



5-2020

HPV Vaccine in Adolescents: How to Increase Uptake

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HPV Vaccine in Adolescents: How to Increase Uptake

by

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A Scholarly Project

Submitted to the Graduate Faculty of the University of North Dakota

in partial fulfillment of the requirements for the degree of

Master of Physician Assistant Studies

Grand Forks, North Dakota

May 2020

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Acknowledgments

First and foremost, all praise to God for his grace and blessings to allow me the opportunity to fulfill my dreams.

I would like to express my deepest gratitude to my husband, family, and friends for all their encouragement, prayers, support, and love along the way. It takes a village, and I, hands down, have the best supporters in my corner.

I would like to thank my professor and advisor, Daryl Sieg, for all his knowledge, patience, and guidance throughout this research. I also would like to thank Abby Moeller, PA-S for her knowledge, friendship, and help to edit this project.

Lastly, I want to recognize my late great grandmother, Nanny. The compassion and love she showed me until her last day left an impression on me. I owe her credit for helping lead me down the path of becoming a physician assistant.

Abstract

The human papillomavirus (HPV) is a sexually transmitted virus that affects both males and females of all ages. An HPV vaccine was developed to help protect against harmful infections caused by the virus. This literature review focuses on the relationship between the HPV vaccine and its low uptake from untoward events, misinformation surrounding the vaccine, and different education methods. PubMed, Clinical Key, and Cochrane electronic databases are used for the literature review. A comprehensive literature review was conducted, and articles utilized were based on the age of the population being 11 to 29 years old, the HPV vaccine's involvement in the article, and the article being published less than 12 years ago. The results concerning untoward events related to the HPV vaccine are low and misinformation is common in the news and social media. The research showed the most effective techniques for educating a parent were direct provider-parent communication and informational videos.

Keywords: papillomavirus infections/prevention, papillomavirus vaccines/ adverse effects, mass media, vaccination/ statistics& numerical data, health education, Gardasil 9 immunizations, adolescents, HPV immunization/ methods.

Introduction

Human papillomavirus has become known as one of the most common sexually transmitted infections, according to the Centers for Disease Control and Prevention (CDC). It is linked with cervical and vaginal cancer in females and anal cancer in both sexes. The HPV vaccine was created for adolescents to help combat the harmful effects of HPV. The purpose of this study is to learn the most effective way to educate adolescents and guardians about the HPV vaccine and to understand the hesitancy that surrounds the vaccine that prevents adolescents from becoming vaccinated.

Statement of the Problem

In today's society, we are experiencing a stigma attached to vaccines that has created much skepticism. Some would suggest that there is more fear of the vaccine than the actual disease it serves to protect against. McGhee et al. (2017) point out that the HPV vaccine has an uptake rate of as little as 12% in some states. Those numbers show a need for digging a little deeper to find out the root of hesitancy. Is this low rate based on vaccines as a whole, or is this directly linked to this specific vaccine? Resolving these fears is a task that must be handled carefully and thoroughly to overcome. It starts with figuring out the most effective way to educate patients and understanding that it will vary from patient to patient. Providers need to have resources available that provide statistics on practical techniques for educating patients about vaccines.

Research Questions

Does direct recommendation from the provider compared to routine practice increase the number of patients vaccinated in the adolescent population? Does educational templates and social media advertisements compared to routine practice increase the number of patients

vaccinated in the adolescent population? Does the usage of factual anecdotes compared to routine practice increase the number of patients vaccinated in the adolescent population? Does vaccination with the HPV vaccine compared to non-immunized adolescents increase the risk of untoward events in the adolescent population?

Methodology

A literature review was conducted using PubMed, Clinical Key, and Cochrane from an electronic database. The search produced 300 articles on misinformation and untoward events about the HPV vaccine and 226 articles from the search on effective methods for educating patients about the HPV vaccine. Articles in the misinformation and untoward event search were excluded if the content did not involve the HPV vaccine, involved participants younger than 11 or older than 29 years, were related to the treatment of genital warts, participants with a history or current cervical cancer, or specified to HIV patients. Articles on the effective methods for educating about the HPV vaccine were excluded if the material was not specific to HPV vaccination, did not include education methods, pertained to a definite race, or did not involve adolescents. The search was further narrowed by reading abstracts to define the studies relative to the research topic. All searches also excluded articles published greater than twelve years ago, involved animals in the study, not peer-reviewed, or not applicable to the English language. A total of 20 articles were found that met the criteria of the research. After review of the full text of articles, a total of 13 were found to be pertinent to the study.

Literature Review

A review of the literature provided evidence that the HPV vaccine has been studied to include the possibilities of untoward events and misconceptions that may be affecting a patient's or guardian's decision to receive the vaccine. Further research shows the percentage of untoward

events and ways to overcome the misinformation surrounding the vaccine. The literature review offers different techniques for educating patients about vaccines that have been studied thoroughly. Statistically, one technique may be more effective than others may.

HPV Vaccination Purpose/Function

Cuzick (2015) conducted a trial comparing the Gardasil vaccine to the new Gardasil 9 vaccine. The study's purpose was to see if there was any added effectiveness of adding five new HPV types to the vaccine. The Gardasil vaccine comprises of four HPV types: 6, 11, 16, and 18. The Gardasil 9 vaccine includes an additional five other types: 31, 33, 45, 52, and 58.

