small reductions in the probability of their death while including measures for non-labor and labor income, value of leisure, and aversion to risk.[96]

Ideally, proper calculations of the value of a human life use relevant income and non-market measurements but labor earnings are the only readily available measurement by age and sex. Therefore, this paper will follow the human income approach to putting a value on a human life. In particular, this study uses the disposable personal income of the average individual fitting the model's characteristics to measure the value of a life.

A paper that conducts a model regarding the impact of treatment over future cases of an illness is Robert Brent's. In his paper examining life expectancy in nursing homes, Robert Brent uses a value of statistical life model that informs how this paper's model will calculate the value of lives lost to the examined cancers. Brent tests whether nursing home residents being sicker leads to lower survival rates of dementia patients in nursing homes. He finds that the value of

[93] J. Steven Landefeld, and Eugene P. Seskin, "The Economic Value of Life: Linking Theory to Practice," *AJPH* 72, no. 6 (1982): 556.
[94] Ibid.
[95] Ibid., 557.
[96] Ibid.

lost years of life per individual living in a nursing home is $1.7 million per person.[97] This number is based on labor market data, takes an equity approach using a 3% discount rate, and uses remaining life expectancy in years to estimate the value.[98] This paper is useful to contextualize the value of a statistical life approach that this HPV study will take on to measure the significance of life lost to the studied HPV-associated cancers.

10.3. Cost-Effectiveness Inside the United States

To analyze the potential benefits of the vaccine, one need first place a numerical value on the medical costs attributable to HPV cancers. In their paper, Harrell Chesson et al. examine estimates of the direct medical costs attributable to HPV to illustrate the potential benefits of vaccination.[99] They find that the medical cost burden of preventing and treating HPV-related disease in 2010 was $8.0 billion, $0.4 billion of which was for treating cervical cancer, $0.3 billion of which was for treating oropharyngeal cancer (OPC), and $6.6 billion of which was for screening and follow-ups (not including vaccination costs).[100] The authors used pap smear incidence and cost data from Kaiser Permanente Northwest and the National Breast and Cervical Cancer Early detection Program and cost of cancer treatment data from private medical claims data.[101] As $6.5 billion was associated with follow-up costs of cervical cancer screening, the authors conclude that HPV vaccination could be cost-effective in removing some of these follow-up costs due to its high success rate. Chesson's paper offers numerical estimates of cancer treatment costs that can be used in this model, though this paper will not directly replicate Chesson's effectiveness calculations.

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[97] Robert J. Brent, "Life expectancy in Nursing Homes," *Applied Economics* (2021): 4.
[98] Ibid., 16.
[99] Harrell Chesson et al., "Estimates of the annual direct medical costs of the prevention and treatment of disease associated with human papillomavirus in the United States," *Vaccine* 30, no. 42 (2012): 6016.
[100] Ibid.
[101] Ibid., 6019.

In her article, scientist Partha Basu notes that HPV vaccine clinical trials demonstrate that the cervical cancer prevention strategy with the lowest incremental cost-effectiveness ratio per QALY is combining HPV vaccination at age 12 with triennial conventional cytologic screening.[102] This offers a baseline estimate of cost-effectiveness, but the article also mentions that this result could change due to price and this is something that this present HPV study will explore further. Basu's article was published prior to the acceptance of the 9vHPV vaccine that will be used in the present study, meaning that the calculations that will be conducted will provide updated results for cost-effectiveness. A useful part of Basu's paper was that it offered different sources that will be examined later in the paper and vaccination efficacy values that are used in this model.

In a separate meta-analysis of the cost-effectiveness of HPV vaccination in the US, Joshua Pink evaluated the economic models that have been performed to address this theory. A key result of the analysis was that the new 9vHPV vaccine (which incorporates a larger number of strains), has been shown to be more cost-effective than the previous two HPV vaccines available in the United States.[103] This sentiment is echoed by David Durham et al. in their study, where on the national level, the 9vHPV vaccine was cost-effective compared with the previous bivalent and quadrivalent vaccines, despite the higher cost per dose.[104] Durham et al. takes their analysis a step further to state that the expansion of coverage would have the greatest health impact in those states with the lowest coverage due to the decreasing marginal returns of herd immunity. In fact, the study deduces that with 9vHPV, coverage would reduce incidence by 73%

[102] Partha Basu et al., "Efficacy and Safety of Human Papillomavirus Vaccine for Primary Prevention of Cervical Cancer: A Review of Evidence from Phase III Trials and National Programs," *South Asian J Cancer* 2, no. 4 (2013): 188.
[103] Joshua Pink et al., "Cost-Effectiveness of HPV Vaccination: A Systematic Review of Modelling Approaches," *PharmoEconomics* 34, (2016): 857.
[104] David P. Durham et al., "National- and State-Level Impact and Cost-Effectiveness of Nonvalent HPV Vaccination in the United States," *PNAS* 113, no. 18 (2016): 5107.

and mortality by 49% compared to equal vaccination rates with the previous two vaccines and would yield 65,000 QALYs.[105] The study also finds that universal HPV vaccination coverage in the United States would be cost-effective at a willingness-to-pay of $159,000 per QALY. These studies not only provide insight into the benefit of using modern HPV vaccine data where only the 9vHPV vaccine is available but offer a benchmark for which to compare the data and model results from this study.

