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Fear of HPV Vaccine Safety Affects Self-Reported Likelihood to Be Vaccinated after Interventions among University Undergraduates

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2012

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An abstract of

A thesis submitted to the Faculty of the
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2017

Abstract

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By Christopher Piccione

Background
Human papillomavirus (HPV) burdens college women and men with the highest risk for acquisition and prevalence. Despite the protection HPV vaccines provide and the little or no evidence of severe side effects associated, vaccination coverage is not on track to meet the Healthy People 2020 goal of 80%. Assessing how fear of HPV vaccine safety affects interventions to increase coverage among 18 to 26 year old university students will shed light on viable catch-up vaccination programs.

Methods
A secondary analysis was performed with data obtained by a HPV Vaccine and Decisions Making Behaviors Survey administered to undergraduate students. Inverse probability treatment weighting (IPTW) was used to create a pseudo data set in which confounding covariates were balanced between persons who perceived the HPV vaccine as unsafe or safe. Odds ratios were calculated with logistic regression models using stabilized weights to identify relationships between perceived vaccine safety and likelihood to be vaccinated after interventions.

Results
Overall, 50 (11.5%) students perceived the HPV vaccine as unsafe, while 386 (88.5%) perceived the vaccine as safe. The odds of being self-reported likely to get the HPV vaccine after CDC recommendation was 59% lower among persons who perceived the HPV vaccine as unsafe compared with those who believed it to be safe (OR = 0.405, 95% CI: 0.22, 0.74). Similarly, the likelihood to be influenced to get the vaccine after an HPV awareness program on campus was 49% lower (OR = 0.512, 95% CI: 0.28, 0.94). All other associations between interventions and perceived vaccine safety registered unstable confidence intervals.

Conclusions
A minority of university undergraduates perceive the HPV vaccine as unsafe, but interventions to address vaccination coverage can be substantially affected by these perceptions. The characteristics of an intervention's target audience should be assessed beforehand to ensure efficacy of catch-up HPV vaccination programs.

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TERMS OF REFERENCE

ACIP	Advisory Committee on Immunization Practices
CI	Confidence Interval
DAG	Directed Acyclic Graph
HPV	Human Papillomavirus
IPTW	Inverse Probability Treatment Weighting
OR	Odds Ratio
US	United States of America

1. BACKGROUND

1.1. Human papillomavirus (HPV)

1.1.1. Introduction

Human papillomavirus (HPV) is the most common sexually transmitted infection, which burdens college women and men with the highest risk for acquisition and prevalence (1). The infection causes cervical cancer, and is associated with cancers of the anus, oropharynx, penis, vagina, and vulva (2). Three inactivated vaccines are licensed for use in the United States (US) that protect for the majority of HPV-associated cancers. Beginning in the latter of 2016, 9vHPV is the only HPV vaccine being distributed in the US. The Advisory Committee on Immunization Practices (ACIP) recommends routine 2- or 3-dose vaccinations for females and males aged 11 or 12 years. Vaccination can be initiated at age 9 years, and is recommended for females through age 26 years and males through age 21 years; males age 22 to 26 years may be vaccinated. Clinical trials demonstrate at least 10 years of protection (3, 4).

1.1.2. Biology

HPV is a DNA virus that targets the basal cells in the stratified squamous epithelium of the cervix, the metaplastic cells at the squamocolumnar junction of the cervix, and the glandular epithelium of the endocervix. The infection is not usually associated with immediate symptoms. The host immune system resolves the majority of infections prior to any onset of symptoms. Individuals may become symptomatic and present with genital warts. Infection can also result in oncogenic changes caused by degradation of host-cell p53 proteins, telomerase activation, or inactivation of retinoblastoma protein. Consequently, the decrease in immune response and onset of host cell mutations can cause cervical lesions or cancer (5). HPV type 16, the most common high-risk type, accounts for more than half of all cervical cancers (6). HPV types 16 and 18 are responsible for 70% of HPV associated cancers (7).

No tests exist to identify HPV infection. Most women discover infection through abnormal Pap test results during cervical cancer screenings. These screenings are only recommended for women aged 30 years and older (8). Although the disease itself cannot be treated, the outcomes (e.g., genital warts, pre-cancerous cell changes, cancers) are treatable. There are also vaccines in the market to protect nine of the 40 types of HPV (6, 9).

1.1.3. Epidemiology

HPV is transmitted by direct, skin-to-skin contact with an infected individual. Most sexually active individuals will be infected with at least one type of HPV type over the course of their lives. Approximately 79 million persons living within the US are currently infected. An estimated 14 to 15 million incident infections occur each year (7, 8, 10).

Infection with HPV is believed to be responsible for nearly all cases of cervical cancer, 90% of anal cancer cases, 71% of vulvar, vaginal, or penile cancer cases, and 72% of oropharyngeal cancer cases. The financial cost of burden in the US is estimated to be 8 billion dollars due to HPV infections (7).