The limitations of this study include the failure to test participants before beginning the trial for infection. This study's strengths include the 95% confidence that Gardasil 9 reduced persistent infections and the data support the greater efficacy of Gardasil 9 without showing biases to either of the two vaccines.

The methods involved a randomized trial of 14,215 women. There were 7,109 women who received Gardasil, and 7,106 women received Gardasil 9 vaccine. The females received a dose of the vaccines at the beginning of the trial and again at two and six months. There were follow-ups every six months for a total of 54 months, which included ThinPrep samples being sent for cytology. If the same infection was present for two consecutive times, six months apart, it was documented as persistent.

The results showed that Gardasil 9 had a 96.6% reduction in the added HPV types. There were 30 cases reported with Gardasil vaccine compared to one case reported with Gardasil 9. The reduction in HPV types 6, 11, 16, or 18 and reduction of persistent infection involving those types was insignificant between the two vaccines. Cuzick (2015) showed a 96% reduction in

persistent infections, with 95% CI (94.4-97.2%), associated with HPV types 31, 33, 45, 52, and 58 with Gardasil 9 vaccines.

Gupta, Glueck, and Patel (2017) provide global perspectives on the HPV vaccines. They explain the disease process of HPV, the need for vaccine protection against HPV, and the issues the current HPV vaccines are facing. The purpose of the research is to explain the complex function of the current HPV immunizations and address the areas that warrant improvement. Throughout the article, the language suggests that it is intended for an audience of scientists working with immunizations.

The research limitations were the lack of specific reasons provided for the low uptake of the HPV vaccine. Cost and the number of dosages required were the only two factors discussed. The strengths include a detailed explanation of what HPV is, the genetic level that HPV vaccines target, and some areas that need to be improved with a vaccine for HPV. The article takes into account developed countries and underdeveloped countries.

Gupta et al. (2017) introduce HPV by describing the virus's genetic makeup and characteristics. Human papillomaviruses are made up of double-stranded deoxyribonucleic (DNA) molecules that are lacking an envelope. They are typically around 50 nanometers in diameter. These viruses will spend their lifecycle in mucosal epithelial tissue. Their genome is made up of two stages, early(E) and late(L). The early stages consist of E1-7 genes and are considered to be the therapeutic area for HPV linked malignancies. The genes function in DNA transcription and replication is responsible for this. The late stages, L1 and L2, are the target areas for prevention.

The HPV vaccines available now are only preventative, thus reactive with either L1 or L2 genes. They cannot treat an infection or any other sexually transmitted illness. There are

currently three vaccines approved for HPV protection: Gardasil, Gardasil 9, and Cervarix. Gupta et al. (2017) noted that each of those vaccines protect against the high-risk types of HPV associated with cervical cancer.

The issues facing the current vaccines are cost and the number of doses required. The government's National Immunization Program does not cover HPV vaccines. In the United States, one dose is costing around \$100-\$120. Developing countries are equally as expensive. Gupta et al. (2017) explained the different trials ongoing to produce an affordable vaccine. Some of those approaches include using alternative expression to create a lab-based virus that expresses the same virus-like particles as the current vaccines.

The goal for the number of doses required is to go from three to one. The new vaccine will require a higher antigen concentration to achieve this goal. This theory will necessitate further research to see if it would provide adequate results while producing similar minimal adverse effects.

Untoward Events of the HPV Vaccine

Douglas (2009) performed research on the HPV vaccine to gather if the vaccine was safe or not. He compiled data from peer-reviewed literature to determine how common and severe adverse reactions were with the Gardasil vaccine. The information collected is from Australia and the United States. The article's audience is the general public, specifically female and male candidates for the vaccine.

This study's limitations include the lack of background given on each participant, data collected from a vague audience, and no correlation between minor adverse events and the HPV vaccine. This research by Douglas (2009) showed strength in addressing populations in the

United States and Australia, using the Vaccine Adverse Event Reporting System (VAERS), and provided detailed information on causative factors with significant adverse events.

The methods used for this research included gathering data from several literature reviews conducted by PubMed. Data was used from all Gardasil vaccines given in Australia between June 2006 to July 4, 2008, and in the United States between June 2006 to April 30, 2008. This amounted to 3.7 million injections in Australia and 12 million in the United States. The reported adverse events include 1013 for Australia and 7802 for the United States.

The results from Australia and the United States were similar in the type of adverse reactions reported, for the most part. 795 cases of 1013 in Australia were mild. The most common reaction, at 203 cases, was soreness/redness to the injection site. Soreness was also the most common reaction reported in the United States. Other common reactions reported were headache, dizziness, nausea, and vomiting. Australia did report eight cases of anaphylactic reactions. However, Douglas (2009) reported that the study failed to explore the whole data, resulting in selection bias. He reevaluated the anaphylactic data, taking the considerations above into account, and came up with around 0.2 cases per 100,000 doses resulted in anaphylaxis. In the United States, the VAERS documented 15 reported deaths following the injection of the HPV vaccine. Douglas found supporting data that had looked into the 15 deaths and found that 10 of those cases were determined to show no direct link between death and the vaccine. Another area of concern in the United States is the link between the HPV vaccine and Guillain-Barre Syndrome (GBS). The VAERS collected 31 reported cases of GBS during this time frame. Ten of those cases were confirmed to be GBS, but five of those ten had received a simultaneous injection of the quadrivalent meningococcal vaccine.