In a cost-effectiveness study between the three types of HPV vaccine that have been available since 2006 (bivalent, quadrivalent, and 9-valent), the 9-valent vaccine has been deemed as the most cost-effective version of the HPV vaccine.[106] The study showed that the quadrivalent vaccine was more cost-effective and medically effective in protecting against HPV related cancers than the bivalent vaccine was.[107] A 2016 UK study found that the incremental cost-effectiveness ratio of quadrivalent vaccination was found when a QALY is valued at £30,000 with its main benefit found in preventing anogenital warts linked to HPV strains 6 and 11.[108] During a 20-year study comparing cross-protection against HPV between the vaccines, the 9-valent vaccine had a cost per QALY of $12,208 compared with a $15,528 cost per QALY for the quadrivalent vaccine.[109] However, the price difference needed to be negligible in these studies, something that did not occur in 2016 when the 9-valent vaccine was rolled out in the United States.[110] This detail is not addressed in current time as the medical community has deemed the quadrivalent and bivalent vaccines no longer comprehensive HPV vaccines for adolescents, and

[105] David P. Durham et al., "National- and State-Level Impact and Cost-Effectiveness of Nonvalent HPV Vaccination in the United States," *PNAS* 113, no. 18 (2016): 5109.
[106] David Yang, "Update on the new 9-valent vaccine for human papillomavirus prevention," *Can Fam Physician* 62, no. 5 (2016): 399.
[107] Mark Jit et. al., "Comparing Bivalent and Quadrivalent Human Papillomavirus Vaccines: Economic Evaluation based on Transmission Model," *BMJ* 343, (2011).
[108] David Yang, "Update on the new 9-valent vaccine for human papillomavirus prevention," *Can Fam Physician* 62, no. 5 (2016): 400.
[109] Ibid.
[110] Ibid., 401.

the 9-valent vaccine is currently the only HPV vaccine available in the United States. An additional factor that was not addressed in this comparative study, is that the dosage schedule for the new 9-valent vaccine is two rather than the previous three doses needed under the quadrivalent and bivalent vaccines, cutting the overall cost of vaccination.[111]

Another study informing how to determine health and economic outcomes of vaccinating a population was conducted by Jane Kim and Sue Goldie. In this study, demographic data of pre-adolescent females in the United States was used to determine health outcomes after vaccination. The results found that the vaccine was beneficial in averting other HPV-related cancers, genital warts, and juvenile-onset recurrent respiratory papillomatosis. The study also found that under the assumption that the vaccine provided lifelong immunity, the cost-effectiveness ratio for a 12-year-old female was $43,600 per QALY gained. This is compared to the practice of just screening for cervical cancer, and it is important to note that this study analyzed the effectiveness of the older vaccine that is no longer used in the United States.[112] By examining the effects of waning immunity after 10 years of vaccination, the cost of vaccination exceeded $140,000 per QALY, highlighting the importance of including the vaccine's efficacy in this paper's analysis. In this dynamic modeling approach, the discount rate used was 3% annually, and the benefit of this model is that it estimates the direct health benefits to people that were vaccinated as well as the unvaccinated benefitting from herd immunity.[113] This study delves further into the impacts of screening changes; however, the present research paper will only be including the effects of a vaccination program, holding the current cervical cancer screening practices constant. Another limitation of the present analysis, which is highlighted below, is that it does not include

[111] Clare Tanton et. al., "Human Papillomavirus in young women in Britain…" *Papillomavirus Research* 3, (2017): 37.
[112] Jane J. Kim and Sue J. Goldie, "Health and Economic Implications of HPV Vaccination in the United States," *N Engl J Med.* 359, no. 8 (2008): 821.
[113] Ibid., 826.

discussions of what would constitute this vaccine being cost-effective for men, especially if cancer screening for male HPV-related cancers is less prevalent in a common medical physical.

10.4. Cost-Effectiveness for Men

Even though the vaccine has had a longer history of use in females, oropharyngeal cancer caused by HPV has high prevalence in males. In their study, Marc Ryser et al. use an agent-based modeling framework to assess the impact of coverage-dependent marginal vaccination costs to determine the value of vaccinating adolescent males in addition to females.[114] They use a sample of sexually active adolescents, divided equally between males and females, and run simulations to determine the infection and transmissibility of HPV without vaccination. Then simulations are run that factor in vaccination at its 2009 rate to identify the costs and benefits of the program.[115] Ryser et al. examine this by running a model where vaccine uptake levels are negatively correlated with sexual activity, and another where uptake is positively correlated, as there is the assumption that vaccination impacts future sexual activity. The limitation of this method is that sexual activity for adolescents is not numerically quantified in this paper, meaning that relationship and sexual relations patterns could change the results. The paper does overall find that the male marginal costs of vaccination are 25-50% higher than the female marginal cost therefore indicating that the most cost-effective vaccination policy so far is vaccinating only women.[116] This is a jumping off point for what I can expect to find in the current paper's study.