HPV vaccine efficacy is substantially high. Over 99% of recipients develop antibodies to the HPV types protected by the vaccines. Some protection for recipients vaccinated after prior exposure may occur, but further research is required (11). No serious adverse effects have been reported after vaccination. The most common adverse reaction is pain, redness, or swelling at the site of injection. Other reported adverse effects have included fever, nausea, dizziness, myalgia, and malaise (7). Despite the protection HPV vaccines provide and the little or no evidence of severe side effects associated, HPV vaccination coverage rests well below other recommended childhood immunizations. Coverage is not on track to meet the Healthy People 2020 goal of 80% (12, 13). In 2015, female HPV vaccination coverage with ≥ 1 dose was 62.8% and with 3 doses was 41.9%. Male coverage with ≥ 1 dose was 49.8% and with 3 doses was 28.1% (14).

1.1.4. Vaccine acceptance & hesitancy

Determinants of vaccine acceptance are complex. Various quantitative studies have been conducted to assess predictors of acceptance for the HPV vaccine. Factors associated with acceptance include: number of sexual partners (i.e., higher number of partners), susceptibility (i.e., persons who estimate current or future risks), vaccine safety, vaccine benefits, parent or healthcare provider recommendations, significant other influences, vaccine effectiveness, fear of shots, cost, ethnicity, and knowledge of HPV (15, 16). Uptake has been related to lower age, being unmarried, religion, knowledge of HPV spread, awareness of connection between HPV and cervical cancer, belief of importance in immunizations, and doctor recommendations (17).

Hesitancy can be steered by contextual influences (e.g., religion, media), individual or social group influences (e.g., perceived risks, social norms), and vaccine-specific issues (e.g., costs, science) (18-20). Perception of HPV vaccine safety has been demonstrated as a significant predictor of acceptance in various quantitative studies. Individuals have expressed concern about potential adverse side effects due to the relative short time frame the vaccine has been publically available (15, 16, 21, 22). Parent restriction among college students to vaccinate was also supported by a study of HPV uptake and barriers for 10% of the sample population (21).

Additionally, qualitative studies have repeatedly determined HPV vaccine hesitancy due to fear of side effects. Respondents to a study of mothers with children aged 9 to 26 years rated vaccine safety and efficacy as the most important factor influencing their decision to vaccinate their children. There was a concern about whether or not the HPV vaccine has been tested enough (23). Likewise, a qualitative study of college women's HPV perspectives among students at a large northeastern university uncovered a narrative of vaccine safety skepticism. Families, health care providers, and peer norms shaped their perceptions (24). An additional in-depth interview study of female college students aged 18 to 26 years found that vaccine safety was not a major influence among vaccinated persons; however, non-vaccinated persons were concerned about short-term and long-term safety and efficacy. Their beliefs about the vaccine originated from news stories, word-of-mouth stories from friends, parent influences, and general concerns about immunizations (25).

1.1.5. Catch-up vaccination programs

Parents have control over vaccination of their children. Pediatricians acknowledge adolescents as not a captive audience for vaccine recommendations. Therefore, current initiatives to improve HPV vaccination coverage are focused on parents and physicians (26-30). A study in 2010 identified that 56% of parents refused HPV vaccination for their children (22). Thus, teens leaving their guardians' homes for college provide an opportunity for catch-up interventions. Impacts of these programs have been diverse. Environmental approaches, such as school-based vaccination programs, have achieved the highest vaccination coverage (31). Other interventions have shown mixed results. Free HPV vaccinations were offered at a US university resulting in similar vaccination rates to the national average (32). An intervention comparing the influence of gain- or loss-framed messages had no effect on vaccine uptake (33). On the contrary, female university students showed an educational video about HPV had significantly higher vaccination coverage relative to the control group (34).

There is limited research on factors that drive some young adults to pursue HPV vaccination while others do not. Analyzing the role fear of HPV immunization plays in vaccination hesitancy among college students will shed light on immediate and long-term public health strategies to improve coverage.

1.2. Inverse probability treatment weighting (IPTW)

1.2.1. Introduction

Inverse probability treatment weighting (IPTW) with observational study data mimics the results of a randomized clinical trial. A synthetic, pseudo data set is created to reduce selection bias by using the propensity score to assign exposure independent of other measured covariates. The propensity score is evaluated through logistic regression with the outcome being the active and control treatment groups. Using the propensity-stabilized weights allows for unbiased estimates of average exposure effects independent of other covariates (35, 36).

1.2.2. Variable selection

The primary purpose of the propensity score is to balance measured covariates between treated and control participants. Therefore, variable selection for IPTW should include prognostically important covariates rather than covariates that affect treatment selection without having an impact on the outcome. In other words, covariate selection for the propensity score model should focus on confounding covariates (37).

1.2.3. Assumptions

Four assumptions are made when using propensity score methods: consistency, exchangeability, positivity, and no misspecification of the model. Consistency means the individual's potential outcome under the treatment is precisely the individual's observed outcome. Exchangeability implies that there are no unmeasured confounders in the study. Positivity means that there is a non-zero probability of receiving the treatment. Specification refers to the input of covariates in the propensity score model; particularly, specification should be assessed when using continuous variables as predictors in the logistic regression model (35).