Geier, Kern, and Geier (2019) conducted a study to see if there was a risk of developing asthma after receiving the HPV vaccine. The study came about from asthma being the leading chronic diagnosis among children in the world. The authors of the study were interested in testing an environmental factor, the HPV vaccine, to determine any association between them. The study hypothesized that there could be a vastly increased number of reported asthma incidents among patients who received the HPV vaccine.

Limitations concerning research conducted by Geier et al. (2019) is the lack of specifying exact component(s) of Gardasil that was the causative agent. Other limitations included the lack of clarification in the asthma episode and the treatment required. The strengths of this study include it using the National Health and Nutrition Examination Survey (NHANES) program to collect data, a 95% CI was met in reported asthma the same year the HPV vaccine was given, and the use of specific demographics, including gender, race and socioeconomic status, was included.

In the study done by Geier et al. (2019), the method employed data from the NHANES program. This program uses an annual questionnaire and physical exam to evaluate adults' and children's health and nutritional status. They reviewed 316,481,004 persons between 2015 and 2016. A total of 60,934,237 persons were selected after narrowing the data to complete demographics provided and documented asthma. They then evaluated each of the asthma diagnosis to create a list. The exposed group received the HPV vaccine, and the unexposed group did not.

Two statistical analyses provided the results of Geier et al. (2019) study. The first was recorded data based on the difference between the age of the first received dose of the HPV vaccine and the initial diagnosis of asthma. There was a total of 459,332 cases reported of the

HPV vaccine exposed persons with documented incident asthma. Year zero had the highest incidence of reported asthma in a person exposed to the HPV vaccine. There were 16,240,688 persons that received the vaccine and 299,245 that had reported incident asthma. This accounts for 65.15% of the total number of reported asthma incidents in an exposed person, and 1.84% of the total reported HPV vaccine exposed persons. Binomial modeling showed a risk ratio equal to 3.83 ($p < 0.0001$). The lowest incidence of reported asthma in a person exposed to the HPV vaccine was year one. There was 5.89% of the total number of reported diagnoses of asthma in an exposed person and 0.18% of the total number of persons receiving the HPV vaccine. Year two demonstrated an increase in numbers compared to year one, with 16.59% reported asthma and a rate of 0.65% of all exposed persons. Year three decreased to 12.37% in reported asthma among those exposed and 0.60% of total exposed persons.

The second statistical analysis Geier et al. (2019) compared reported incidence of asthma in exposed persons and incidence of asthma in nonexposed persons in the same year. The data was broken down between genders, as well. When looking at both genders together, it was expressed that there was an increased risk in reported incidence of asthma when receiving the HPV vaccine in the same year. The analyses calculated a 7.88% risk ratio, with a 95% CI (1.75-35.46). The excess risk was 0.0161. The compared percentage between HPV vaccine exposed and unexposed was 1.84% and 0.23%, respectively. The data revealed that the females did not significantly differ in asthma in exposed versus nonexposed groups. However, the males showed a significant increase asthma incident in the HPV vaccine exposed group. Risk ratio 19.01% with a 95% CI (2.31-156.25).

Mauro et al. (2019) performed a retrospective study on the HPV immunizations among adolescent females. The objective of the study was to identify any adverse effects if they took

place. The experiment took place in Sao Paulo State, Brazil, and the Adverse Event Following Immunizations (AEFI) data system was used to gather information.

Their study was limited by the difficulty in determining the relationship between the vaccine and the adverse events. The information included was limited to a retrospective study and did not include an analysis of the reactions to understand the causative agent. The strengths include providing statistics on the HPV vaccine and adverse events in a large population of females, a broad timeframe, and unbiased research.

The method of the study done by Mauro et al. (2019) analyzed all data between March 01, 2014 to December 31, 2016 from the AEFI regarding the HPV vaccine given to adolescent females. A clause was included that stated the adverse events recorded in the AEFI database are not necessarily linked to the vaccine, and a severe reaction is based on requiring 24 hours stay in the hospital, cause permanent disability, or death. Non-severe are any other reactions not meeting the above criterion.

The results yielded 3,390,376 HPV injections given and 475 reported cases of adverse events between March 01, 2014, and December 31, 2016. Ten of the adverse events were determined to be inadequate for the study. Severe adverse events accounted for 39 cases with a duration greater than six hours in 46% of the cases. The majority of untoward events were documented in the first year accounting for 318 non-severe events and 19 severe. The second year saw 63 non-severe cases and 18 severe, and the final year had 43 reported non-severe events and only two severe. The most common reported untoward event was 197 cases of syncope. Other everyday adverse events were dizziness, headache, and nausea, with the non-severe events lasting less than 6 hours in 90% of the cases. The 39 severe cases showed 34 non-severe type reactions resulting in a 24-hour hospital stay. There were two reported cases of GBS.

