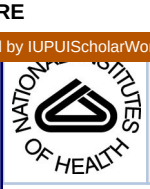

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Educational interventions to increase HPV vaccination acceptance: A systematic review

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Abstract

Background—The Human papillomavirus (HPV) vaccine has been available for protection against HPV-associated cervical cancer and genital warts since 2006. Nonetheless, uptake has varied among countries and populations within countries. Studies have found that individuals' knowledge and attitudes toward the vaccine are associated with immunization uptake. The purpose of the current review is to summarize and evaluate the evidence for educational interventions to increase HPV vaccination acceptance.

Methods—We searched the databases of PubMed and Web of Science for English-language articles describing educational interventions designed to improve HPV vaccination uptake, intention or attitude.

Results—We identified 33 studies of HPV vaccination educational interventions: 7 tested the effectiveness of interventions with parents, 8 with adolescents or young adults, and 18 compared

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the effectiveness of different message frames in an educational intervention among adolescents, young adults or their parents. Most studies involved populations with higher educational attainment and most interventions required participants to be literate. The minority of studies used the outcome of HPV vaccine uptake. Well-designed studies adequately powered to detect change in vaccine uptake were rare and generally did not demonstrate effectiveness of the tested intervention.

Conclusions—There is not strong evidence to recommend any specific educational intervention for wide-spread implementation. Future studies are required to determine the effectiveness of culturally-competent interventions reaching diverse populations.

Keywords

Papillomavirus vaccines; Decision making; Intervention studies; Education; Attitude to health; Systematic review

1. Background

Human papillomavirus (HPV) is among the most common sexually transmitted infections with a global prevalence of 11–12% among women and with rates as high as 16–24% in some regions including sub-Saharan Africa, Eastern Europe and Latin America [1]. It is also the causative agent of nearly all cervical cancer, the second most common cancer in women worldwide [2]. Currently, there are two HPV vaccines that confer protection against HPV-associated cervical cancer, as well as other anogenital cancers. The bivalent Cervarix® vaccine protects against HPV types 16 and 18 which cause roughly 70% of all cervical cancer [3]. The quadrivalent vaccine, Gardasil® protects against types 16 and 18 as well as types 6 and 11 which cause more than 90% of genital warts in men and women [4]. In 2006 the U.S. was the first country to approve the quadrivalent vaccine for females, extending this approval to use in males in 2009. The bivalent vaccine was approved for females in the U.S. in 2009 and was licensed in other countries in Europe as well as Australia and the Philippines prior to 2009 [5]. Both vaccines are recommended for use as a 3-dose series over 6 months before the onset of sexual activity and typically starting between ages 10 to 13 years [6,7].

According to the World Health Organization's monitoring system, HPV vaccine had been introduced in 57 countries by 2013 [8]. Overall, countries that have school-based vaccination programs, such as Australia, Great Britain and Portugal, have achieved the highest (80% or greater) female vaccination coverage rates [9], though Denmark has reached very high vaccination rates (3-dose coverage of over 80%) through administration by general practitioners [10]. Studies conducted in countries with national HPV immunization programs have demonstrated clear benefits of mass vaccination in terms of reductions in viral prevalence and associated disease burden. For instance, a recently published study from Australia found lower rates of high-grade cervical abnormalities and high-grade cytology among vaccinated women versus unvaccinated women (hazard ratio 0.72; 95% confidence interval (CI) = 0.58–0.91) [11]. Further Australian data, collected during the first 5 years of their national immunization program, found that the incidence of genital warts decreased more than 50% among females under 30 and more than 70% in heterosexual

males of the same age [12]. Similarly, incidence data from Denmark shows that genital warts have declined an average of 3.1% every year since 2007 [10]. In the US, vaccine-type HPV prevalence decreased over 50% among females ages 14–19 years in the first 4 years post-licensure [13]. The vaccine is also safe; there have been no post-marketing surveillance reports of severe side effects [8,14–17].

Despite an excellent safety and efficacy profile, HPV vaccine uptake has varied between countries and between populations within countries. This is the case in Europe as well as among low and middle income countries that have universal vaccination programs [7]. Among high income countries with low coverage rates are France (28.5% for the full 3-dose series) and the United States. (34% for full coverage) [7,16]. A recent systematic review of studies mostly conducted in the U.S. examining correlates of HPV vaccine uptake in teenage girls identified the following personal cognitive factors: having higher vaccine-related knowledge, having a healthcare provider as a source of information and maintaining positive vaccine attitudes [9]. Therefore, interventions that improve understanding of, and positive attitudes toward HPV vaccine may increase HPV vaccination coverage. Previous successful behavioral interventions to increase compliance with other preventive health recommendations such as increasing sun protection behavior [18], improving dental hygiene [19], and increasing adherence to cervical and breast cancer screenings [20], for example, have employed various education delivery methods, including classroom lectures for adolescents [18], brief online education for parents [19], and home visits for women [20]. In our present systematic review, we focus on published evaluations of educational interventions designed to increase HPV vaccine acceptance in patients eligible to receive the vaccine, or their parents.”