1.2.4. Diagnostics

The assumption of exchangeability cannot be formally tested. Subject matter knowledge is the primary resource to mitigate issues of unmeasured confounding in a study. Positivity and misspecification can be assessed to some degree using balancing scores. Positivity can be assessed by stabilized weights. A mean value far from one or an extreme maximum weight is indicative of non-positivity. Potential misspecification of the propensity model can be analyzed using absolute standardized differences. Literature suggests an arbitrary threshold <0.25 indicative of confounder balance between exposure groups; however, some authors have proposed standardized differences >0.1 indicative of meaningful imbalance (35, 38, 39).

2. MANUSCRIPT

Fear of HPV Vaccine Safety Affects Self-Reported Likelihood to Be Vaccinated after Interventions among University Undergraduates

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Conflicts of Interest: The authors report no conflicts of interest.

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Condensation

University undergraduates that perceive the HPV vaccine as unsafe comprise a minority of the undergraduate population, but interventions to address vaccination coverage can be substantially affected by perceptions of vaccine safety; thus, it is critical to understand an intervention's target audience prior to any action.

Short version of title: Undergraduates' Perceptions of HPV Vaccine Safety Affects Intervention Outcomes

Abstract

Background

Human papillomavirus (HPV) burdens college women and men with the highest risk for acquisition and prevalence. Despite the protection HPV vaccines provide and the little or no evidence of severe side effects associated, vaccination coverage is not on track to meet the Healthy People 2020 goal of 80%. Assessing how fear of HPV vaccine safety affects interventions to increase coverage among 18 to 26 year old university students will shed light on viable catch-up vaccination programs.

Methods

A secondary analysis was performed with data obtained by a HPV Vaccine and Decisions Making Behaviors Survey administered to undergraduate students. Inverse probability treatment weighting (IPTW) was used to create a pseudo data set in which confounding covariates were balanced between persons who perceived the HPV vaccine as unsafe or safe. Odds ratios were calculated with logistic regression models using stabilized weights to identify relationships between perceived vaccine safety and likelihood to be vaccinated after interventions.

Results

Overall, 50 (11.5%) students perceived the HPV vaccine as unsafe, while 386 (88.5%) perceived the vaccine as safe. The odds of being self-reported likely to get the HPV vaccine after CDC recommendation was 59% lower among persons who perceived the HPV vaccine as unsafe compared with those who believed it to be safe (OR = 0.405, 95%

CI: 0.22, 0.74). Similarly, the likelihood to be influenced to get the vaccine after an HPV awareness program on campus was 49% lower (OR = 0.512, 95% CI: 0.28, 0.94). All other associations between interventions and perceived vaccine safety registered unstable confidence intervals.

Conclusions

A minority of university undergraduates perceives the HPV vaccine as unsafe, but interventions to address vaccination coverage can be substantially affected by these perceptions. The characteristics of an intervention's target audience should be assessed beforehand to ensure efficacy of catch-up HPV vaccination programs.

Key Words

human papillomavirus (HPV), perceived vaccine safety, catch-up vaccination, university health, inverse probability treatment weighting (IPTW), propensity score

2.1. Introduction

Human papillomavirus (HPV) is the most common sexually transmitted infection, which burdens college women and men with the highest risk for acquisition and prevalence (1). The infection causes cervical cancer, and is associated with cancers of the anus, oropharynx, penis, vagina, and vulva (2). Three inactivated vaccines are licensed for use in the United States that protect for the majority of HPV-associated cancers (3). In 2015, female HPV vaccination coverage with ≥ 1 dose was 62.8% and with 3 doses was 41.9%. Male coverage with ≥ 1 dose was 49.8% and with 3 doses was 28.1% (14).

Despite the protection HPV vaccines provide and the little or no evidence of severe side effects associated, HPV vaccination coverage rests well below other recommended childhood immunizations. Coverage is not on track to meet the Healthy People 2020 goal of 80% (12, 13). Determinants of vaccine acceptance are complex. Hesitancy can be steered by contextual influences (e.g., religion, media), individual or social group influences (e.g., perceived risks, social norms), and vaccine-specific issues (e.g., costs, science) (18-20). Perception of HPV vaccine safety has been demonstrated as a significant predictor of acceptance in various quantitative and qualitative studies (15, 16, 21-25, 40).

Current initiatives to improve HPV vaccination coverage are focused on parents (26-30). Therefore, teens leaving their guardians' homes for college provide an opportunity for catch-up interventions. Impacts of these programs have been diverse. Free HPV vaccination programs, as well as gain- or loss- framed messaging campaigns, have shown no effect on vaccine uptake; on the contrary, HPV educational videos have significantly increased vaccination coverage relative to control groups (31-34). There is limited research on factors that drive some young adults to pursue HPV vaccination while others do not.

The objective of this study was to assess how perception of HPV vaccine safety could potentially affect outcomes of interventions to increase immunization coverage among 18 to 26 year old college students. The intention was to evaluate future interventions that could improve vaccination coverage among persons who perceive the vaccine as unsafe. Factors that influence health care decision-making and sources of vaccine information were considered when assessing the impact perception of safety has on interventions. Analyzing the role fear of HPV immunization plays in vaccination hesitancy among college students will shed light on immediate and long-term public health strategies to improve coverage.