Misinformation of the HPV Vaccine

Abdelmutti and Hoffman-Goetz (2010) performed an analysis on the public opinions related to Gardasil, HPV infection, and cervical cancer from January 01, 2006 to December 31, 2007. The research material gathered from four magazines: two from Canada and two from America. The magazines were selected based on the highest views. Canada and America were chosen for the study because Gardasil is manufactured and marketed in both places by the same company, Merck & Co. and Merck Frosst. The research agenda was to investigate if any scare tactics were applied in the news stories and how much influence the media may have on public opinion.

There were a couple of limitations to this study including: lacks p-values, only involves four magazines, and is not specific to a group or specific audience. The strengths of this analysis are that it addresses the influences the media can have on the public, uses accredited database to analyze news articles, and presents an adequate timeframe.

This analysis's method included using LexisNexis Academic and Factiva archives to gather stories from the four chosen magazines. Narrowing the search of the database down, a total of 15 articles with the highest views were selected. The risks were categorized based on scare tactics, such as threats of death or illness, human-made sources, dangerous to small children, promiscuities, and pharmaceutical gains.

The results from Abdelmutti and Hoffman-Goetz (2010) included a table illustrating the percentage of each scare tactic that was cited in the magazines. The topic of HPV accounted for 49% of the articles. The threatening of death or illness accounted for 12% in Canada and 7% in America. Cervical cancer made up 20% of the stories with most of the attention also revolving around threaten deaths or illness, with 5% in both Canada and America. Gardasil yielded 43%

total number of citations. The subjects used to cause alarm were human-made source (8% Canada, 2% America) and danger to small children (5% Canada, 0% America). Promiscuities and pharmaceutical gain were documented under ‘other themes’ and made up 16% of the citations in Canada and America.

Faasse, Porsius, Faasse, and Martin’s (2017) backgrounds consist of psychology, design engineering, rehabilitation medicine, plastic and reconstructive surgery, and neuroscience. The group conducted a study in New Zealand to evaluate how often the media reported adverse events from Gardasil vaccination over a seven and a half years span and if their reporting was driven from Gardasil related internet searches. Their purpose was to understand better why Gardasil has a lower uptake, although HPV has been linked to practically all cervical cancer cases. The authors predicted that an increase in news reports would directly affect the number of adverse events reported after Gardasil injection.

This study’s limitations include the lack of data to determine if the patient or guardian of the patient with a reported adverse event had seen news reports or did an internet search about Gardasil before or at the time of the reaction. It is also unknown what Gardasil topics were reported in the news or exactly what type of Gardasil questions or concerns were found in the Google searches. The strengths of this study include a wide range of years used to collect data. The authors created a linear regression module graphing the relationship of news articles on Gardasil, internet searches related to Gardasil, and Gardasil immunizations during each month.

The methods conducted by Faasse et al. (2017) were based on a nonbiased selection from the Center for Adverse Reactions Monitoring (CARM) system and the Suspected Medicine Adverse Reaction Search (SMARS) archive between January 2009 through July 2016. This data included the patient’s demographics, the adverse reaction reported, the medicine assumed

responsible, and the date. Google Trends was then used to review Google searches for Gardasil related topics during that timeframe. Next was to compile data from the media, including all primary news sources from the web to newspapers, journals, and magazines. The search was narrowed by using search terms relevant to the topic, such as Gardasil, vaccination, HPV, and cervical cancer. This generated 311 unique articles that were between the set timeframe. A linear regression analysis was used to document data from each of the above variables while using year and number of vaccinations given as the controls. A log transformation was used for entering independent variables to clarify the information for a more straightforward interpretation.

The results of the research reported that 720,163 Gardasil immunizations were given. The months had a mean average of 7914 injections per month. The total adverse events reported were 523, along with 1280 symptoms. This accounted for a rate of 73 adverse events per 100,000 injections. The adverse events were reviewed in the 31 months following the Food and Drug Administration's (FDA) approval of Gardasil, which was 54 adverse events per 100,000 injections. The peak of adverse events reported was in April 2009 with 35 cases. The most common reported side effects were headache, dizziness, and nausea. From January 2009 through July of 2009, the number of adverse events reported was equivalent to the number of news coverage. News reporting was highest during this time. In March 2009, there were 35 articles published. Google searches were relatively lower during this time. By January 2010 through July 2010, Google searches were slightly more significant than the adverse events reported, and news coverage was significantly less. The numbers of the three were relatively close from January 2011 through July 2014, with Google searches being slightly higher than the others. This study provides insight that as coverage increased on Gardasil's topic in the news so did the number of adverse events reported and the Gardasil related Google searches.

McGhee et al. (2017) performed a study to learn ways to increase the overall number of persons receiving the HPV vaccine. This group is a part of the United States National Cancer Program. The long-term objective is decreasing, possibly eliminating, cancers associated with HPV. The authors approached this task by exploring why the numbers may be low in the first place. Data was taken from the states with the highest reported uptake and states with the lowest reported uptake. Data taken into account included socioeconomic status and misconceptions about the HPV vaccine's purpose and safety.

This study's limitations are that it was written by the President Cancer Panel Members and could be argued that there may be some bias toward the HPV vaccine. The study also does not acknowledge any adverse events as a possibility of decreased numbers. The strengths of this study include producing results of why the HPV vaccine has a lower uptake than other vaccines and suggestive ways of increasing the uptake. The study included a table that recorded the data of probable percentages HPV was responsible for cancer listed. It considers the global perspective and explains the strategies for increasing the uptake of the HPV vaccine.