In fact, Harrell Chesson et al. reiterate this finding in their paper, finding that cost-effectiveness of male vaccination depends on female vaccination rates and that increasing female

[114] Marc D. Ryser et al., "Impact of Coverage-Dependent Marginal Costs on Optimal HPV Vaccination Strategies," *Epidemics* 11, (2015): 33.
[115] Ibid., 34.
[116] Ibid., 38.

vaccination coverage is probably more efficient.[117] The limitation is that this comparison draws a cost-effectiveness distinction between female and male vaccination campaigns but does not answer or provide evidence that either are cost-effective by themselves.

In a study done in Italy to determine the cost-effectiveness of HPV vaccination in adolescent males, Ersilia Sinisgalli et al., conducted a systematic meta-analysis. Eleven articles were identified by the criteria set and their data collected to find that only 53% of the results deemed vaccinating males to be cost-effective.[118] The rest found it only to be effective for women to prevent cervical cancer. This paper indicates that male vaccination is potentially not as cost-effective, which will be tested in this current paper, but that the subject is also not as studied as the cost-effectiveness for adolescent females.

In their meta-analysis, Mohamed-Béchir Ben Hadj Yahia et al., found a result similar to Sinisgalli et al.'s, but indicated that targeting vaccination of homosexual men could be cost-effective.[119] 17 studies and 12 different models were analyzed and found that if cervical cancer is the only targeted disease for the vaccine, vaccinating men and women reaps a $64,764/QALY benefit compared to vaccinating only women.[120] When the potential benefit of all HPV-related diseases was factored into the model and there was a 75% vaccination rate, the estimated ICER went up to $202,785/QALY, exceeding the cost-effective threshold set by the World Health Organization of $50,000/QALY.[121] The results point to cost-effectiveness of vaccinating males being present only if female vaccination rates are lagging behind 40%, something that will be

[117] Harrell W. Chesson et al., "The Cost-Effectiveness of Male HPV Vaccination in the United States," *Vaccine* 29, no. 46 (2011): 8448.
[118] Erisilia Sinisgalli et al., "HPV Vaccination for Boys? A systematic review of economic studies," *E&P* 39, no. 4 (2015): 56.
[119] Mohamed-Béchir Ben Hadj Yahia et al., "Extending the Human Papillomavirus Vaccination Programme to Include Males in High-Income Countries: A Systematic Review of the Cost-Effectiveness Studies," *Clin Drug Investig* 35, (2015): 474.
[120] Ibid.
[121] Ibid., 475.

explored in further literature. This offers a foundation for which to interpret this paper's results when the male cost-effectiveness model for preventing OPC cases and deaths is conducted.

10.5. Cost-effectiveness Outside the United States

In a meta-analysis by Rashidul Mahumud et al., cost-effectiveness across 12 studies was compared by examining whether the ICER/DALYs (disability adjusted life years) averted was less than three times the country's per capita Gross Domestic Product (GDP).[122] Nine studies examined this question using a dynamic model similar this current paper's model, two used a static model, and one used the Markov model. In all, ten of the featured studies concluded that the 9vHPV vaccine was cost-effective, four of which found this true in gender-neutral vaccination policies.[123] Overall, this article details an overwhelming consensus in the economic community is that the HPV vaccine is cost-effective for adolescent females, but it does not detail whether this is true for males. This study will recreate the study analyzing the effects on females as well as performing a study on men both with full vaccination and current vaccination rates.

As described by parental concerns in section seven of this paper, necessity of the vaccine with the prevalence of pap smears was debated. In a study analyzing whether a national HPV screening program alone or paired with an HPV vaccination program was cost-effective in Nigeria, Obinna Ekwunife and Stefan Lhachimi created a microsimulation framework following one million women.[124] To identify the suitable cervical cancer prevention policy, an incremental costs-effectiveness ratio (ICER) was used to represent the average incremental cost associated with one additional disability adjusted life year (DALY) averted when discounted at a rate of

[122] Rashidul A. Mahumud et al., "Cost-Effectiveness Evaluations of the 9-Valent Human Papillomavirus (HPV) vaccine: Evidence from a Systematic Review," *PLOS ONE*, (2020).
[123] Ibid.
[124] Obinna Ekwunife and Stefan Lhachimi, "Cost-Effectiveness of Human Papillomavirus (HPV) vaccination in Nigeria: A Decision Analysis Using Pragmatic Parameter Estimates for Cost and Programme Coverage," *BMC Health Services Research* 17, (2017).

3%.[125] The result indicated that the paired program resulted in an aversion of $7,930/DALY which proved cost-effectiveness against the threshold of $9,610/DALY set by the authors.[126] However, the screening program alone did not prove to be cost-effective in Nigeria. This study offers insight into how cost-effectiveness of HPV vaccination can be measured in a developing country and what results could be found by running a similar analysis in the United States.

A similar study was conducted by Ariel Bardach et al. to study the cost-effectiveness of implementing a bivalent or quadrivalent vaccination scheme in comparison to the current policy of vaccination in Venezuela. This study used a Markov cohort model that simulated the natural history of HPV in cervical cancer incidence while including just screening practices vs. with quadrivalent or bivalent vaccinations.[127] Expected costs of cancer screening and treatments were estimated using a micro-costing approach using data from the Oncologic Institute in Caracas, Venezuela. The health outcomes in this paper were measured in QALYs and number of cancer cases and deaths. An important contribution of this paper is that the probability of a vaccine being cost-effective depends heavily on the pricing, which will be considered in this research paper's discussion. Another limitation of this paper, like other papers described above is that male cost-effectiveness was not considered.