2.2. Methods

2.2.1. Design

Perceived likelihood of receiving the HPV vaccination among a variety of interventions dependent upon persons' believed safety of the vaccine was investigated in this study. The secondary analysis was performed with data obtained by a HPV Vaccine and Decisions Making Behaviors Survey collected between October and November of 2014 of university students in Georgia. The Emory University approved this study as IRB exempt.

2.2.2. Survey

The 50-item survey drew from existing theories and models (e.g., Health Belief Model, Transtheoretical Model, and Theory of Planned Behavior) to assess topics regarding HPV vaccine, healthcare decision-making, personal health history and behaviors, sexual health history and behaviors, and demographic information (41-43). Items were also adapted from a previously implemented survey by one of the co-investigators and the validated Youth Engagement with Health Services (YEHS!) survey (21, 44, 45).

Participants were questioned about their agreement with the statement, "The HPV vaccine is safe." Responses on a 4-point Likert scale ranged from strongly disagree to strongly agree. Additionally, participants were asked how fourteen potential interventions would influence their decisions about getting the HPV vaccine on a 5-point Likert scale ranging from much less likely to much more likely. An additional option of "don't know" was presented. Other sets of questions included 5-point Likert scales for influences of healthcare decision-making, 5-point Likert scales for confidence/trust in information about health topics from various sources, relationship to a primary care doctor, financial independence, sex, and race.

2.2.3. Study population

The survey population consisted of students at an urban private religious-affiliated university and a rural public university in Georgia. Participants had to be enrolled in an introductory undergraduate course, at least 18 years of age, and able to read and understand English. No purposive sampling for race, ethnicity, sex, or other socio-demographic characteristics was performed (44).

2.2.4. Data analysis

The exposure of interest, perceived safety of the HPV vaccine, was dichotomized by yes (agree and strongly agree) versus no (disagree and strongly disagree). The outcome of interest, perceived influence of interventions, was categorized by more likely (much more likely and a little more likely) versus no increase in likelihood (much less likely, a little less likely, and no change). Values of “don’t know” were set as missing. Additional covariates for influences of healthcare decision-making and confidence/trust in sources were dichotomized by low (none and little) versus medium to high (some, much, and very much). Any observations with missing values for the exposure or covariates of interest were dropped from the sample.

Inverse probability treatment weighting (IPTW) was used to mimic the results of a randomized clinical trial and reduce selection bias. A synthetic, pseudo data set was created in which perception of HPV vaccine safety was the treatment logistically regressed on covariates of interest (Table 1). Using the propensity-stabilized weights allowed for unbiased estimates of average exposure effects independent of other covariates (35, 36). Odds ratios (ORs) were calculated with bivariate logistic regression models using the stabilized weights to identify relationships between perceived safety of HPV vaccination and believed influences of interventions.

Covariate selection for the propensity score model focused on confounding covariates (37). A Directed Acyclic Graph (DAG) was modified from a prior study on factors associated with HPV vaccine uptake (17). An online tool, DAGitty (http://www.dagitty.net) was used to produce minimally sufficient adjustment sets for confounders (Fig. 1) (46). Potential misspecification of the propensity model was analyzed using absolute standardized differences. Literature suggests an arbitrary threshold <0.25 indicative of confounder balance between exposure groups; however, some authors have proposed standardized differences >0.1 indicative of meaningful imbalance (35, 38, 39). Likewise, positivity was assessed by stabilized weights. A mean value far from one or an extreme maximum weight is indicative of non-positivity (35).

IPTW and balance diagnostics were performed using R (R Core Team, 2016). Descriptive statistics and bivariate logistic regressions were performed using SAS software, Version 9.4 (Cary, NC). Results were considered statistically significant if $p < 0.05$.

2.3. Results

The survey resulted in an 89.2% response rate at the urban private university, and a 97.4% response rate at the rural public university. All respondents aggregated into a single sample population regardless of institution type had an overall response rate of 93.1%, or a total of 527 students. The HPV vaccine was perceived unsafe by 60 (11.4%) of these students. The subset of data excluding participants with any missing values for the exposure or covariates of interest consisted of 436 students (44).

Overall, 50 (11.5%) students in the data subset perceived the HPV vaccine as unsafe, while 386 (88.5%) perceived the vaccine as safe. A significant difference existed between perception of safety and HPV vaccination status ($p<0.0001$). Sixteen of the 21 covariates had standardized differences greater than 0.1, and four had standardized differences greater than 0.25 (Table 1). The propensity score model resulted in a mean stabilized weight equal to 1.004 with a standard deviation of 0.417. The minimum and maximum weights were equal to 0.177 and 5.220, respectively. After balancing, four of the 21 covariates had standardized differences greater than 0.1; none were above 0.25 (Table 1; Fig. 2).

There was a significant difference in likelihood to be vaccinated for two interventions depending on perception of vaccine safety. The odds of being self-reported likely to get the HPV vaccine after the CDC guidelines recommended immunization was 59% lower among persons who perceived the HPV vaccine as unsafe compared with those who believed it to be safe (OR = 0.405, 95% CI: 0.22, 0.74). Similarly, the likelihood to be influenced to get the vaccine after an HPV awareness program on campus was 49% lower among persons who perceived the vaccine as unsafe compared with those who believed it to be safe (OR = 0.512, 95% CI: 0.28, 0.94). All other associations between interventions and perceived vaccine safety registered unstable confidence intervals (Table 2).

