



## Interventions to increase uptake of the human papillomavirus vaccine in unvaccinated college students: A systematic literature review

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### ABSTRACT

**Objective:** The purpose of this systematic review is to summarize the best available evidence on interventions that could be implemented in the college environment to increase HPV vaccination uptake in college students who were not previously vaccinated.

**Methods:** Pubmed, CINAHL, PsycINFO, Cochrane, and EBSCO were searched in December 2017 to identify all literature meeting the following criteria: human subjects, English language, HPV, HPV vaccination, and college. PRISMA recommendations were followed. We focused only on manuscripts that reported vaccine uptake, excluding studies that only reported vaccine intentions. We identified 2989 articles; 101 relevant after screening; nine eligible for final qualitative review.

**Results:** Vaccine uptake rates ranged from 5% to 53%. Theory-based variables (e.g., perceived susceptibility and self-efficacy) were associated with vaccine uptake in most studies. A study exposing participants to a narrative video about HPV vaccination led by a combination of peers and medical experts produced the greatest difference in HPV vaccination initiation compared to a control group (21.8% vs 11.8%) of all the studies reviewed.

**Conclusions:** Few interventions resulted in substantial HPV vaccine uptake. A combination of peer and provider encouragement may be the most effective method to increase vaccine uptake in this population.

### 1. Introduction

Human papillomavirus (HPV) is the most common sexually transmitted infection in the United States, with an estimated 14 million individuals newly infected annually (Satterwhite et al., 2013). HPV is responsible for > 38,000 cases of cancer in the United States each year, including 91% of all anal and cervical cancers, 75% of vaginal and vulvar cancers, and 63% of penile cancers (Viens, 2016). Each year > 4000 women die from cervical cancer alone in the U.S. (Singh, 2017). An effective HPV vaccination that can prevent most of the cancers from ever developing has been available since 2006. It has been recommended as a routine vaccination at 11 or 12 years of age for females since 2006 and for males since 2011 (Meites, 2016). Catch-up vaccination is recommended for females through age 26 and through age 21 for males. Vaccination is recommended through age 26 for men who

have sex with men and transgender persons. Three doses of HPV vaccine are recommended for males and females 9 to 26 with primary or secondary immunocompromising conditions (Meites, 2016).

Despite these recommendations HPV vaccination uptake remains suboptimal. The 2016 National Immunization Survey report for adolescents estimates that 49.5% of females and 37.5% of males were up-to-date on HPV vaccination (Walker, 2017). A variety of reasons for poor uptake have been identified including cost, the need for multiple visits to complete the series, and concerns that getting vaccinated will encourage teens to engage in risky sexual behavior (Forster et al., 2010; Holman et al., 2014; Quinn et al., 2014). Data indicate that young women aged 18–26 are less likely to initiate and complete the HPV vaccination series compared to those aged 13–17 (Tan et al., 2011). This is unfortunate as early adulthood is a prime opportunity for cancer prevention using the vaccine. While many may not perceive themselves