11. MODEL

As explained by health economist David Meltzer, expected utility provides a framework for analyzing the effects of changing medical expenditures on one's lifetime utility. Medical interventions, such as immunization, affect one's expected utility by changing survival

[125] Obinna Ekwunife and Stefan Lhachimi, "Cost-Effectiveness of Human Papillomavirus (HPV) vaccination in Nigeria: A Decision Analysis Using Pragmatic Parameter Estimates for Cost and Programme Coverage," *BMC Health Services Research* 17, (2017).
[126] Ibid.
[127] Ariel E. Bardach et al., "Health Economic Evaluation of Human Papillomavirus Vaccines in Women from Venezuela by a Lifetime Markov Cohort Model," *BMC Public Health* 17, (2017).

probabilities and health quality during life and this produces two costs of the intervention.[128] These two costs are the direct intervention cost and the net expenditures due to the change in survival probabilities. Cost-benefit analysis done in this paper uses the utility maximization principle that allocation of resources should produce benefits of the same amount of extra utility gained per individual. The idea of diminishing marginal returns to utility will also be used in this paper because there is a level of herd immunity (85% vaccination) that can be reached where vaccinating additional individuals produces a significantly lower societal benefit. The goal of this study is to analyze whether investing in full United States adolescent vaccination offers benefits producing at least the same utility as the next best option.

This study also encapsulates a social dilemma where the decision to vaccinate entails a choice between taking on a substantial cost now or getting an illness with a larger cost of treatment later. In a classic social dilemma scenario, individuals are better off defecting regardless of what the other does. However, if all individuals defect, everyone is made worse off than if all cooperated, which would mean no inoculation due to its high price tag. Therefore, discounting delayed outcomes will enable cost-effectiveness to be analyzed to see whether the individual and societal benefit of vaccinating everyone is economically effective, especially if the benefits would not be reaped for several decades.

Economically, the principle of discounting can apply to healthcare program analysis, especially those at which most of the costs are incurred presently and benefits occur farther in the future.[129] The idea of discounting is based on the economic concept of "positive time preference" meaning that due to an assumption that humans are rational, society prefers to benefit from

[128] David Meltzer, "Accounting for future costs in medical cost-effectiveness analysis," *Journal of Health Economics* 16, (1997): 37.
[129] Johan L. Severens and Richard J. Milne, "Discounting Health Outcomes in Economic Evaluation: The Ongoing Debate," *Value in Health* 7, no. 4 (2004): 397.

consumption sooner rather than later.[130] In this model, uniform discounting will be used as the impact of time is independent of the nature of future events and to preserve consistency in costs and benefits that yield outcomes at different points in time. Current practice in economic evaluation is to use a uniform discount rate of 3% for the first 30 years of analysis and that the rate may decrease over a greater length of time due to diminishing marginal utility of benefits. As discussed in section nine, most previous literature has utilized a discount rate of 2-4% when measuring benefits and costs of implementing a healthcare program, and an average of 3% is the rate that this present study will use.

In this study's model, we analyze the benefit of treating a group of 100,000 people by medical and mortality costs saved versus the cost of the full-dose vaccine administration. My base case for this analysis will be the cost-effectiveness if no female or male is vaccinated. In addition, I will discount back the benefits received in cervical cancer prevention a certain number of years after the vaccine (defined in the next section) to today's dollars. The benefit is measured as the total cost of treating all patients with cervical cancer minus the cost of life lost in the patients that die of the ailment discounted back a certain number of years. The cost of life lost is measured between the average age of cervical cancer diagnosis for United States women to the average life expectancy of United States women. This model will serve as a baseline to estimate cost-effectiveness of the vaccine for women, after which the current rate of vaccination and full vaccination rate will also be tested for the vaccine's cost-effectiveness. I will then test all three cases for the remaining ages to see if age of inoculation affects the vaccine's effectiveness.

Once the trial is completed for women, I conduct the same model for men but by using the incidences and death of oropharyngeal cancer (OPC) in men as it is the most prevalent HPV

[130] Johan L. Severens and Richard J. Milne, "Discounting Health Outcomes in Economic Evaluation: The Ongoing Debate," *Value in Health* 7, no. 4 (2004): 398.

related cancer for men. The assumptions made for the variables used in building and conducting this model are:

I. The number of cervical cancer and OPC cases and deaths for women and men, respectively, are taken from the CDC's Cancer Statistics Data. The total number of women diagnosed with cervical cancer out of 100,000 women in 2007 was 8.0, 3.0 of whom died.[131] The total number of men diagnosed with OPC out of 100,000 men in 2007 was 17.0, 4.0 of whom died.[132] To represent the base-case scenario, the 2007 cancer numbers (before vaccination) will be used. These values will be used in the model to calculate the cost of treatment for all cancer cases and the cost of life lost for the mortal cases.