2.4. Discussion

The HPV vaccine was considered unsafe by 11% of students in the sample. Considering national vaccination coverage for females and males with ≥ 1 dose is 62.8% and 49.8%, respectively, the study's findings suggest that vaccine hesitancy due to fear of adverse effects is not the singular cause for low coverage (14). The finding is supported by other studies, which establish a small but significant effect size for fear of side effects on HPV vaccine acceptability (16, 40).

The IPTW methodology was advantageous compared with previous studies. Controlling other measured covariates through propensity scoring allowed us to determine an independent difference in self-reported likelihood to be vaccinated after an intervention depending on perceived safety of the HPV vaccine. Perception of vaccine safety was significantly associated with interventions where the CDC guidelines recommended immunization or an HPV awareness program was hosted on campus. The odds of being influenced to receive the vaccination were lower for these two interventions (59% or 49% lower, respectively) among those who perceived the vaccine as unsafe compared with those who believed it to be safe. In other words, there were reverse effects for these interventions in which those perceiving the vaccine as unsafe were significantly less likely to be influenced to receive vaccination after the intervention.

The reverse effects may be suggestive of self-reinforcing effects of biased assimilation or credibility heuristic. Biased assimilation is the tendency of individuals to accept information that corroborates prior beliefs and challenge information that does not. Credibility heuristic refers to the tendency to accept credibility of an argument based on preexisting connections to the source of information (20). College students who perceive the HPV vaccine as unsafe may be negatively predisposed to interventions from the CDC or those without symptom prevention messages in accordance with these mechanisms. The differences may also exist simply because these interventions are the easiest to ignore. For example, participants fearing vaccine safety were more receptive of receiving

HPV vaccination when engaged through interactive interventions such as social media/app campaigns, although the differences were unstable. These interventions were advantageous over TV/radio/print campaigns, which are less interactive. Future studies may assess the potential value of more engaging, technology-based interventions on influencing vaccination among individuals who perceive the HPV vaccine as unsafe.

The findings also suggest that encouragement from significant others may have enough strength to overcome concerns about safety. Recommendations from friends, which lack an intimate relationship, suggested no difference between groups. Moreover, talking to someone who had a good experience or interventions that did not disseminate knowledge of HPV or the vaccine, including free vaccinations or vaccines offered on campus, did not influence vaccination likelihood among persons who perceived the vaccine as unsafe relative to those who believed it to be safe. Additionally, physician encouragement and parental focus have been valuable methods to increase HPV vaccination coverage, but our findings suggested a decreased likelihood to be vaccinated for those with concerns of vaccine safety (21, 40). The discordance may suggest college students act autonomously of physician and parental recommendations at this age. Thus, it is critical to understand an intervention's target population prior to any action.

Despite the benefits of IPTW, the methodology may potentially be a limitation of the study. Effectiveness is largely dependent upon correct assessment of confounders. Creating a weighted sample with balanced distributions of covariates that affect the exposure but not the outcome can result in increased bias of the exposure-effect estimate (35). Balancing diagnostics identified absolute standardized differences greater than 0.1

but less than 0.25 for only four covariates, which suggested a low probability of model misspecification in this study.

The cross-sectional design of the study was an additional limitation due to self-report bias. Participant self-reported likelihood to receive the HPV vaccine after various interventions may not be representative of actual likelihood to be vaccinated. An explicit explanation of vaccine safety was also not addressed in the survey. Perceived safety risks can be a topic for further research on HPV vaccination.

Overall, perception of HPV vaccine safety has been reported as a significant predictor of vaccine uptake in prior studies; however, our findings suggested that undergraduate students who fear adverse effects comprise a minority of the university undergraduate population. Nonetheless, interventions to increase vaccination coverage can be substantially affected by perceived vaccine safety. The target population of any HPV intervention should be assessed for consequential characteristics beforehand to ensure efficacy. Navigating the role fear plays in vaccine hesitancy will be a critical obstacle as we progress towards the Healthy People 2020 goal of 80% HPV vaccine coverage.

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2.6. Tables

Table 1. Characteristics of individuals perceiving the HPV vaccine as safe or unsafe among an original subset (N=436) and an inverse probability treatment weighted (IPTW) subset of data from HPV Vaccine and Decision Making Behaviors survey[a]