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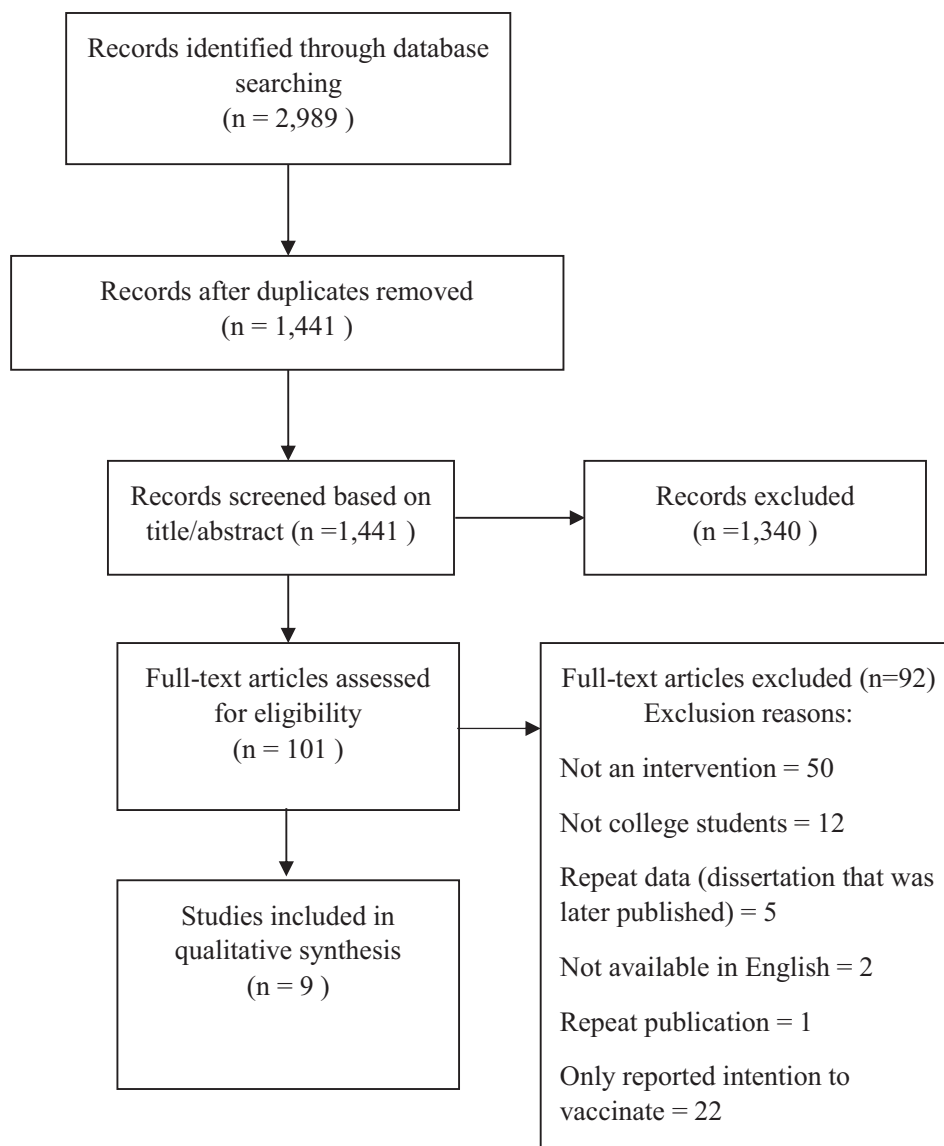


Fig. 1. Flow diagram of article selection.

to be at risk, average lifetime probability of acquiring HPV is 84.6% for females and 91.3% for males with at least one sexual partner of the opposite sex (Chesson et al., 2014). There is an urgent unmet need to identify effective strategies to encourage catch-up vaccination for those who reach young adulthood unvaccinated.

College campuses represent an opportunity to fill this need for a significant portion of the young adult population. College students are able to make their own health care decisions, are usually required to have health insurance, and have regular access to campus health centers (McBride et al., 2010; Turner and Hurley, 2002; United States Government Accountability Office, 2008). The American College Health Association included HPV vaccination as an objective in Healthy Campus 2020 (American College Health Association, 2012). For an institution to invest in an intervention to improve the long-term health of students, there must be good evidence that it impacts the targeted health behavior. Previous research has demonstrated that the correlation between HPV vaccination intention and behavior is not as high as would be expected (Juraskova et al., 2012). For this reason, focusing on actual HPV vaccination uptake as compared to intention to get vaccinated is important to guide program planning. The purpose of this systematic review is to provide the best available evidence on interventions that could be implemented in the college environment to

increase HPV vaccination uptake in young adults and to summarize, evaluate, and provide recommendations based on the results.