II. The average age of diagnosis of the individual cancers tested will be taken from the American Society of Clinical Oncology and used to calculate how long the effects of vaccination for each age tested would take to cause an effect. This age of effect will be represented by the average age of cancer incidence (diagnosis), denoted as 49 years of age for cervical cancer in women and 62 years of age for OPC in men.[133][134]

III. The discount rate represents the social opportunity cost of investing in the vaccination program instead of the "next-best" alternative program. A consensus among previous literature detailed in section 10 is to use a 3% discount rate on costs and benefits when measuring cost-effectiveness of healthcare programs.

IV. The cost of death/life lost will be used to measure the benefits of cancer death prevention in this model. The cost of life lost will be the average income one would have earned each year

[131] "United States Cancer Statistics Data Visualizations: Cervix," *Centers for Disease Control and Prevention*, last modified 2018.
[132] "United States Cancer Statistics Data Visualizations: Oral Cavity and Pharynx Cancer in Males," *Centers for Disease Control and Prevention*, last modified 2018.
[133] Cancer.Net Editorial Board, "Oral and Oropharyngeal Cancer: Statistics," *American Society of Clinical Oncology (ASCO)*, last modified 2021.
[134] Cancer.Net Editorial Board, "Cervical Cancer: Statistics," *American Society of Clinical Oncology (ASCO)*, last modified 2021.

from the age of death to the age of retirement (designated as 67).[135] Using data from the United States Census Bureau, the average income of a male between the ages of 45 and 64 in 2018 was $77,878 and the average income of a female between the ages of 45-64 in 2018 was $47,913.[136] These income values are what will be used as a measurement of life lost per year for the current vaccination and full vaccination calculations. The 2007 average income values for women between the ages of 45 and 54 years old was $37,645 and for men between the ages of 55 and 64 years old was $58,800.[137]

a. Although most previous literature have used QALYs to measure value of life lost, this model will assume equal quality of life lost and will value an individual's life without including potential spillover effects. QALYs have also been subject to scrutiny by economists due to the subjective way of quantifying one's value to society.
b. Previous literature shows estimates of annual direct medical costs of preventing and treating HPV-associated diseases, including cervical cancer and OPC. The baseline cost per case of cervical cancer in 2010 U.S. dollars was $38,800 and the baseline cost per case of OPC in 2010 U.S. dollars was $43,200.[138] This model will convert these values into 2018 U.S. dollars for the current-vaccination and full-vaccination modeling, and 2007 U.S. dollars for the no-vaccination model by using the Bureau of Labor Statistics' Consumer Price Index (CPI) for Medical Care.[139] The values can be converted due to the assumption that medical technologies and cost of care have not

[135] The average age of retirement to receive social security benefits is between 65 and 70, depending on the amount of benefits one would like to forgo presently to receive an additional benefit later on. This model will use the age in between this range of 67.
[136] "Source of Income-Number with Income and Mean Income of Specified Type of People 15 Years Old and Over, by Age, Race, Hispanic Origin, and Sex," *United States Census Bureau,* last modified in 2020.
[137] Ibid.
[138] Harrell Chesson et al., "Estimates of the annual direct medical costs of the prevention and treatment of disease associated with human papillomavirus in the United States," *Vaccine* 30, no. 42 (2012): 6017.
[139] "Consumer Price Index for All Urban Consumers: Medical Care in U.S. City Average," *Bureau of Labor Statistics,* last modified in 2021.

changed dramatically in eight years. Therefore, this model assumes that the average cost of cancer treatment has gone up at the same rate as average general medical costs. The CPI calculations are as follows:

Reference Base: 2008-2010
January 2010 CPI: 400.24
January 2007 CPI: 351.07
Index Point Change: $351.07 - 400.24 = -49.17$
Percent Change: $\frac{-49.17}{400.24} = -0.123 * 100 = -12.3\%$
Cervical Cancer Treatment Cost in 2007: $38{,}800 * 0.877 = \$34{,}027.60$
OPC Treatment Cost in 2007: $43{,}200 * 0.877 = \$37{,}886.40$

Reference Base: 2010-2018
January 2010 CPI: 400.24
January 2018 CPI: 484.70
Index Point Change: $484.70 - 400.24 = 84.46$
Percent Change: $\frac{84.46}{400.24} = 0.211 * 100 = 21.1\%$
Cervical Cancer Treatment Cost in 2018: $38{,}800 * 1.211 = \$46{,}986.80$
OPC Treatment Cost in 2018: $43{,}200 * 1.211 = \$52{,}315.20$

c. According to the vaccine database, in 2018 the 9vHPV vaccine's CDC cost was $168.10 and the vaccine's private sector cost was $217.11.[140] For this model, an average price of $192.61 per dose will be used. Since each vaccination in this model is defined as a two-dose set, the total average price of vaccinating an individual is $385.22. A limitation is that the price of the vaccine used in this study will not include considerations of vaccine delivery costs, which could raise the price of administration.

d. The second scenario that will be modelled in this study is whether the vaccine is cost-effective in trying to advance vaccination rates past current levels. The current vaccination levels for up to date (UTD) vaccination in 2018 for adolescent females,

[140] "Vaccine for Children Program (VFC)," *Centers for Disease Control and Prevention*, last modified 2018.

based on the CDC NIS data, was 54% and 49% for males.[141] These are the vaccination rates that will be used to represent the current vaccination rates in the model.