Characteristic	Perception of HPV Vaccine Safety, N (%)		Original		Weighted
	Unsafe (N=50)	Safe (N=386)	p-value[b]	SMD	SMD
Female	36 (8.3)	263 (60.3)	0.5796	0.084	0.099
HPV vaccinated	13 (3.0)	241 (55.3)	<0.0001	0.789	0.051
Financially independent	5 (1.2)	28 (6.4)	0.4897	0.098	0.012
Primary doctor	33 (7.6)	294 (67.4)	0.1183	0.226	0.190
Race/ethnicity					
White, only	33 (7.6)	276 (63.3)	0.4027	0.262	0.172
African American, only	5 (1.2)	21 (4.8)			
Asian, only	6 (1.4)	52 (11.9)			
Hispanic	2 (0.5)	22 (5.1)			
Other/combination	4 (0.9)	15 (3.4)			
Confidence/trust (ref = low)[d]					
School health/resource center	39 (8.9)	340 (78.0)	0.0466	0.271	0.048
Newspapers/magazines	17 (3.9)	168 (38.5)	0.1998	0.196	0.052
Television/radio	15 (3.4)	136 (31.2)	0.4643	0.112	0.044
Internet sources	32 (7.3)	249 (57.1)	0.9437	0.011	0.109
Doctor	47 (10.8)	378 (86.7)	0.0957	0.201	0.045
Governmental agencies	39 (8.9)	320 (73.4)	0.3924	0.124	0.163
Family	44 (10.1)	357 (81.9)	0.2719	0.152	0.071
Friends	29 (6.7)	254 (58.3)	0.2767	0.161	0.021
Decision making (ref = low)[e]					
TV/magazine ads/social media	13 (3.0)	106 (24.3)	0.8273	0.033	0.066
Parents'/guardians' beliefs	43 (9.9)	346 (79.4)	0.4352	0.111	0.004
Friends' beliefs	22 (5.1)	202 (46.3)	0.2674	0.167	0.046
Finances	34 (7.8)	228 (52.3)	0.2249	0.186	0.004
Type of/lack of insurance	28 (6.4)	206 (47.3)	0.7254	0.053	0.010
Religious beliefs	13 (3.0)	51 (11.7)	0.0162	0.326	0.022
Family health history	33 (7.6)	273 (62.6)	0.4919	0.102	0.046
Hx care for chronic conditions	17 (3.9)	166 (38.1)	0.2247	0.186	0.012

Abbreviation: SMD, standardized difference.
[a] Only participants with no missing observations for covariates of interest were eligible.
[b] Fisher's exact test was utilized for race/ethnicity; Pearson chi-square tests for all other analyses.
[d] Low confidence/trust in information about health topics included none and little; medium to high confidence/trust included some, much, and very much.
[e] Low influence for health care decision-making included none and little; medium to high influence included some, much, and very much.

Table 2. Odds of self-reporting likelihood to get the HPV vaccine by perceived safety of the vaccine among an inverse probability treatment weighted (IPTW) subset of data from HPV Vaccine and Decision Making Behaviors survey[a]

Intervention[b]	Likelihood to be vaccinated[c]	Perception of HPV Vaccine Safety, N (%)		OR	95% CI
		Unsafe	Safe		
TV/radio/print campaigns focused on preventing genital warts (N=419.3)	No	32.7 (7.8)	227.5 (54.3)	Ref.	Ref.
	Yes	18.2 (4.3)	140.9 (33.6)	0.897	0.49, 1.65
TV/radio/print campaigns focused on preventing cancer (N=422.3)	No	27.3 (6.5)	186.0 (44.0)	Ref.	Ref.
	Yes	23.6 (5.6)	185.5 (43.9)	0.864	0.48, 1.56
Social media/app campaigns focused on preventing genital warts (N=421.1)	No	29.1 (6.9)	247.7 (58.5)	Ref.	Ref.
	Yes	21.4 (5.1)	123.0 (29.2)	1.480	0.81, 2.69
Social media/app campaigns focused on preventing cancer (N=416.8)	No	23.4 (5.6)	197.1 (47.3)	Ref.	Ref.
	Yes	25.5 (6.1)	170.8 (41.0)	1.257	0.69, 2.29
If a parent/guardian encouraged you to (N=423.7)	No	9.1 (2.2)	43.2 (10.2)	Ref.	Ref.
	Yes	41.7 (9.9)	329.6 (77.8)	0.599	0.27, 1.31
If a friend encouraged you to (N=422.5)	No	19.6 (4.6)	131.8 (31.2)	Ref.	Ref.
	Yes	31.3 (7.4)	239.8 (56.8)	0.880	0.48, 1.61
If a doctor encouraged you to (N=404.5)	No	6.6 (1.6)	35.8 (8.9)	Ref.	Ref.
	Yes	40.7 (10.1)	321.4 (79.5)	0.688	0.28, 1.68
If your partner/significant other encouraged you to (N=413.7)	No	8.6 (2.1)	91.4 (22.1)	Ref.	Ref.
	Yes	42.3 (10.2)	271.4 (65.6)	1.668	0.77, 3.60
If the CDC guidelines recommended you to (N=415.1)	No	21.9 (5.3)	85.2 (20.5)	Ref.	Ref.
	Yes	29.0 (7.0)	279.0 (67.2)	*0.405	0.22, 0.74
An HPV awareness program on campus (N=419.7)	No	32.6 (7.8)	178.5 (42.5)	Ref.	Ref.
	Yes	17.8 (4.3)	190.9 (45.5)	*0.512	0.28, 0.94
If the HPV vaccine was offered on campus (N=413.0)	No	25.8 (6.2)	147.9 (35.8)	Ref.	Ref.
	Yes	24.7 (6.0)	214.7 (52.0)	0.659	0.37, 1.19
If the HPV vaccine was free (N=402.8)	No	18.9 (4.7)	112.7 (28.0)	Ref.	Ref.
	Yes	26.8 (6.6)	244.5 (60.7)	0.652	0.35, 1.22
Talking to someone who had a bad side effect (N=410.2)	No	35.6 (8.7)	290.9 (70.9)	Ref.	Ref.
	Yes	10.1 (2.5)	73.6 (18.0)	1.115	0.53, 2.35
Talking to someone who had a good experience (N=416.8)	No	24.8 (5.9)	135.5 (32.5)	Ref.	Ref.
	Yes	25.6 (6.2)	230.9 (55.4)	0.607	0.34, 1.10