2. Methods

2.1. Search strategies

We searched both the PubMed and Web of Science databases to ensure comprehensive capture of both the medical and social sciences literature (Web of Science having greater coverage of the social sciences than PubMed). We entered relevant MeSH (Medical Subject Headings) keywords (*papillomavirus vaccines* and *decision making*, *behavioral research*, *intervention studies*, *communication*, *education* or *attitude to health*) and limited the search by *English language*. Realizing that some studies were conducted prior to licensure of the HPV vaccine, we searched the maximum date coverage range available in PubMed at the time the search was conducted. Abstracts of all articles with a publication date between 1946 to August 20, 2013 were reviewed for relevance to the study topic. Full-text articles were obtained for studies pertaining to the evaluation of educational interventions to increase HPV vaccination attitudes, intentions or uptake. Two authors independently reviewed the articles to determine relevance for inclusion. In addition, the references of retrieved papers and a recent systematic review of parental vaccine hesitancy interventions [21,22] were searched for studies that might have been missed in the original search strategy.

2.2. Inclusion and exclusion criteria

We included trials that employed both randomized and nonrandomized designs, as well as quasi-experimental designs (i.e., comparing pre- and post-intervention outcomes). Educational interventions designed to improve patient or parental knowledge or attitudes, and which measured the following outcomes were included: (1) receipt of HPV vaccine (any dose or completion of the 3-dose series), (2) intention to receive HPV vaccine, or (3) attitude toward HPV vaccine. Non-English articles and conference abstracts were excluded. In addition, pilot or descriptive projects which reported only qualitative or anecdotal results were also excluded. Finally, studies that did not focus primarily on populations eligible to receive HPV vaccine or their parents or that did not subset results in a way that we were able to extract information on these target groups were also excluded.

2.3. Data extraction

A form was created and used to extract data from all articles to ensure a standardized process was applied. The elements included in the data extraction form were adapted from the GRADEprofiler evidence profile tool for creating Cochrane Reviews Summary of Findings tables and assessing the quality of the evidence. All items captured are reflected in the data presented in Tables 1–5 [23]. Two reviewers independently extracted data from each article and forms were reviewed jointly afterward to achieve consensus.

2.4. Data analysis

Studied interventions were too heterogeneous to perform meta-analysis and outcomes were reported in many different ways. To standardize reported outcomes as much as possible and thereby enhance the reader's ability to compare effects across studies, reviewers calculated the relative risk (RR) and 95% confidence interval (CI) whenever sufficient data were provided, and outcomes involved a comparison of event probabilities. When response categories for HPV acceptance survey items included *undecided/no response* and *no*, these two categories were combined into a single category for comparison to *yes* responses. Generated RR and 95%CI are reported for post-intervention responses in tables along with the authors' stated results as they appeared in the original articles. Some studies reported multiple outcomes. In such cases, we reported them in the following hierarchy: *receipt of HPV vaccine* in preference to *intention to receive HPV vaccine* in preference to *attitude toward HPV vaccine.* Our preferences for this hierarchy of outcomes were based on our understanding that intention to vaccinate is an approximation of vaccination behavior, while positive attitude is generally considered a precursor to intention [24].

If studies reported both between- and within-group comparisons, we preferentially reported between-group comparisons. If studies reported participant intention to receive the HPV vaccine free of cost or for a fee, we reported the outcomes for the free-of-cost vaccine since this removed the confounding factor of financial barriers. If studies included subgroup analysis or interaction terms between the intervention and other variables, we preferentially reported outcomes for the overall groups and main effects of the intervention, respectively.

2.5. Critical appraisal

Each article was evaluated for risk of bias based on the methods suggested by the Cochrane Collaboration [25] including: condition allocation strategy, concealment of condition assignment to participants, research staff blinding, and inclusion of intent to treat analysis. Because the Cochrane criteria support evaluation of clinical trials, we omitted two other appraisal categories as not applicable to this review: loss to follow up (since the vast majority of included studies were conducted in one sitting) and confounding (since there is no consensus regarding which participant factors and theoretical constructs are highly associated with vaccination behavior) [9]. Beyond the Cochrane criteria, we included four additional appraisal categories to meet the objectives of this review: adequate reporting of participant eligibility criteria (e.g., exclusion of participants with prior HPV vaccination), inclusion of a no-treatment or standard-treatment control condition, adequate reporting of interventional and outcome details for the primary research question, and outcome assessment at any point beyond immediately post-intervention. Appraisal of each category and of an overall risk of bias rating (*low*, *medium* or *high*) for each article was performed by two reviewers. Any discrepancy in risk-of-bias rating was discussed to achieve consensus.