McGhee et al. (2017) gathered HPV vaccine series records from each state and created a table to demonstrate where each state's percentage ranked. The percentages were based on 13 to 17 years old in 2012 and the number that received the HPV vaccine series. Only two states had a range greater than 50%, Rhode Island and Delaware, 57.7% and 50.4%, respectively. The majority of states were in the 30-39% range, with a total of 28 states. Eleven states had less than 29%, with the lowest percentage being from Mississippi at 12.1%. The group then configured a table to demonstrate the probable percentage of cancer caused by HPV in the US in 2012. The most common cancer site was the cervix, with 11,967 reported cases. The probability of HPV was 96%, and 76% that the strand of HPV was 16 or 18. The next highest reported site was the

oropharynx with 11,726 cases, 63% likelihood of being caused by HPV, and 95% chance that, if caused by HPV, it was HPV 16 or 18. Cancer of the anus accounted for 4,767 persons with a 93% possibility it was caused by HPV and a 93% chance it was linked to HPV 16 or 18.

McGhee et al. (2017) created four goals to increase the number of HPV vaccine series given globally. The first goal was to increase the number of vaccines given in the clinic. The authors want to increase the number of HPV eligible persons who are offered the vaccine during their routine visits. They suggested the provider have a conversation with the parents about the safety of the vaccine, the beliefs about vaccines, and the sexual behavior topics in adolescents. The panel also recognized the concerns from the clinical standpoint of equal reimbursement from the vaccine. The second goal focused on addressing compliance from the patient and guardians. The common refusals from guardians were their child not being sexually active, it not being needed for a male, or that the idea of the vaccine encouraged sexual activity among adolescents. The panel agreed that the CDC needed to make more informative material available regarding the HPV vaccine to educate patients and guardians. The third goal addressed the need for more places offering the HPV vaccine, such as pharmacies and school programs. The final goal focused on how to increase the global uptake of the HPV vaccine. McGhee et al. (2017) discussed making the HPV vaccine affordable for the lower and middle-class countries.

Schuler, Hanley, and Coyne-Beasley (2014) discussed that the HPV vaccine's male uptake was relatively low, with less than 9% in qualified males. The authors wanted to explore the reasons for this low uptake. They specifically wanted to study the effect concerns about vaccine-associated infertility (VAI) had on the numbers. During this study, the authors wanted to see any correlation between VAI and a lack of knowledge related to the HPV vaccine and diseases it protects against.

The limitation of this study includes a restricted geographic area for the participants. This study's strengths included conducting a study on males after the HPV vaccine was FDA approved for them and evaluating VAI in males, which was not previously studied.

The methods included a cross-sectional survey of parents to boys in determining VAI concerns. The parents were selected from a pediatric clinic with a son between 9 to 21 years of age. The survey consisted of a series of questions to evaluate concern of infertility with the HPV vaccine, knowledge of HPV related diseases, knowledge about the HPV vaccine, and the likeliness their son would receive the HPV immunization. Exclusion from the study involved any parents that had sons who had already received the HPV vaccine. The analyses conducted used a multivariate model to allow for demographics for each parent. An alpha value of 0.05 was considered statistically significant.

The results of the cross-sectional study involved 270 participants. There were 47% not concerned with VAI, 39% concerned, and 14% preferred not to answer. The outcome of knowledge about HPV diseases resulted in 88% had insufficient knowledge and 12% with high knowledge. An adequate understanding of the HPV vaccine showed that 72% felt like they did not have enough information to decide if their son should receive the injection, and 28% agreed that they had enough information to make the decision. Although more parents felt they did not have enough information to decide if their son should receive the HPV vaccine, 63% agreed to probably vaccinate their child next year as opposed to the 37% that probably would not. When comparing parents concerned about VAI to HPV disease knowledge, there was no significant difference in the adjusted odds ratio (AOR) (AOR high knowledge= 1.18, 95% CI= 0.53-2.65). The analysis showed that parents concerned about VAI also had a higher percentage of agreeing

they did not have enough information about the HPV vaccine compared to those that did (AOR= 2.22, 95% CI= 1.22-4.03).

Effective Techniques to Educate Patients About Vaccines

Connors, Slotwinski, and Hodges (2017) conducted a study to evaluate if provider and parent communication has any increased effect on a parent's decision to vaccinate than other interaction methods. The group noted that their study was due to the increasing vaccination hesitancy among parents and the concern of a potential outbreak of vaccine-preventable diseases.

This study's limitation included the data consisting of insufficient evidence, according to the Melnyk Pyramid. The data collected was not directly related. The topics are broad and not concise to provider-patient interaction regarding vaccination. This study's strengths include its ability to provide efficacious strategies for providers when communicating with parents about vaccination, it being unbiased in the selection, and giving a parent's perspective on what they found to be helpful or not helpful in their decision to vaccinate.

The methods performed by Connors et al. (2017) used PubMed and the Cumulative Index to Nursing and Allied Health Literature (CINAHL) to conduct a systematic review from March 2011 to March 2016. The authors were able to gather a total of 41 articles (n=41). Covidence 2015 was utilized to give a systematic review of the titles and abstracts of each article. Any articles that were duplicate, biased, or did not involve provider-parent communication were excluded. A total of nine (n=9) studies meet the criteria.