Abbreviation: OR, odds ratio; CI, confidence interval.

[*] p-value < 0.05.

[a] Only participants with no missing observations for covariates of interest were eligible.

[b] N is the sum of weights used in the bivariate regression model.

[c] No likelihood to get vaccinated included much less likely, a little less likely, and no change; yes included a little more likely and much more likely. Don't know responses were excluded.

2.7. Figures

Figure 1. DAG showing potential confounders within the relationship between perceived safety of HPV vaccine and self-reported likelihood to get the vaccine after an intervention (46).

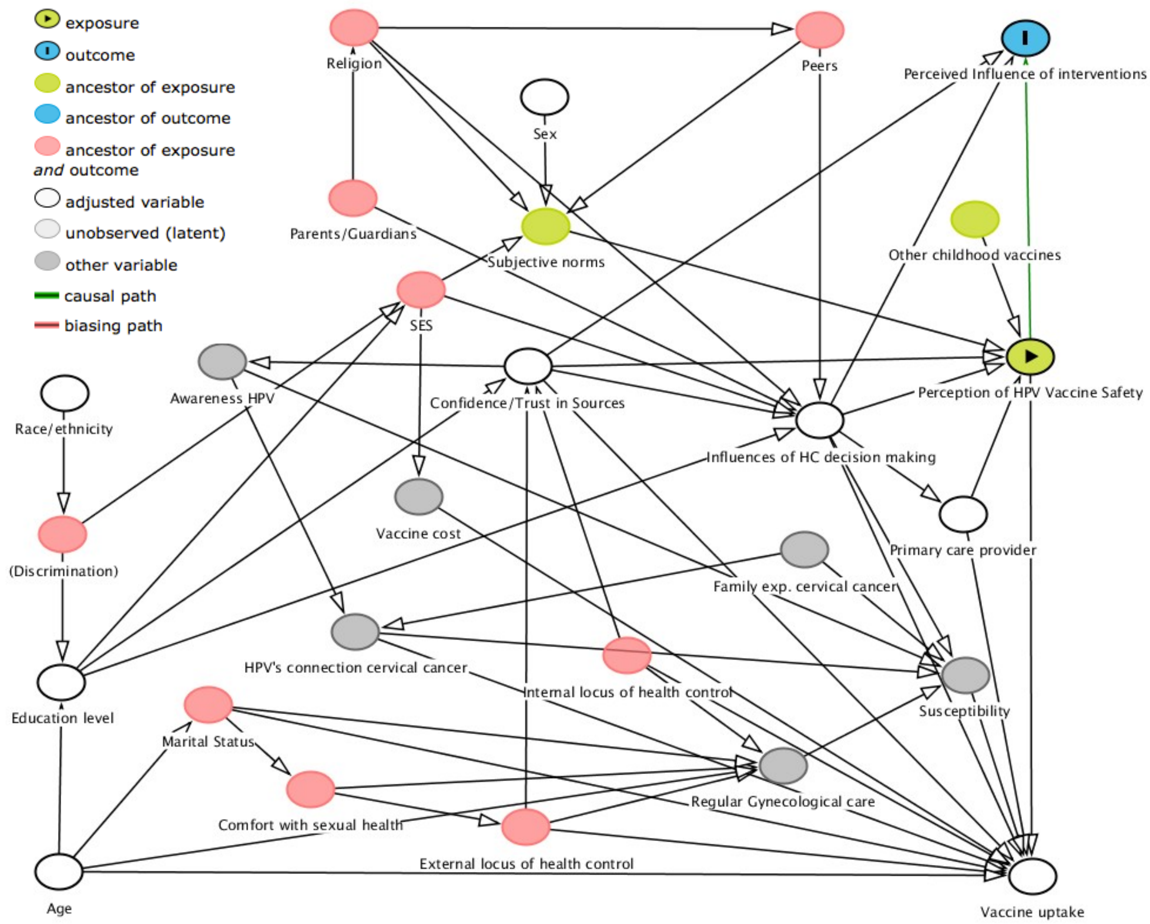
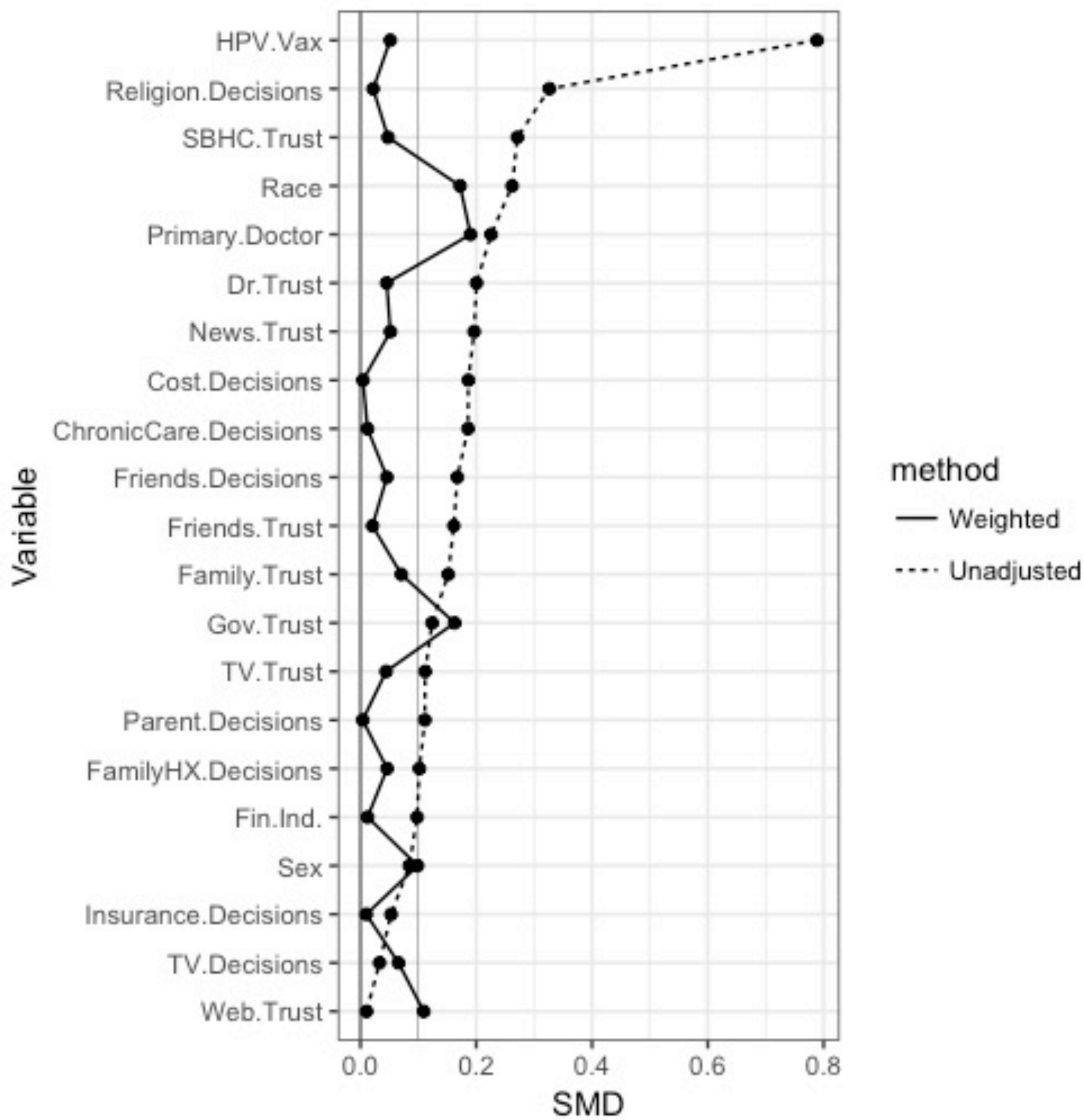