3. Results

3.1. Study characteristics

Our search resulted in a total of 33 relevant articles included in this review (Fig. 1). Studies were classified into the following categories: *parental education* (7 studies), *adolescent/young adult education* (8 studies) and *comparative message persuasiveness* (18 studies). If the primary aim of a study was to evaluate the impact of a single educational intervention, compare different delivery modes for the same educational content (e.g., video vs. written information) or the "dose response" (i.e., differential effect of increasing the quantity, length of exposure or extent of education) of two or more educational interventions, the study was categorized as either *adolescent/young adult* or *parental education* as appropriate. If the primary aim of a study was to determine the differential effect of two or more interventions with essentially the same educational content but varying message frames, tones or messengers, the study was considered to be in the realm of *comparative message persuasiveness.*

3.2. Critical appraisal

In terms of risk of bias, we judged seven studies to be of low risk, fifteen of medium risk and eleven of high risk (Table 1). While the majority of included studies were randomized trials, most did not specify whether group assignment was concealed to participants or study personnel and did not include a standard-treatment or no-treatment control group. Most studies did not evaluate interventions with the preferred outcome, HPV vaccination receipt, but rather a proxy of acceptance (intent or attitude). Over half (55%) of the studies did not adequately report interventional and outcome details for the primary research question. Specifically, these studies lacked sufficient descriptions of: their survey measurement scales' items or scoring, the educational content of their interventions, the main effects or significance levels of their outcomes, and the numbers of participants allocated to initial treatment conditions and/or completing protocol.

3.3. Parental education

We identified seven articles that tested interventions to educate parents of minors in the recommended age range for HPV vaccination (Table 2). Of these, five were conducted in the United States [26–29] and other two were from India [30] and China [31]. Less than half the studies were randomized, controlled trials [27,28,32] with most designed as quasi-experimental comparisons of parental intentions to vaccinate pre- versus post-intervention [26,29–31]. All but two of the studies [26,27] exclusively surveyed parents of girls and none of the studies involved any follow-up assessment beyond the period immediately following the intervention. All of the studies used the primary outcome of self-reported indicators of HPV vaccine acceptability rather than actual vaccination behavior (i.e., child's HPV vaccination status post-intervention), although in the study by Spleen et al., the authors did assess self-reported HPV vaccination receipt one month post-intervention among nine, non-randomly-selected participants [29]. It would not have been possible to assess actual vaccination receipt in four of the studies since they were conducted prior to HPV vaccine licensure in the study country [26,27,30,31].

The format for five of the parental educational interventions was written information fact sheets from 1 to 2 pages in length [26–28,30,31]. Although some of the studies provided more detailed descriptions of the content of the fact sheets given to participants, all provided information on aspects of the potential morbidity associated with HPV infection and informed parents of the current or future availability of an HPV vaccine to protect children against infection. Of the studies examining the effectiveness of parental information sheets, the two that were randomized, controlled trials [27,28] found no difference in HPV vaccination intention between the experimental and control conditions. The three studies that exclusively compared HPV vaccination intention pre- to post-intervention found a significant increase in intention to vaccinate in parents after they had read the information sheet with risk ratios (RR) and 95% confidence intervals (CI) ranging from 1.60 (1.23–2.08) to 2.88 (2.47–3.36) [26,30,31] while the study by Kennedy et al, which reported results both within-group as well as between-groups, did not ($P = 0.74$) [28].

Just two studies examined the effects of parental educational interventions that were not fact-sheet based. Spleen et al. tested the effectiveness of a 1-h slide presentation about HPV infection to parents of girls in Appalachian Pennsylvania. This study found increases in scores for intention to accept the HPV vaccine after the presentation of less than 1 point on a 4 point-scale ($P = 0.002$) although it should be noted that 31% of the sampled parents had daughters who had already started the HPV vaccination series at the time of the intervention [29]. A study by Kepkaet al. [32] tested the effectiveness of a Spanish-language radio advertisement (referred to as *radionovela* in the study) to educate Latino parents about HPV vaccination. This study did not find any difference in intention to vaccinate one's daughter's between the experimental and control conditions, (RR = 0.86 (95%CI 0.65–1.13)), although it may have been under-powered as it enrolled only 60 participants.

3.4. Adolescent/young adult education

Our search strategy yielded eight educational studies which targeted adolescents or young adults (Table 3). Half of the studies targeted younger adolescents in secondary or high

school [33–36]. Participants' ages, specified in all but one of these studies, ranged from 12 to 16 years overall. The other half of the studies either partially [37] or exclusively recruited participants from colleges [33,36,38,39]. The age range of these participants ranged from 18 to 26 years in the two studies in which age criteria were specified [37,39]. Three studies were conducted in the United States [37–39], two in England [33,36], and one study each in Sweden [34], Hong Kong [35] and Canada [40]. Half of the studies involved both male and female participants [34,36,38,40] and half were limited to females [33,35,37,39]. All but one of the studies [33] were conducted after the HPV vaccine was licensed in the country from which participants were recruited.

Formats for the educational interventions involving adolescent and young adult participants varied. The interventions tested in three of the studies were brief HPV educational videos ranging in length from 3 to 10 min [33,37,40]. Two studies tested hour-long, live presentations delivered at school [34,35]. Three studies tested written HPV fact sheets [36,39,40] and one an online fact sheet with a question-and-answer section and a self-quiz [38].