The randomized trial results showed that parents reacted better to presumptive interaction from the provider rather than a participatory approach. A study with 111 participants resulted in parents opposed vaccine recommendation 83% with a participatory approach versus 26% that resisted with presumptive interactions ($p < 0.0001$). Another study Connors et al. (2017) reviewed

found that providers need to use layman's terms when explaining what the HPV vaccine protects against, how HPV occurs, and emphasize the importance of male adolescents receiving the vaccine. A cross-sectional study in Canada in 2011 indicated that the concerns parents had about the vaccine's safety were not fully addressed by the provider. The study found 17.3% of parents felt that they were met with confrontation when discussing whether or not to vaccinate their child with the provider. Regarding successful strategies, a conversation centered around the parents' concerns or their background was met with 74% and 68%, respectively, compliance in receiving the vaccine. When administering the HPV vaccine, there was a 72% success rate when the parent had information regarding the vaccine before the visit.

Cory et al. (2019) conducted a study to discover whether educational videos or educational handouts were more effective at teaching patients and parents about the HPV vaccine. The authors comment on the suboptimal uptake of the HPV vaccine, especially among lower socioeconomic classes. This research aims to understand the best route for increasing knowledge and acceptability among patients and parents where the HPV vaccine is concerned.

The limitations of this study are the participants limited to females only and the selection being bias. The strengths of this study include the format of the randomized, control trial, and the investigational phase identifying potential educational interventions.

The methods utilized included an investigational phase and a randomized, controlled study. During the investigational phase, the study conducted a cross-sectional survey from May 2013 to January 2014 to gather data on what women knew about the HPV vaccine. The survey involved 200 women that were patients at the University of Pennsylvania Obstetrics and Gynecology health system. The study also included a semi-structured discussion where 15 of the 200 women were chosen at random. The survey included demographics of the women and their

knowledge of HPV vaccine protection, their opinions of the vaccine, and if they had received the vaccine. An interview was recorded by a telephone call. This part of the study asked the women to explain their knowledge of the HPV vaccine, what influenced their decision to be for or against the vaccine, and what learning method was most appealing between handouts and videos. There were 256 participants, and they were randomized into one of the three groups: the control, the educational handout, and the informative video. The study by Cory et al. (2019) used the following to analyze the data:

In the exploratory phase, Chi-square and Wilcoxon rank sum test were used to compare categorical and continuous characteristics, respectively, between acceptors and nonacceptors. In the randomized, controlled trial phase, Chi-square and Kruskal-Wallis tests were used to compare categorical and continuous characteristics, respectively, between study arms. (para. 11)

P-values less than 0.05 in the investigational study and less than 0.025 in the randomized, controlled study were considered statistically acceptable.

The results reported that 51% (n= 109) of women during the investigational phase were open to receiving the HPV vaccine. However, only 41% (n= 82) of the women started the HPV vaccination series, and only 19% (n= 28) completed the entire series. Those supporting the vaccine had a better initial understanding and knowledge about the HPV vaccine and what it prevents (51% versus 22.4%, $p < 0.01$). The recorded interview revealed that those opposed to the HPV vaccine stated it was due to not understanding its purpose. Those in support of the vaccine acknowledged the reasoning to be due to the protection it offered against cervical cancer. They also identified their medical providers as a trusted resource and most influential in their decision-making regarding health. The randomized, controlled trial included the control group (n= 85), the

educational handout group (n= 84), and the educational video group (n= 87). The participants' average income was less than \$25,000 (48.3%, n= 123), and the majority of females listed their race as African Americans (80.6%, n= 207). Following the intervention, the educational video group reported a 51.7% (n=45) of participants were in support of the HPV vaccine. That was the highest among the three groups. The educational handout reported 33.3% (n=28) in support of the vaccine (p=0.02), and the control group documented 28.2% (n= 24) in support of the vaccine (p<0.01). The majority of the women in both the educational video and handout group stated the material had increased their knowledge about the HPV vaccine, 97.7% and 92.9%, respectively.

Ortiz, Smith, and Coyne-Beasley (2019) performed a systematic literature review to research how the media may affect the attentiveness and attitude of HPV and the vaccination for HPV.

The limitations of this study include it being unable to access all of the data regarding HPV on social media due to private accounts. The strengths of this study include it being unbiased research, and a significant amount of data was collected from a broad timeframe.

The methodology consisted of a systematic review of scholarly articles published before December 31, 2018. Ortiz et al. (2019) defined social media as internet sources and platforms that allowed for interaction between users and the ability to share content and personal opinions.