## 2. Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) was utilized to guide the systematic review of the literature (Moher et al., 2009). PRISMA offers structured guidance for reviews and provided the basis for the review protocol used in the current study. Potential articles were identified via searches of Cochrane, PubMed, CINAHL, PsycINFO, and EBSCO databases. Each search was limited to articles in the English language and those that utilized human subjects. In order to identify all available literature, no date limits were applied. The databases were searched in December 2017 using the terms “HPV” AND “college” AND “vaccine” and repeated by substituting “vaccination” as the last search term. The Cochrane database was search with the terms “HPV” AND “vaccine” as well as “HPV” AND “vaccination.” A total of 1441 non-duplicate articles were identified through these searches.

All identified articles were screened for full-text review. Inclusions for full-text review included (1) focused on college students, (2) focused on HPV vaccination, and (3) included some intervention or program to

increase uptake of the vaccine. Articles were excluded if they only included a pediatric or non-student population, focused on parent/caregiver interventions, were survey studies that did not include an intervention, were not peer-reviewed, or were not directly related to HPV vaccination. Two authors (MB and AC) screened titles and abstracts for inclusion in the full-text review, with a third author (LW) resolving any discrepancies. A total of 101 articles were identified for full-text review. The data charting process was conducted via a Qualtrics data entry form. The form was tested by the team, with all team members completing reviews of several articles to ensure the abstraction process was uniform. Data items abstracted included study design and duration, population (inclusion criteria, demographics, HPV vaccination status), intervention and comparison treatment descriptions, treatment allocation, blinding, HPV vaccine outcomes and follow-up length, integrity of and adherence to the intervention, management of missing participants, other variables assessed (e.g., knowledge, attitudes about vaccines), and funding source. The charting was conducted by three authors (AC, EG, and MC) and a fourth author (MB) resolved any discrepancies. Additionally, references in all articles for which a full-text review was completed were scanned for potential identification of any references that may not have been identified in the original search. No additional references were identified. After full-text review, 92 articles were excluded. Studies were excluded after full text review if they did not report on an intervention, did not focus on college students, were dissertations whose peer-reviewed publications were included in the review, did not have full text available in English, were a repeat publication of the same study data, or only reported on intention to get the HPV vaccination rather than reporting actual vaccine uptake. HPV vaccine uptake was the main outcome abstracted. See Fig. 1 for the PRISMA flow diagram which describes the article selection process. An inductive content analysis of the abstracted data was conducted to identify themes by two authors separately (MB and EG) and then reviewed and confirmed by all authors. Data were organized and reported by the identified themes.

### 3. Results

The nine articles selected for review are summarized in Table 1. All of the studies were randomized controlled trials except for one. Most of the studies (7 of 9) only included female participants. All of the studies were conducted in the United States, except for one which was conducted in Australia. Six studies tested interventions in controlled lab settings, two did so in health care clinics, and one in a health fair setting. The risk of bias at the study level was assessed utilizing the Cochrane Collaboration's tool for assessing risk of bias and potential biases are identified in Table 1 (Higgins and Green, 2011).

#### 3.1. HPV vaccine uptake rates

There was wide variation in the length of follow-up (4 weeks to 10 months) and the rate of HPV vaccine initiation and completion (5–53%) across the studies. Only one randomized trial demonstrated increased uptake of at least one dose in the intervention compared to the control condition (Hopfer, 2012). However, studies varied widely in actual rates of vaccine uptake and often utilized two interventions without a control condition for comparison. For example, Bennet et al. had a 7.83% uptake of one dose in the intervention group and 8.73% in the control group whereas Juraskova et al., which examined two interventions head-to-head, achieved 32% uptake of at least one dose in one group and 44% in the other group (Bennett et al., 2015; Juraskova et al., 2011). Differences in uptake rate may be related to the length of time participants were followed and whether they reported uptake based on at least one dose or completion of the vaccine series. One study assessed vaccine uptake at four weeks post-intervention (Perez et al., 2016) and four assessed this at two to three months post-intervention (Bennett et al., 2015; Hopfer, 2012; Juraskova et al., 2011;

Venkatesan, 2011). Three studies went at least as long as a semester, with one assessing uptake at six months after the intervention, (Patel et al., 2012) one at seven months, (Richman et al., 2016) and one at ten months. Five of the studies utilized chi-square analyses to compare HPV vaccine uptake rates between the treatment groups and three of the studies utilized regression methods that permitted controlling for covariates (Hopfer, 2012; Patel et al., 2012; Venkatesan, 2011).