Of note, three studies were randomized controlled trials that used the preferred outcome of vaccination behavior [34,37,39]. The outcome of interest in two of the three studies was receipt of the first dose of HPV vaccine. The first of these studies was conducted by Patel, et al. and tracked HPV vaccine uptake via medical record review up to 6 months after the intervention [39]. For this intervention, college-aged women were given a written fact sheet, discussed the contents with the study coordinator and received a second copy in the mail two weeks later. The comparator group received a different HPV vaccination fact sheet ("with similar content") once with no reminder mailing and no review of the content. Rate of receipt of the first dose of HPV vaccine in the intervention group was low (5.5%) and did not differ significantly from that of the control group. The other study was conducted by Gottvall et al. and tested the impact of an hour-long lesson on HPV and condom usage for high school students with handouts and online resources [34]. The comparator groups in this study did not receive any education on these topics. Rate of self-reported receipt of the first dose of HPV vaccine in the intervention group was also low (16%) and not significantly different from that of the control groups [34,39]. Vanderpool et al. conducted a trial comparing completion rates of the 3-dose HPV vaccination series among young women who received the first dose from study personnel [37]. In this study, the difference between the intervention and control conditions was viewing a 13-min video about HPV or not. Both conditions received a CDC-produced HPV vaccine fact sheet and a t-shirt. The authors report 11% more participants in the intervention versus control group received all 3 doses of HPV vaccine within 9 months as assessed via medical record review (RR = 1.36; 95%CI = 1.03–1.79) [37].

The remaining studies of adolescent and young adult education assessed effects on behavioral intention or attitudes rather than actual vaccination behavior. Four of the five studies were randomized, controlled trials [33,36,38,40]. All five found significant improvement by their chosen measure as assessed immediately post-intervention. However, only one of these studies re-assessed outcome 1 month later, and it found no significant difference between intervention and control groups at follow up [38].

3.5. Comparative message persuasiveness

We identified eighteen articles with interventions that tested how the framing of messages about the HPV vaccination influenced vaccine acceptance [41–58] (Table 4). Four of the studies recruited parents exclusively [41,44,46,55], thirteen recruited college aged-participants [42,43,45,47–53,56–58], and one recruited a broad sample of adults from which we report the subgroup analysis involving parents with minor girls eligible to receive the HPV vaccine [54]. Three of the studies involving parent participants only included parents of girls [41,54,55] and two included parents of boys or girls [41,46]. Of the studies involving college-aged participants, seven included women only [43,45,48,49,51–53], three men only [42,47,50] and three included both men and women [56–58]. Overall, the age of participants (when reported) for college-based samples was 18–26 years old [42,43,51,52,56–58]. Thirteen of the studies were American [41,42,47–51,53–58], two were Canadian [45,46], two were Australian [43] and one was Irish [44]. All four studies with Gerend as the lead author as well as a fifth conducted by Leader, et al. were conducted prior to the licensure of the HPV vaccine for the study's target population (namely males and females or males exclusively) [47–50,54]. The rest were conducted post-licensure [41–46,51–53,55–58]. Because the objective of all eighteen studies was to compare two or more framing messages, all included at least one comparison group although only four included a standard-treatment or no-treatment control condition [41,43,51,58]. All studies in this category assigned treatment condition randomly.

In terms of format, the majority of the interventions in this category were presented as written materials either as 1–2 page brochures and fact sheets [41,44,47–50,52,53,55] or as online content [45,46,54,56–58]. One intervention involved slide presentations [42], another radio advertisements [43], and a third videos [51].

Researchers took a variety of approaches to framing the HPV vaccination message including comparing: (1) gain—(advantages of getting vaccinated) versus loss—(disadvantages of not getting vaccinated) framed messages; (2) different delivery formats (e.g., narrative versus informative presentation styles, color priming with red versus gray, and graphic versus non-graphic presentation of HPV infection risk statistics); and (3) different message content foci (cervical cancer versus genital warts prevention) (Table 5).

The most common message-framing model tested was gain versus loss framing with nine studies represented. None of these found any main effects of gain versus loss framing on HPV vaccination intention [44–46,55]. However, some studies did find that gain/loss framing affected HPV vaccination intention under particular circumstances (as demonstrated by significant interactions with other variables including aspects of sexual history [48]; number of vaccinations required for immunity [49]; among persons primed with red versus gray color [50]; among persons characterized as present-versus future-minded [57]; and among persons characterized as avoidance- versus approach-oriented [48,56]).

There were five studies that compared messages focusing on the different diseases prevented by HPV vaccination [42,50,52–54]. Although these studies were conducted with a variety of types of participants (parents, young men, and young women), none found a differential direct effect of their messages on HPV immunization intention [42,50,52,54]. However, one

study found that self-efficacy and response efficacy sequentially mediated the positive indirect influence of their genital warts prevention message (vs. a cervical cancer prevention message) on HPV vaccination intention among young women [53].

Sixteen studies in this category examined the effect of message framing on HPV vaccination intention only and none of these studies assessed outcomes beyond immediately post-intervention [41–50,53–58]. We here highlight the two message framing trials that used the preferred outcome of interest, HPV vaccine uptake [51,52]. Both of these studies assessed vaccination receipt by participant self-report 2 months after the intervention. In a large study by Hopfer et al., female college students in the experimental condition viewed brief videos with a narrative message delivered by different source types: peers, medical experts and combined peers and medical experts [51]. Compared with the control group, only the combined peer-expert group reported statistically higher vaccination rates. The effect size was relatively large with participants in the combined peer-expert group twice as likely to report having been vaccinated. The other study to use self-reported HPV vaccination as the outcome of interest included a smaller sample. It involved 75 female college students with half reading a fact sheet explaining the benefits of HPV vaccine for cervical cancer prevention only and the other half reading a fact sheet explaining the benefits for prevention of cervical cancer and genital warts [52]. This study did not find a statistically significant difference between the two groups in immunization rates.