12. DATA

A large piece of the data used in this model are the vaccination rates for adolescents per year broken down into different demographic groups. This data is compiled from the annual National Immunization Survey for Teens published by the Center for Disease Control and Prevention (CDC).[142] This survey is a random-digit-dialed survey of parents or guardians of 20,000 randomly selected adolescents, between the ages of 13 and 17, each year. Every year, the vaccination data of these individuals are compiled into a panel-formatted data set that reports the percentage of the randomly sampled survey respondents who are up to date on a particular vaccine or who, in the case of HPV vaccination, received one dose out of the two recommended. The data also breaks the percentages down by each age between 13 and 17 years old, gender, and for whether they live in a Metropolitan Statistical Area (MSA). Although data has been collected for HPV vaccines since 2011, I will be using the 2018 vaccination data for the vaccination rates of men and women in my model as it is the most comprehensive and recent data.

[141] NIS-Teen Survey, "TeenVaxView Publications and Resources," *Center for Disease Control and Prevention*, last modified 2021.
[142] Ibid.

Table 1. 2018 Vaccination Rates for Males and Females Based on Dose Amount and Age

	2018 Age (years)					Composite (%)
Dosage (Sex)	**13**	**14**	**15**	**16**	**17**	**2018**
1 Dose (Female)	61.1	68.6	70.7	73.5	76.3	69.9
95% CI Upper Bound	65.2	72.5	74.5	76.8	80.0	71.6
95% CI Lower Bound	56.9	64.4	66.5	69.8	72.2	68.1
UTD (Female)	38.9	52.7	54.7	57.5	66.0	53.7
95% CI Upper Bound	42.9	56.8	59.0	61.6	70.1	55.6
95% CI Lower Bound	35	48.5	50.4	53.3	61.8	51.8
1 Dose (Male)	64.0	65.1	68.7	69.2	64.7	66.3
95% CI Upper Bound	67.9	68.7	72.1	73.0	68.5	68.0
95% CI Lower Bound	59.9	61.3	65.0	65.2	60.7	64.6
UTD (Male)	40.9	47.7	53.2	51.8	50.0	48.7
95% CI Upper Bound	45.3	51.8	57.3	56.1	54.3	50.6
95% CI Lower Bound	36.5	43.6	49.1	47.5	45.7	46.8
1 Dose (All)	62.6	66.9	69.7	71.2	70.1	68.1
95% CI Upper Bound	65.4	69.6	72.3	73.8	72.8	69.3
95% CI Lower Bound	59.7	64.1	66.9	68.5	67.3	66.8
UTD (All)	39.9	50.3	54	54.5	57.5	51.1
95% CI Upper Bound	42.9	53.2	56.9	57.5	60.5	52.5
95% CI Lower Bound	37.0	47.3	51.0	51.5	54.4	49.8
Count	3,455	3,641	3,666	3,731	3,342	17,835

Source: NIS-Teen Survey, "TeenVaxView Publications and Resources," *Center for Disease Control and Prevention*, last modified 2021.

13. RESULTS

The first part of the comparison that will be done is calculating how much it costs to vaccinate 100,000 people at the 2018 vaccination rate compared to the costs of treatment foregone and life lost. The values in Table 2 are represented by the following variables:

- Column II represents the age at which the female or male adolescent was fully vaccinated against HPV in 2018.
- Column III represents the costs of cervical cancer and OPC treatment and death foregone by vaccinating at 2018 rates. The cost values for each age and gender are calculated using the below equation:

Equation 1

$$\left[\frac{total\ cost\ of\ treatment}{(1+discount\ rate)^{(average\ age\ of\ cancer\ diagnosis - age\ of\ vaccination)}} * (\#\ of\ people\ with\ cancer\ per\ 100{,}000\ individuals)\right] +$$

$$\left\{\frac{\sum_{n=average\ age\ of\ cancer\ diagnosis}^{age\ of\ retirement-1} ai_n \left(\frac{1}{(1+r)}\right)^{67-n}}{(1+discount\ rate)^{(average\ age\ of\ cancer\ diagnosis - age\ of\ vaccination)}} * (\#of\ people\ dying\ of\ cancer\ per\ 100{,}000\ individuals)\right\}$$

- The above equation represents the calculations for the baseline values. The same equation will then be used with the current vaccination rate and the difference in costs between the two numbers per age and gender are the values displayed in Column III.
- Column IV represents the number of people that would be fully vaccinated in 2018 for every 100,000 people.
- Column V represents the cost of vaccinating the number of people in column IV, calculated by:

$$number\ of\ people\ getting\ fully\ vaccinated\ in\ 2018 * (two\ dose\ vaccine\ price)$$

- Column VI represents the cost ratio between columns III and V, calculated by:

$$\frac{Column\ V}{Column\ III}$$

Table 2. Cost and Benefit Evaluation between Baseline Math and 2018 Vaccination Rates

I	II	III	IV	V	VI
Gender	**Age of Vaccination**	**Treatment and Death Costs Foregone with Vaccination**	**People Getting Vaccines per 100,000**	**Vaccine Cost**	**Cost Ratio Between Columns III and V**
Female	13	$ 102,261.46	38,900	$ 14,985,058.00	14,654
	14	$ 209,179.12	52,700	$ 20,301,094.00	9,705
	15	$ 230,956.71	54,700	$ 21,071,534.00	9,124
	16	$ 260,239.61	57,500	$ 22,150,150.00	8,511
	17	$ 337,943.58	66,000	$ 25,424,520.00	7,523
Male	13	$ 60,556.20	40,900	$ 15,755,498.00	26,018
	14	$ 96,673.49	47,700	$ 18,374,994.00	19,007
	15	$ 128,149.12	53,200	$ 20,493,704.00	15,992
	16	$ 124,501.64	51,800	$ 19,954,396.00	16,027
	17	$ 118,315.20	50,000	$ 19,261,000.00	16,279

Source: The data used to calculate these values were compiled from various sources and explained in the Model section of this paper.