The results produced 325 articles. By the end of the screening process, 44 articles were found to be inclusive of the research. There were 29 articles based directly off of social media engagement of HPV and/or HPV vaccination, “including Twitter (n= 14), YouTube (n= 6), Facebook (n=3), Google+ (n= 1), Myspace (n= 1), Instagram (n= 1), and other social spaces, such as comment sections and discussion boards (n= 5)” (Ortiz, Smith & Coyne-Beasley, 2019). The other 15 articles involved interviews and experiments with social media and HPV and HPV

vaccination. The results determined that Twitter and YouTube were the most popular social media platforms that users used to engage in conversations about HPV and the vaccination. The study suggests this to be due to how easily both sites are to access and search directly for content. Looking at how HPV and the HPV vaccine were interpreted on social media, the authors labeled the data as either positive or negative, encouraging HPV vaccination or discouraging, or neutral. When the study focused on Twitter, it was found that from October 2013 through April 2014, there were 25.1% of tweets about HVP immunization described as negative (n= 20,994). From August 2014 through July 2015, there were similar results, with 25.3% having a negative tone (n= 48,940). Positive tweets during this time accounted for 39% of tweets. However, the number of times negative and positive data was retweet was equivalent at 9.1 versus 9.7, respectively. This information confirms that negative information was surfaced nearly as much as positive despite there being 14% less original tweets.

The YouTube search showed that 57% of videos were anti-vaccine, followed by pro-vaccine at 31%, and the remainder neutral. Myspace and Instagram had less content about HPV and HPV vaccination. The majority of Myspace's content between November 2005 to May 2008 was described as positive at 52% (n= 157), and 43% (n= 129) viewed as a negative tone. Instagram had data collected using the hashtag HPV from three days, September 7, 21, and October 4, 2018. This totaled to 45% (n=150) of the post discussing HPV vaccination, and 79.2% of those posts were in favor. Negative content was found to be a mix of incorrect data, conspiracy theories of pharmaceutical gains and the government profit, and fears of adverse events from the vaccine. Positive content used evidence-based information to explain the protection, efficacy, and safety of the HPV vaccine.

To determine the impact of negative content on HPV vaccination on social media, one study reported results of a survey given to 1,263 parents of adolescents not yet vaccinated for HPV. It was analyzed that the HPV vaccine's harmful effects were more likely to be found on social media (30%) as opposed to posts about the harmful diseases the HPV vaccine prevents (11%). The parents that only saw the harmful information on social media were less likely to vaccinate. The ones that heard both harmful stories and information about the HPV vaccine's protection were more likely to opt for a delayed schedule for vaccinating. Ortiz et al. (2019) also looked at the effects of using social media to promote the HPV vaccine from the articles gathered for this study. They found that a few campaigns had been successful with social media and increased HPV vaccine uptake. However, several of the studies they looked at did not have the same success. While knowledge increased, the vaccinating uptake did not.

Teoh (2019) is a gynecologic oncologist. She published a journal article addressing the influences that media can have on the HPV vaccination.

This study's limitations include its ability to offer only the potential effects of promoting on social media and the unknown demographics of the survey participants. This journal's strengths include the statistics provided on the type of interaction that appears to resonate more with a parent and the comparison of social media platforms.

The analysis that was conducted involved reviewing different social media platforms for their effects on the HPV vaccine. A comparison of Twitter and YouTube was performed, and it was noted that Twitter's content regarding HPV vaccination was the majority in support. In contrast, YouTube's data revealed that 57% of the content regarding the HPV vaccine were in favor of anti-vaccination. As a whole, pro-vaccine information was from providers in health care and involved facts based on evidence-based medicine. The messages with pro-vaccine content

were focused on preventing the HPV diseases and not so much on the safety of the vaccine. The anti-vaccine material on social media addressed the opposite. It emphasized the harmful effects of the vaccine and the monetize scheme from the government and pharmaceutical companies. The study found that often the adverse side effects were not backed by evidence-based research. Instead, it was usually personal stories discussing the harm that had occurred.

The analysis's results explain the effects social media can have on the uptake of the HPV vaccine. As many as 62% of Americans use social media to stay up to date on the daily news. A model was created that showed 60% of the HPV vaccine's discrepancy was due to social media, and the other 40% was faulted to the socioeconomic status. It was noted that the results could not determine the type of social media propaganda used and if it was persuasive for or against the vaccine. A cross-sectional survey of 564 parents to adolescents was performed in 2018 to give more insight into the effects of the HPV vaccines on social media. Approximately 45% of parents answered 'yes' to having heard stories about HPV vaccinations on social media. The survey compared harmful stories to preventative stories and found that harmful stories were predominant over preventative stories, 19% to 11%, respectively. The remaining 15% had heard both types of stories. The survey's results also yielded information to support a personal conversation about protection the HPV vaccine offers was more likely to remain with a parent as were conversations about harm, 33% to 24%, respectively ($p < .01$).

Discussion

Cuzick's (2015) study showed the added protection with Gardasil 9 compared to Gardasil. However, the study confirmed that each vaccine offered equal protection against the HPV types they shared.

Gupta, Glueck, and Patel (2017) gave a global perspective on the HPV vaccines and how the cost and number of doses required contributed to the low uptake of the vaccine. The study was not able to provide conclusive tactics for increasing the uptake of the HPV vaccine.

Untoward events contribute to why the HPV vaccine has a lower than expected uptake. Douglas (2009) findings resulted in five reported cases of GBS following the HPV vaccine in the United States out of twelve million injections of the HPV vaccine. Mauro et al. (2019) also reported similar findings with two GBS cases reported following the HPV vaccine out of roughly three million injections. An epidemiological evaluation was conducted, and it was determined that the likelihood of developing GBS following the HPV vaccine was equivalent to the happenstance of it occurring in any other vaccination offered in the ages 9 to 26 years (Douglas, 2009). The most common reactions reported were redness and soreness at the site of injection and syncope (Douglas, 2009; Mauro et al., 2019). The HPV vaccine is deemed as safe as all other approved vaccinations (Douglas, 2009).