4. Discussion

We identified 33 studies of HPV vaccination educational interventions: 7 tested the effectiveness of interventions with parents, 8 with adolescents or young adults and 18 compared the effectiveness of different message frames. Unfortunately, our review did not identify any clearly superior interventions meriting strong recommendation for wide-spread implementation. Well-designed studies adequately powered to detect change in vaccine uptake were rare and generally did not demonstrate effectiveness of the tested intervention.

In comparing the outcomes of the randomized trials of educational interventions for adolescents and young adults versus parents, it seems that adolescents' and young adults' intention to receive HPV vaccination may be more readily influenced by educational interventions. In fact, all five of the adolescent/young adult education studies examining effect on vaccination intention or attitude found significant improvement as assessed immediately post-intervention regardless of the format and content of the education. This is in contrast to none of the three randomized trials targeting parents. Perhaps the difference is due in part to the study setting: most of the studies involving adolescents and young adults occurred at school or university where students may have been already primed for learning. Nonetheless, even among adolescents and young adults, there is no evidence that the positive intentions and attitudes achieved by HPV educational interventions are durable or that they impact vaccine uptake. In the only adolescent/young adult education study to include a follow-up assessment, higher intention to be vaccinated seen immediately post-intervention was extinguished after 1 month [38]. Furthermore, the two educational trials involving adolescents/young adults that used receipt of the first dose of HPV vaccine as the primary outcome found no significant increase in uptake as a result of their interventions

[34,39]. Since virtually all of the interventions were completed in a single session with minimal or no reinforcement at a later time, it is possible that the positive effect of a single-episode educational intervention on HPV vaccination intention may not be robust enough to affect vaccination behavior among adolescents and young adults who have yet to receive the first dose. On the other hand, enhanced single-session education may increase compliance with completion of the 3-dose series among participants who are given the first dose at the time of the education as demonstrated by Vanderpool et al. [37]. This is worth noting for further exploration since rates of completion of the series understandably lag behind rates of series initiation [7,16].

Two recent reviews have included HPV immunization educational interventions in their searches: one focused on parental acceptance of childhood vaccines [22], and the other included any intervention to increase HPV acceptance [5]. These two reviews include 9 [22] and 7 [5] articles relevant to HPV vaccination education, respectively. The findings of these other reviews are similar to our own in that many of the identified studies were methodologically deficient and results were difficult to generalize [5,22].

The most common message-framing dichotomy tested in studies we identified as part of this review was gain- versus loss-framing. None of the nine studies showed significant main effects of gain-/loss-framing. Our negative findings are consistent with a recent meta-analysis which found no significant difference between gain and loss frame messages in persuading people to be vaccinated [59]. Taken together, we can surmise that the relationship between gain-/loss-message frame and HPV vaccine acceptance, if it exists at all, is complex and only relevant under particular circumstances and when moderated by other factors.

Another common framing theme among the identified studies was varying the specifics of HPV disease prevention messages provided to participants, most often between cervical cancer and genital warts prevention messages. Since none of these studies found any difference in vaccination intention between treatment conditions, it is possible that HPV vaccination educational interventions need not focus on one particular aspect of disease prevention to be effective.

One of the major challenges we found with the studies included in this review was the limited generalizability of their findings. Despite the fact that cervical cancer mortality disproportionately affects socioeconomically disadvantaged populations [60], only thirteen (39%) of the studies in this review included populations outside the university setting. Of these, only six tested an intervention that did not require participants to be literate [29,32–35,37]. Only one study tested a culturally-tailored intervention in a population at risk for under-immunization (specifically Hispanic Americans), and this study was likely under-powered [32]. Since many of the studies were conducted pre-licensure or in the early years of the HPV vaccine usage in the study country, it was reasonable and appropriate at that time to test educational interventions among anyone eligible to receive or consent for vaccination. However, at this juncture, new research should shift focus to populations at higher risk of disease or under-vaccination.

One limitation of our review is that our search was restricted to English-language publications. Therefore, the results are difficult to generalize beyond Western European, Australian and North American populations. Furthermore, the vast majority of reviewed studies comparing different message frames for HPV vaccination education were conducted in the U.S. (72%). Given that social norms and beliefs differ by culture, care must be exercised when extrapolating the findings of this review to other populations.

Comparing the studies identified in this review and their conclusions highlighted the potential for bias in different approaches for testing educational interventions. For instance, all four of the parental educational studies that compared within-group attitudes or intentions (from pre- to post-intervention) found a significant improvement [26,29–31]. However, none the three that utilized a randomized controlled design found improvement between groups [27,28,32]. When restricted to analyzing within-group data alone, there is no way to determine whether improvement in participant HPV vaccination acceptance may have been partly due to unintended learning about the vaccination from a detailed survey, or to social desirability bias because participants gained a sense of the study's aims. This increases the chances of researchers making the type I error of incorrectly concluding that improvements were the result of the intervention and underscores the importance of the randomized, controlled design for future studies.