#### 3.2. Interventions

None of the studies, briefly described in Table 1, used the same intervention. Interventions ranged from tailored messages on websites to gain and loss-framed video messages, stigmatizing and fear-oriented messages to enhanced reminder systems. Most (7 of 9) used some sort of educational intervention (Bennett et al., 2015; Gerend and Shepherd, 2012; Hopfer, 2012; Juraskova et al., 2011; Patel et al., 2012; Perez et al., 2016; Richman et al., 2016). The studies that achieved at least a 20% uptake of at least the first dose utilized interventions that would be relatively easy to implement as they are relatively inexpensive and easy to disseminate widely. Hopfer demonstrated a 21.8% vaccination uptake rate of at least one dose in the group that watched a peer and medical expert-led video about the vaccination (Hopfer and Clippard, 2011). Juraskova et al. achieved a 44% uptake rate of one dose with an information leaflet that describe the vaccines protection from cervical cancer and genital warts and Richman et al. achieved completion of two doses in 53% and three doses in 34% of the intervention group which received monthly health education and reminder prompts (Juraskova et al., 2011; Richman et al., 2016).

#### 3.3. Combined peer and provider impact

While only one of these interventions had a significant impact on increasing uptake compared to the comparison condition in each study, there was a common intervention component associated with a non-significant but positive impact on vaccine uptake in three of the studies. Hopfer found the highest uptake in the combined peer and medical expert-led vaccination video condition (Hopfer, 2012). Long et al. increased the number of vaccines administered year-to-year with the inclusion of language-specific education to Chinese students provide by peer educators, and Venkatesan reported that participants who got the first vaccine dose were more likely to have consulted family and friends in addition to their healthcare provider compared to participants who did not get the vaccine (Long et al., 2017; Venkatesan, 2011). A combination of both peer and provider support may be critical to increasing college students' uptake of the vaccine.

#### 3.4. Knowledge and perception of HPV and HPV vaccine

While the primary outcome of interest was HPV vaccine uptake, most of the studies (8 of 9) included in this review also included assessment of knowledge and perceptions related to HPV and the HPV vaccine. Few of the studies (3 of 9) included the descriptive statistics for knowledge measures by group and pre/post intervention and there was no common method of assessing knowledge. Bennett et al. (2015) reported an increase in the proportion of participants with high levels of HPV and HPV vaccine knowledge after the intervention, increasing from 32% to 50% of the participants. However, they noted that in the multivariate model, knowledge was not associated with vaccine uptake (Bennett et al., 2015). Richman et al. (2016) found a greater increase in knowledge of HPV and the HPV vaccine in the treatment group compared to the control group, but they did not include knowledge in the predictor model so the impact on vaccine uptake is unclear (Richman et al., 2016). Others reported no difference in HPV-related knowledge between the intervention and control groups and did not include knowledge as a predictor of vaccine uptake (Juraskova et al., 2011; Perez et al., 2016). Assessment of perceptions related to HPV and the