Table 2 demonstrates how much money is expected to have been saved in cervical cancer/OPC treatment and death costs due to the vaccination rates in 2018. The comparison is between the future savings from vaccinating at 2018 rates and if there had been no vaccination. By comparing columns III and V, one can determine that the cost of vaccination at the 2018 rates are between 7,523-14,654 times higher than the costs foregone (depending on the age and gender of the vaccinated individual). Therefore, the vaccination in 2018 was not cost-effective when comparing the treatment and death costs foregone and the 2018 price of the two-dose vaccine.

The second comparison that will be done is comparing the additional costs and benefits of maximizing the vaccination rate by raising the vaccination rate from its 2018 level to 100% of the population. The values in Table 3 are represented by the following variables:

I. Column II represents the age at which the female or male adolescent was fully vaccinated against HPV in 2018.

   a. Column III represents the difference between the costs foregone calculated with 100% vaccination rates and those in Table 2 Column III. The values for each age and gender are calculated using the following steps:

      1. Performing the calculations demonstrated in Equation 1 using the fully vaccinated values.
      2. Taking the difference between the costs calculated in the baseline trial and those calculated in step 1.
      3. Then taking the difference between the values in Table 2 Column III and those calculated in step 2.

   b. Column IV represents the additional number of people that would be fully vaccinated in 2018 for every 100,000 people if the vaccination rates were increased to 100%. Calculated by:

$$(100 - 2018\ vaccination\ rate) * 100{,}000$$

   c. Column V represents the cost of vaccinating the number of people in column IV. Calculated by:

$$column\ IV\ values * (two\ dose\ vaccine\ price)$$

   d. Column VI represents the cost ratio between columns III and V, calculated by:

$$\frac{Column\ V}{Column\ III}$$

Table 3. Cost and Benefit Evaluation between 2018 Vaccination Rates and Full Vaccination

I	II	III	IV	V	VI
Gender	**Age of Vaccination**	**Costs Foregone by fully vaccinating from current rates**	**Additional # of People Getting Vaccines per 100,000**	**Additional Vaccine Cost**	**Cost Ratio Between Columns III and V**
Female	13	$ 21,081.87	61,100	$ 23,536,942.00	111,645
	14	$ 125,564.13	47,300	$ 18,220,906.00	14,511
	15	$ 144,833.27	45,300	$ 17,450,466.00	12,049
	16	$ 171,532.47	42,500	$ 16,371,850.00	9,544
	17	$ 246,575.23	34,000	$ 13,097,480.00	5,312
Male	13	$ 6,141.90	59,100	$ 22,766,502.00	370,675
	14	$ 40,626.76	52,300	$ 20,147,006.00	49,590
	15	$ 70,420.99	46,800	$ 18,028,296.00	25,601
	16	$ 65,041.66	48,200	$ 18,567,604.00	28,547
	17	$ 57,071.42	50,000	$ 19,261,000.00	33,749

Source: The data used to calculate these values were compiled from various sources and explained in the Model section of this paper.

Table 3 demonstrates how much money could be expected to be additionally saved in terms of future cervical cancer/OPC treatment and death costs if vaccination rates had been 100% in 2018, compared to the actual 2018 rates. The comparison is between the additional future savings from vaccinating at 100% rates compared to those at the 2018 rate of vaccination. The additional vaccine cost is the additional costs associated with vaccinating the people that were not vaccinated under the 2018 rates. By comparing columns III and V, we show the cost of moving society from 2018 vaccination rates to full vaccination is between 5,312-111,645 times higher than the costs foregone (depending on the age and gender of the vaccinated individual). Therefore, vaccinating at 100% instead of 2018 vaccination rates would not have been cost-effective when comparing the additional treatment and death costs foregone and the 2018 price of the two-dose vaccine.

14. LIMITATIONS

There are two main limitations of these results that offer potential for future research. The first is that my study only uses the costs foregone associated with costs of cancer treatment and death; it does not include the vaccine's ability to lower the incidence of pre-cancerous lesions. This demonstrates that the vaccine has a wider positive effect on the medical community than is defined in this paper and it is possible that the vaccine's benefits could reduce the use of certain medical treatments, including pre-cancer treatments.

The second limitation of this study is that the marginal benefit calculation does not include a partial externality of vaccination to society in the form of herd immunity. This was excluded from this model's calculations due to the difficulty of quantifying these effects but could produce a positive impact on the costs foregone due to vaccination. Depending on how much of an impact the herd immunity effects have on the costs foregone, the cost-effectiveness of the vaccine could change.