5. Conclusion

Given the association between HPV vaccination acceptance and individual knowledge, attitudes and beliefs, finding effective HPV vaccination educational interventions is essential to reducing HPV-associated morbidity and mortality [9,61–63]. Studies to date have largely focused on written informational handouts targeted toward educated populations. Future studies should focus on culturally-competent interventions to reach a more diverse population. Trials should be adequately powered, employ strong research methodology and examine HPV vaccine uptake as the primary outcome.

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Abbreviations

HPV	human papillomavirus
RR	relative risk
CI	confidence interval

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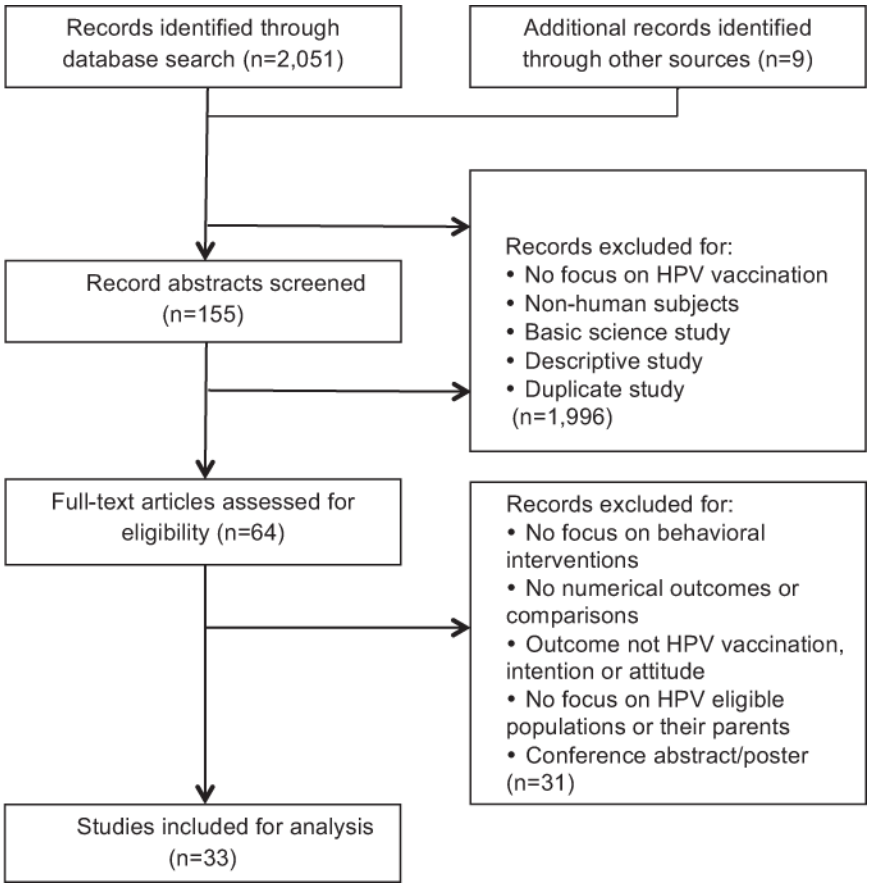

Fig. 1.
Flow chart of included and excluded studies.

Table 1

Quality appraisal of included studies.

Total studies (33)	**Yes *N* (%)**	**No *N* (%)**	**Unclear *N* (%)**	**N/A *N* (%)**
Were eligibility criteria adequately reported (inclusion and exclusion)?	28 (85)	5 (15)	0	0
Were there two or more comparative groups?	28 (85)	5 (15)	0	0
Was group assignment random?	25 (76)	1 (3)	2 (6)	5 (15)
Was group assignment concealed to participants?	9 (27)	1 (3)	18 (55)	5 (15)
Was study staff blinded to group assignment?	4 (12)	0	24 (73)	5 (15)
Was a no-treatment or standard-treatment control group included?	10 (30)	18 (55)	0	5 (15)
Was the outcome assessed actual receipt of HPV vaccine?	5 (15)	28 (85)	0	0
Were interventional and outcome details for the primary research question adequately reported?	15 (45)	18 (55)	0	0
Were outcomes assessed at any time beyond immediately post-intervention?	6 (18)	27 (82)	0	0
Was intent to treat analysis completed?[a]	0	8 (24)	1 (3)	24 (72)
Overall risk of bias[b]	Low *N* (%) 7 (21)	Medium *N* (%) 15 (46)	High *N* (%) 11 (33)	

[a] For studies in which assessment required mailed responses or follow up.

[b] Risk for all studies was classified as indicated by consensus rating of the quality of the evidence in the above-listed domains; only randomized, controlled trials could be classified as *low risk of bias*.

Table 2

HPV vaccine parental education interventional trials.