**Table 1**  
Summary of articles selected for systematic review.

Author (year)	Research design, randomization method, and bias assessment	Sample and sample size	Intervention/duration	Outcome & explanatory variables	Intervention effects
Bennett et al. (2015)	Randomized controlled trial Randomized via automated algorithm and stratified by age (< 21 or ≥21) Potential performance and detection biases due to lack of blinding of participants, personnel, and outcome assessment	Non-HPV vaccinated female U.S. university undergraduate and graduate students aged 18–26 who (n = 661) (67.3% undergraduate students, 27.5% graduate students, 5/1% professional students)	Participants were randomized to receive an individually tailored online education intervention (“Me First”) or the control website showing the CDC vaccine information statement; intervention was one time viewing	HPV vaccine uptake (including how many doses) 3 months after randomization HPV/HPV vaccine knowledge, risk perception, and intention were also assessed	No significant difference in HPV vaccine uptake (7.83% intervention vs. 8.73% control completed first dose; 3.31% intervention vs. 3.61% control completed two doses; 0.60% intervention vs. 1.2% control completed three doses)
Gerend and Shepherd (2012)	Randomized controlled trial Potential selection, performance and detection biases due to lack of clear randomization method, blinding of participants, personnel, and outcome assessment	Non-HPV vaccinated female U.S. university students aged 18–26 and not pregnant (n = 739)	Participants were randomized to be exposed to one of three HPV vaccine education videos a) a gain-framed video message focused on vaccination benefits (n = 250); b) a loss-framed video message focused on costs of not getting vaccinated (n = 243); or c) a control video with no framed information (n = 246); intervention was a one-time viewing	HPV vaccine uptake of at least one dose 10 months after the intervention Perceived susceptibility, severity, and barriers, attitudes, subjective norms, self-efficacy, and vaccination intention were also assessed	No significant difference in HPV vaccine uptake across the three experimental conditions (5% gain frame, 6% loss frame, 7% control)
Hopfer (2012)	Randomized controlled trial Potential selection, performance and detection biases due to lack of clear randomization method, blinding of participants, personnel, and outcome assessment	Non-HPV vaccinated female U.S. university undergraduate and graduate students aged 18–26 who had not previously been seen at the university’s campus health center (n = 404)	Female students were presented with videos of HPV vaccine decision narratives that included HPV susceptibility, vaccine self-efficacy, and vaccine safety narratives, and narratives prompting college women to vaccinate themselves regardless of their data status. The video narratives were either delivered by peers (101 viewed these videos), by medical experts (50 viewed these), or presented by a combination of both peers and medical experts (101 viewed these), or control videos of information without narratives, the campus website about HPV and the vaccine or no message (these control conditions, viewed by a total of 152 participants, were collapsed for analysis as one control group)	HPV vaccine uptake of at least one dose 2 months after the intervention HPV knowledge was also assessed	The peer and medical expert-led vaccination video was associated with increases in receiving at least on HPV vaccine dose (21.8% compared to peer alone (17.8%), provider alone (6.0%), and control (11.8%).
Juraskova et al. (2011)	Randomized controlled trial Potential selection, performance and detection biases due to lack of clear randomization method, blinding of participants, personnel, and outcome assessment	Non- HPV vaccinated female Australian university undergraduate students under the age of 27 (n = 159)	Participants were randomized to be exposed to an information leaflet either about the HPV vaccine protecting against cervical cancer or a leaflet about protecting against cervical cancer plus genital warts (which tested whether a potentially “sexualized” or stigmatized message would impact uptake)	HPV vaccine uptake of at least one dose 2 months after the intervention HPV/HPV vaccine knowledge, perceived severity, susceptibility, barriers and benefits, along with cues to action and vaccine preference and intention were also assessed	No significant difference in HPV vaccine uptake across the two experimental conditions (32% in the leaflet about cervical cancer only group, 44% in the leaflet about cervical cancer plus genital warts group)
Long et al. (2017)	Single arm pre-post study Potential selection, performance, detection, attrition, and reporting biases	Chinese students at a U.S. university	Pharmacy school operation immunization utilized a peer to peer model with two Chinese pharmacy students speaking in the Chinese language to Chinese students to encourage HPV vaccination. An email was also sent to a UW Chinese freshmen student email list and prepared flyers in simplified Chinese at flu shot clinics on campus.	Overall HPV vaccination rate at the university (no information about number of doses per patient)	HPV vaccinations increased by 41% compared with the same period the year before (331 vs 235 HPV vaccine doses) and 83.7% (277) of the doses were administered to Chinese students
Patel et al. (2012)	Randomized controlled trial	Female U.S. university undergraduate and graduate students aged 18–26 who	Participants were randomized to receive HPV-specific patient education plus	HPV vaccine uptake of at least one dose 6 months after the intervention as	Overall, 14 (5.5%) participants received at least 1 HPV vaccine dose within <i>(continued on next page)</i>