Figure 2. Absolute standardized differences in unadjusted and stabilized IPTW subset of data from HPV Vaccine and Decision Making Behaviors survey.



3. PUBLIC HEALTH IMPLICATIONS

3.1. Summary

Various studies have identified perception of HPV vaccine safety as a significant predictor of vaccine uptake. Understanding the role fear of adverse effects associated with the immunization plays in vaccine uptake will guide future public health programs aimed at increasing vaccination coverage. University undergraduates offer a viable opportunity for catch-up interventions to this aim. These individuals are leaving their guardians' homes, and are beginning to develop autonomy in their decision-making behaviors. There is limited research on particular factors that motivate some young adults to vaccinate while others do not. Trepidations associated with vaccine safety among these individuals should be considered when designing catch-up vaccination programs to ensure efficacy.

3.2. Possible Future Directions

Perceived safety risks associated with the HPV vaccine can be a topic for further research among college students. Acknowledging that approximately one in ten students may be concerned with HPV vaccine safety, it would be beneficial to understand the specific reasoning behind these fears when addressing vaccination coverage. These instilled fears may potentially influence the impact of physician and parental encouragement to be vaccinated, which have been valuable methods to increase HPV vaccination coverage. Thus, further understanding of this population will be critical to improving vaccination coverage.

Additionally, future studies may assess the potential value of more engaging, technology-based interventions on influencing vaccination among young adults. Interventions that are easier to ignore and neglect may have no impact on persons who already perceive the vaccine as unsafe. Assessing strategies to target this select population may provide insights into health programs that will influence immunization among persons fearing or ambivalent of vaccine safety.