Author, year and journal	Intervention (I) and control (C)	Outcome (O) and assessment (A)	Population	Setting	Time frame	Results RR (95%CI) or M ± SD[a]
Basu, 2007 J Obstet Gynaecol Res[30]	Comparison of attitudes pre- to post-intervention I: Fact sheet about cervical cancer and HPV vaccine. Afterwards a trained social worker was available to answer questions C: No control condition	O: HPV vaccination intention for daughters A: Single survey item (agree, refuse, undecided) assessed pre- and immediately post-intervention	522 middle/high income parents with at least high-school education with one or more girls age 9–26	Middle/high income residential complexes in Kolkata, India	04/2008–09/2008 pre-licensure	2.88 (2.47, 3.36)[b]
Chan, 2007 J Adolesc Health[31]	Comparison of attitudes pre- to post-intervention I: One-page fact sheet that detailed the effectiveness of the HPV vaccine on reducing HPV infection and by implication cervical cancer C:No control condition	O: HPV vaccination intention for daughters A: Single survey item (agree, disagree, undecided) assessed pre- and immediately post-intervention	170 mothers of girls age 8–18 at first visit to gynecology clinic	Gynecology clinic in Hong Kong	01/2006–06/2006 pre-licensure	1.60 (1.23, 2.08)[c] Authors reported change in agreement to vaccinate as: *agree:+20%, disagree:* −8%, *undecided:* −25% P<0.001
Davis, 2004 J Low Genit Tract Dis[26]	Comparison of attitudes pre- to post-intervention I: Fact sheet about HPV prevalence, seriousness and route of transmission, as well as diagnosis, treatment and brief details about the HPV vaccine C: No control condition	O: "Do you want your child/ children to receive the HPV vaccine?" A: Single survey item (yes vs. no + no response) assessed pre- and immediately post-intervention	506 parents and guardians of boys and girls age 10–15	Clinics at the Medical College of Georgia in Augusta	05/2003–08/2003 pre-licensure	1.37 (1.25, 1.51)[d] Authors reported change in agreement to vaccinate as: *yes:* +20%, *no*: −3%, *no response*: 17%.
Dempsey, 2006 Pediatr[27]	Randomized, controlled trial I: Fact sheet about epidemiology and morbidity associated with HPV infection based on CDC vaccine fact sheet and a baseline paragraph about HPV and the vaccine C: Baseline paragraph about HPV and the vaccine	O: HPV vaccination acceptability for 3 potential age groups: "infants," preadolescents (8–12) and "older teenagers" A: Average score of 3 items (each 10-points with higher scores indicating higher acceptability) assessed in a survey mailed with information sheet	840 parents of boys and girls ages 8–12 Some college (53.4%), High school or less(9.3%) White (75.2%), Asian (11. 4%), Black (5.1%) Hispanic (4.1%)	Seattle area: recruited using mailings to enrollees of an area HMO	Pre-licensure (date not specified)	I: 6.56 (6.28–6.84) C: 6.28 (5.99–6.57) Between-group *P* = 0.17
Kennedy, 2011 J Health Commun[28]	Randomized, controlled trial I: Two-page fact sheet adapted from the CDC mailed to participants C: No information sheet	O: HPV vaccination intention for daughters if physician recommended A: Single survey item, (0 = strongly disagree, 10 = strongly agree) assessed in a survey mailed with information sheet	205 parents of girls ages 11–18 Income of <$50,000 (38%) White (77%), non-White (23%)	US: recruited using mailings to participants from a commercial sample vendor	03/2008 post-licensure	I: 5.9±3.1 C: 5.7 ± 2.7 No *P value* provided Pre-intervention: 5.8 ± 3.0 Post-intervention: 5.9 ± 3.1 *P* = 0.17

Author, year and journal	Intervention (I) and control (C)	Outcome (O) and assessment (A)	Population	Setting	Time frame	Results RR (95%CI) or M ± SD[a]
Kepka, 2011 J Commun Health[32]	Randomized, controlled trial I:5 min radio novel a about cervical cancer, HPV infection, HPV vaccine, concerns about the HPV vaccine and decision making activities related to vaccine uptake C: Prostate cancer radio announcement	O: "How likely is it that your daughter will receive the vaccine in the next 12 months? (Very Probable)" A: Single survey item (yes vs. no) assessed immediately post-intervention	60 Hispanic parents and guardians of girls ages 9–17 Income of <$36,000 (77%)	Lower Yakima Valley, Washington: recruited at community events	07/2009–09/2009 post-licensure	0.86 (0.65, 1.13)[e] Authors reported results as 61% of intervention vs. 67% of control group answered *very probable* *P* = 0.58
Spleen, 2012 J Cancer Educ[29]	Comparison of attitudes pre- to post-intervention I: One-hour educational slide presentation about HPV infection, disease and vaccine which included time for discussion lead by health educators C: No control condition	O: HPV vaccination intention for daughters within 1 month and within 6 months A: Two survey items reported separately (0 = extremely unlikely, 3 = extremely likely) assessed pre- and immediately post-intervention	38 parents of girls ages 9–17, 12 of whom had already started HPV vaccination series White non-Hispanic (95.5%), Hispanic (2.7%), other (1.8%)	Appalachian Pennsylvania: recruited via sources such as newspaper ads, flyers and newsletters	2008–2009 post-licensure	1 month:[f] Pre-intervention: 0.72 Post-intervention: 1.38 P = 0.002 6 months: Pre-intervention: 1.46 Post-intervention: 1.84 P = 0.07 No standard deviations for means reported

[a] RR (95%CI) = relative risk (95% confidence intervals) where RR > 1 indicates higher and RR < 1 indicates lower HPV vaccine acceptance. M ± SD = mean ± standard deviation.