**Table 1 (continued)**

Author (year)	Research design, randomization method, and bias assessment	Sample and sample size	Intervention/duration	Outcome & explanatory variables	Intervention effects
Perez et al. (2016)	Randomized via a computer randomization program with assignment revealed after consent	attended the university's health service gynecology clinic for routine exam, and had not previously received the HPV vaccination (n = 256)	reminder letter or standard care in which HPV vaccination is briefly mentioned to all patients	documented in medical record HPV/HPV vaccine knowledge, personal beliefs, and intention to vaccinate were also assessed	6 months of study enrollment. Data is not provided separately for each treatment condition, although the authors report no difference between the treatment groups.
	Potential performance and detection biases due to lack of blinding of participants, personnel, and outcome assessment; reporting bias due to incomplete outcome reporting Randomized controlled trial	Non-HPV vaccinated female U.S. university undergraduate students aged 18–26 (n = 70)	Participants participated in either an active intervention (AI) or an attention control (AC) group. AI received HPV education content specific to knowledge gaps identified among young adult women, motivational and skills-building content, information on where to access and how to pay for the vaccine, reminder tools and guidance to communicate vaccine interest with parents and providers. AC watch video clips on women's health topics.	HPV vaccine uptake of at least one dose 4 weeks after the intervention Motivation to get vaccinated and perceived efficacy and difficulty were also assessed	No significant difference in HPV vaccine uptake across the two experimental conditions. Data is not provided in aggregate nor separately for the treatment groups, although the authors report no difference between the treatment groups.
Richman et al. (2016)	Randomized controlled trial	Male and female U.S. university undergraduate and graduate students aged 18–26 who were voluntarily initiating the first HPV vaccine dose from the campus student health center (n = 264)	Participants were randomized to receive an electronic message per month for 7 months (health education and reminder messages) or standard care which provided a paper card with date of next appointment	HPV vaccine uptake and completion 7 months after the intervention HPV and HPV vaccine knowledge were also assessed	No significance in HPV completion across the two experimental conditions. HPV vaccine dose 2 was completed by 53% of intervention group and 52% of control group. HPV vaccine dose 3 was completed by 34% of intervention group and 32% of control group.
	Potential selection, performance and detection biases due to lack of clear randomization method, blinding of participants, personnel, and outcome assessment Randomized controlled trial	Non-HPV vaccinated female U.S. university undergraduate students mean age 19.03 (2.49) years recruited from an undergraduate Psychology pool (n = 72)	Participants were randomly assigned to listen to either a high or low threat fear communication about HPV. High threat messages emphasized the susceptibility to HPV among college-aged women using personalized language whereas the low threat message describe susceptibility to HPV among women in general and included the low prevalence rates for cervical cancer.	HPV vaccine uptake of at least one dose 6 weeks after the intervention Attitudes, intentions, information seeking behavior and knowledge retention about HPV/HPV vaccine were also assessed	3 participants (6.25%) obtained the vaccine (data not presented by intervention group). Participants who got the vaccine reported that they were more likely to have consulted friends and family in addition to their doctor.
Venkatesan (2011)	Assigned to condition via a coin flip Potential performance and detection biases due to lack of blinding of participants, personnel, and outcome assessment; reporting bias due to incomplete outcome reporting				

HPV vaccine (e.g., perceived susceptibility, perceived risks and benefits, subjective norms, and self-efficacy) were guided by theories, including the Health Belief Model, the Theory of Planned Behavior, Culture-Centric Narrative Theory, and Exemplification Theory. Variables from these theories were found to be associated with vaccine uptake. For example, Gerend and Shepherd (2012) found that perceived susceptibility, perceived barriers, intentions, subjective norms and self-efficacy predicted vaccine uptake and Hopfer (2012) found that vaccine intent mediated the impact of the intervention on vaccine uptake (Gerend and Shepherd, 2012; Hopfer, 2012; Juraskova et al., 2012).