15. COST-EFFECTIVENESS DISCUSSION

This study aimed to examine whether the benefits accrued by rolling out the HPV Gardasil-9 vaccine in the long term justified the high price tag needed to be paid for today. The benefits accrued were measured by the cost of treating cervical cancer/OPC (depending on the individual's sex) and the cost of loss of life from the people that died of the illness. The costs of the vaccine were determined by the average market price of the vaccine published by the CDC. The total cost of treatment and death were calculated for every population of 100,000 individuals using cancer rates from the CDC and discounted at a rate of 3% to determine how much the costs would be without vaccination in today's dollars. Then the same calculations were conducted for the 2018 rate of vaccination and full vaccination to identify how the additional benefits of costs

foregone would compare to the costs of vaccinating the individuals. The comparison yielded that neither the campaign to vaccinate at 2018 levels, nor the goal of fully vaccinating adolescents was cost-effective at the current price of the Gardasil-9 vaccine. This demonstrates that vaccinating adolescent females and males with the current price may not have been the best use of funding in order to prevent cervical cancer and OPC.

A potential avenue for future cost-effectiveness research on the HPV vaccine is to study the cost-effectiveness of the vaccine at a price outside of it current patented one and with a different dosage schedule. It is possible that if either of these vaccine factors changed the cost-effectiveness could as well. For example, if the patent expired, it is possible that the vaccine could become cost-effective. However, based on the results in section 13, the vaccine's price would have to fall to 1.5% or less of its current price to make it cost-effective for females and to 0.3% of its current price for males, vaccinated at age 17, and even lower for the other ages of vaccination.

There are studies that demonstrate promise for the vaccine to be as effective at a one-dose efficacy as it is at the current two-dose efficacy. In their study, Joshi et al. conducted a multi-center cluster randomized trial of one vs. two vs. three doses of the quadrivalent HPV vaccine. The studied analyzes the antibody production of 18,000 unmarried girls aged 10-18 years over a 48 month period divided into four vaccination groups: a three-dose group, two two-dose groups, and a one-dose group.[143] The study found that the frequencies of cumulative incident HPV 16 and 18 infections over 7 years from vaccination were similar across all vaccinated groups and that the antibody titers for HPV 16 and 18 increased over the study period in one-dose

[143] Smita Joshi et al., "Can a Single Dose of Human Papillomavirus (HPV) Vaccine Prevent Cervical Cancer? Early findings from an Indian study," *Vaccine* 36, no. 32 (2018): 4784.

recipients.[144] The HPV prevalence among unvaccinated women in the study was higher than the group receiving one-dose, indicating the single-dose schedule's potential to provide robust protection. Further research, especially regarding the single-dose efficacy of the new Gardasil-9 vaccine is required before a single-dose efficacy can be put in place to replace the current two-dose schedule. If this change occurs, then the price of vaccinating an individual would be cut in half, potentially affecting the vaccine's cost-effectiveness.

These results should be prefaced with the statement that this paper is not intended to discount the suffering of the people who suffer from cervical cancer or OPC, but to address where the best use of resources is to help the largest number of people. Contrary to much of the existing literature, this paper demonstrates that HPV vaccination is not cost-effective in the United States given the current price of the Gardasil-9 vaccine.

16. CONCLUSION

This analysis finds that there were two underlying assumptions within the CDC/FDA prescriptions during the three main events in the HPV vaccine timeline. The two assumptions were that the language initially placed a larger burden on women to protect society's reproductive health and that there was a greater concern for female over male long-term health. These two assumptions shaped parental concerns and media response to the vaccine, to a point that has hindered uptake rates and shaped the feminization of the vaccine. A central question that the parental discussion unveiled was the heavily marketed nature of the vaccine and the question of how profitability had been affecting the HPV vaccine discussion. To understand the efficacy and necessity of the vaccine, this paper also found that the 9vGardasil vaccine was not cost-effective at 2018 inoculation levels nor at 100% vaccination. Therefore, with the current price of

[144] Smita Joshi et al., "Can a Single Dose of Human Papillomavirus (HPV) Vaccine Prevent Cervical Cancer? Early findings from an Indian study," *Vaccine* 36, no. 32 (2018): 4790.

the vaccine and oropharyngeal and cervical cancer treatments, investing in increasing the uptake rates of vaccination is not the most efficient use of financial resources.

A potential avenue for expanding this research is to do a similar analysis of parental concerns and economic benefits for certain populations in the United States to determine if a targeted inoculation campaign could be efficient and beneficial for long-term societal health. This could include analyzing the impact of income level, insurance status, or a non-patented vaccine price.

By combining the fields of STS and Economics, this paper offers a comprehensive view on the ideas behind parental concerns regarding vaccination. The STS portion was focused on an individual level impact of the prescriptions, whereas the Economics portion took a more societal lens. Both are helpful is building a comprehensive understanding of HPV vaccine politics. Cost-effectiveness analysis is key in health economics to determine whether financial resources should be invested into a program and STS analysis is used to dig deeper into why the scientific discussion evolved in a certain way. As a large parental concern over HPV vaccination was the belief that it was a large marketing push, identifying whether the vaccine is cost-effective in preventing certain cancers offers greater insight into the importance of the parental discussions. This offers some credibility to the parental concerns and the idea that a different approach to reducing cervical cancer cases would be beneficial to explore.

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