Geier, Kern, and Geier (2019) looked specifically at the relationship between asthma and the HPV vaccine. Their study could not prove what exact components of the HPV vaccine that were the causative agent, but it revealed that the males had a noted increase in asthma cases following the HPV vaccination compared to the unexposed group (Geier et al., 2019). Further studies would need to be conducted to determine what causative agents in the vaccine were attributed to the onset of asthma and to determine if the asthma episode was long term or an acute event.

The HPV vaccine's media attention was mainly focused on adverse effects instead of the protective factors it offered. McGhee et al. (2017) linked as great as 96% of cervical cancer connected to HPV. However, most of the magazines' stories used scare tactics such as the

possibility of death or illness with receiving the vaccine (Abdelmutti & Hoffman-Goetz, 2010). When comparing the articles associated with the HPV vaccine to cervical cancer, the journalist used more negativity, such as death, illness, and pharmaceutical gain, when discussing the HPV vaccine than cancer (Abdelmutti & Hoffman-Goetz, 2010). As the HPV vaccine was reported more often in the news media, the reporting of adverse reactions increased. Google searches for the HPV vaccine also increased (Faasse et al., 2017). These results illustrate precisely how influential the media can be on their viewers (Faasse et al., 2017).

Infertility was the most common concern associated with the HPV vaccine and males (Schuler et al., 2014). Upon further research, it was determined that the actual leading cause of low uptake in males was parents lacking knowledge about the vaccine and infections associated with HPV (Schuler et al., 2014). A more astounding percent of parents lacked knowledge about HPV infections than their fear of infertility associated with the vaccine (Schuler et al., 2014).

Failing to understand effective ways of educating the patients and parents also contributes to the low uptake. Direct provider-patient communication using layman's terms resulted in parents being better informed and more receptive to vaccine information (Connors et al., 2017). A confrontational standpoint from the provider to the parent resulted in the parents rejecting the vaccine (Connors et al., 2017). When educational videos and pamphlets were used, almost a hundred percent of the participants stated that they had increased their knowledge about the HPV vaccine (Cory et al., 2019).

Social media makes up a substantial amount of the current population's time. However, using social media as an educational platform for the HPV vaccine presents as an issue. Currently, more harmful effects of the vaccine are likely found online than the harmful effects of diseases caused by HPV (Ortiz et al., 2019). Social media contributes to the largest amount of inconsistent

information spread on the HPV vaccine, and the other causative factor was contributed to populations of lower socioeconomic status (Teoh, 2019). The studies on using social media to increase the HPV vaccine uptake had inconsistent results. This area warrants further research due to more than half of the population using social media as a news outlet or a way to stay up to date (Teoh, 2019).

Conclusion

This literature review revealed how complex it is to understand why the HPV vaccination uptake is low and what factors could increase the uptake. Multiple avenues need to be considered if a solution is going to be achieved. I agree from a pharmaceutical perspective with Gupta et al. (2017). Making the vaccine cost-effective, readily available to all, and requiring fewer injections would increase compliance, thus likely to increase uptake. I found that the HPV vaccine's hesitancy is directly related to the coverage that news media shares on the vaccine and the negative attitude spread on social media (Ortiz et al., 2019). Since the HPV vaccine is currently approved by the FDA, it was already known that the untoward events made up a substantially low percentage. However, I found that untoward events and misconceptions make up the majority of the media coverage and social media newsfeed concerning the HPV vaccine (Ortiz et al., 2019). This research paper supports the need to further explore multimodal strategies that would debunk the false information spread about the vaccine. With social media being a widely viewed platform amongst most of today's population, it offers an opportunity to be gateway for successfully educating the public about the HPV vaccine (Teoh, 2019). Further research is needed to make that envision a reality. Lastly, and possibly most influential, the research shows it begins in the patient's room. Connors et al. (2017) revealed that provider-patient communication is proven to be the most effective. It can be further concluded that educational

videos produced a positive response in knowledge and vaccine uptake (Cory et al., 2019). There is a gap in the public's knowledge of what HPV is and the harmful effects it can have on the body, especially among lower socioeconomic population. The research strongly suggests that a provider explaining exactly what the HPV vaccine protects against, the side effects associated with the HPV vaccine, and giving a personal recommendation to the parent regarding a vaccine can be beneficial. I was not able to find a study that had been conducted on factual anecdotes to determine the outcome they had on educating patients. That leads me to believe that provider-patient communication that is forthright while offering empathy to the patient's concerns and providing educational videos on HPV and the vaccine are the mainstay to successfully increasing the HPV vaccine uptake.

Applicability to Clinical Practice

The information provided within this literature review offers valuable information that will allow a provider to educate their patients about the HPV vaccine. A provider will be able to utilize this evidence-based medicine in practice to offer their patients the best treatment.

The research I conducted clearly supports investing the office visit time with direct provider to parent education which emphasizes understanding and empathy of parental concerns, but provides solid clinical evidence. Educational videos have shown promising results regarding improving the uptake of the HPV vaccine as well. In closing, further research and media attention should be conducted to address the negative fabrications related to the vaccine.

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