#### 4. Discussion

The suboptimal HPV vaccination uptake in the U.S. population warrants attention to reach the Healthy People 2020 goal of 80% of all adolescents completing the HPV vaccine series (Immunization and Infectious Diseases | Healthy People 2020, 2019). Effective interventions are needed to improve catch-up vaccination rates. College health centers are optimally positioned to facilitate catch-up vaccination as college students are making their own health decisions, over 80% have health insurance that would cover the cost of the vaccination, and have easy access on campuses to complete the multi-shot vaccination (United States Government Accountability Office, 2008). Determining what kind of health education program will be effective at increasing vaccination rates is essential. To date there has been nearly no replication of specific interventions to increase HPV uptake in the young adult population making it difficult to identify interventions to recommend for adoption. Current literature indicates that provider recommendations are one of the main predictors of HPV vaccine uptake in adolescents (Dempsey et al., 2019; Holloway, 2019). It is interesting to note that the only intervention in this review that significantly increased HPV vaccine uptake was an educational intervention that utilized a joint peer and medical provider message, which was found to be more effective than a message from a peer or provider alone (Hopfer, 2012). The interventions that achieved the highest vaccination rates appear to be relatively easy to implement, such as videos, leaflets, and monthly reminders (Hopfer, 2012; Juraskova et al., 2011; Richman et al., 2016). Replication of these interventions to examine effectiveness in other samples is needed. Further, there is a clear gender gap in the literature as few studies have examined the impact of intervention vaccine uptake by male students.

Importantly, all but one of the studies had a non-significant treatment effect. Differences in the sample characteristics, the control groups' exposures, and other health care access and educational variables are potential drivers of the variation in findings related to vaccine uptake. The lack of significant differences between the intervention and control conditions may indicate that simply participating in a study related to HPV vaccination impacts uptake and thus the control conditions may have had higher uptake than would naturally have occurred. Manipulating messages to increase the perceived threat, tailoring educational messages, and reminder letters were utilized in studies that found < 10% of participants went on to receive the HPV vaccine (Bennett et al., 2015; Patel et al., 2012; Venkatesan, 2011). While Juraskova et al. (2011) did not find a significant difference between two interventions, HPV vaccine uptake rates were relatively high in both the group exposed to a leaflet focused on the protective effect of the vaccine (32% uptake) and the group exposed to a leaflet with a more stigmatizing message (42% uptake) (Juraskova et al., 2012). There is clearly a need for further investigation of specific intervention components to develop optimal intervention strategies.

There are several limitations to the current literature and review. There are only a small number of studies that examine HPV vaccine uptake as an outcome variable following an intervention among college students. While many health behavior theories indicate that intention is a precursor to behavior, there remains a need for studies that demonstrate actual efficacy at completion of the behavior, in this case HPV

vaccination. Further review of studies investigating vaccination intention as the primary outcome may be warranted to provide insight into promising interventions that could be tested for impact on actual vaccination uptake. An additional limitation is the small number of studies that included male participants. Only one study explicitly included male participants (Richman et al., 2016) and another was a general health education approach at a college of pharmacy operation immunization program which likely exposed both male and female students but did not report any data by sex (Long et al., 2017). As a result, no conclusion can be made about whether these interventions would potentially have any impact on male HPV vaccination uptake. This is unfortunate as boys are less likely to be vaccinated as adolescents compared to girls (Walker, 2017). Further, several of the studies had a relatively short follow-up period. It is possible that participants went on to eventually receive the vaccine after the follow-up assessment, which may result in an underestimation of the impact of the interventions. However, there is no clear reason to expect that there would have been differences across the treatment conditions in delayed uptake.

#### 5. Conclusions

While there are many studies demonstrating improvement in vaccination intention, very few interventions targeting college students have demonstrated effectiveness at increasing actual HPV vaccine uptake. Based on nine studies that reported vaccine uptake rate as an outcome, uptake rates for at least one dose of the vaccine varied from 5% to 53%. Program planners should focus on interventions that have demonstrated the ability to improve vaccination rates. This review finds that interventions that engage both peers and medical professionals may be the most effective way to increase uptake.

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