[b] Authors reported agreement to vaccinate separately for males and females. Reviewers combined responses of *undecided* plus *refused* and combined all responses for mother and father participants to calculate RR (95%CI).

[c] Reviewers combined "undecided" and "disagree" to calculate RR (95%CI).

[d] Reviewers combined *no* and *no response* categories to calculate RR (95%CI).

[e] Reviewers calculated RR (95%CI).

[f] For 9 participants, authors also reported (self-report of) receipt of HPV vaccine for self or daughters (44.4%) 1-month post-intervention (unknown if any of these had already received any doses prior to intervention).

Table 3

HPV vaccination adolescent/young adult education interventional trials.

Author, year and journal	Intervention (I) and control (C)	Outcome (O) and assessment (A)	Population	Setting	Time frame	Results RR (95%CI) or M ± SD[a]
Brabin, 2010 Vaccine[33]	Unclear if trial was randomized I:10-min educational video about HPV and the HPV vaccine including personal stories for adolescents and a fact sheet about the HPV vaccine for their parents C: Fact sheet about the HPV vaccine for parents	O: Desire to receive HPV vaccine A: Single survey item assessed 6–8 months post-intervention	553 girls ages 12–13	Schools in Manchester, UK	2007–2008 pre licensure	1.08 (1.01, 1.16) Authors reported results as 90% of intervention group and 83% of control group "want the vaccine," $P = 0.015$
Doherty, 2008 Int J Sex Health[38]	Randomized, controlled trial I: Online HPV fact sheet including question/answer section, personal story and self-quiz C: No online fact sheet	O: HPV vaccination A: Change in average score of 7 items including: willingness to obtain the vaccine (1 = strongly disagree, 5 = strongly agree) assessed immediately post- and one month post-intervention	119 male and female college students White (93%), Asian-American (3%), Black (1%), other (3%)	4 psychology courses at Bates College, Maine	Post-licensure (date not specified)	Immediately post-intervention: I: 2.7 ± 2.8 C:1.2±1.9 $P = 0.036$ 1 month post-intervention: No significant difference Average scores 1 month post-intervention depicted graphically only (no numerical results reported).
Gottvall, 2010 Int J STD AIDS[34]	Unclear if trial was randomized I: One-hour lesson about HPV and preventive methods focusing on vaccination and condom use, folder about HPV and prevention and incentives to view project's website about HPV and other STIs C: Two groups: C1: No educational materials, completed baseline survey C2: No educational materials and did not complete baseline survey	O: Receipt of HPV vaccine A: Self-report two months post-intervention	276 first-year male and female high school students Swedish (76%)	3 high schools in Sweden	10/2008–5/2009 2009 post-licensure	1.36 (0.72, 2.56)[b] Authors reported HPV vaccination rates for I (16%) vs. C1 (14%) vs. C2 (11%) Authors also reported intention and attitudes (not shown here)
Krawczyk, 2012 J Am Coll Health[40]	Randomized, controlled trial I: Two groups: I1:1: 5-min educational video about HPV and the HPV vaccine video presented by a healthcare provider	O: HPV vaccination intention A: Single item, 7 point scale (1 = not at all to 7 = definitely) assessed	200 male and female college students White (61%), non-White (38.5%)	McGill University, Montreal	10/2009 to 03/2010 post-licensure	I1: 4.39 ± 1.86 C: 3.88 ± 1.77 $P<0.05$ I2: 4.57 ± 1.90 C: 3.88 ± 1.77 $P<0.05$

Author, year and journal	Intervention (I) and control (C)	Outcome (O) and assessment (A)	Population	Setting	Time frame	Results RR (95%CI) or M ± SD[a]
	I2: Fact sheet about HPV and vaccine I2: Fact sheet about HPV and vaccine C: Fact sheet about general cancer prevention strategies	immediately post-intervention	Income of > $100,000 (46%)			I1 vs. I2: no significant difference
Kwan 2011 Patient Educ Couns[35]	Comparison of attitudes pre- to post-intervention I: One-h educational slide presentation followed by a question/answer session conducted by a gynecologist oncologist C: No control condition	O: "How likely is it that you would take the HPV vaccine now?" A: single item (yes/no) assessed immediately post-intervention	943 adolescent girls Parents with secondary school education or more (91.6%)	4 secondary schools in Hong Kong	07/2008–11/2008 post-licensure	1.15 (1.10, 1.20)[c] Authors reported intent pre- (74.9%) vs. post-intervention (86.2%).
Lloyd, 2008 J Adolesc Health[36]	Randomized, controlled trial I: Fact sheet about HPV prevalence, detection, prevention, treatment and symptoms C: Two groups C1: Fact sheet about chlamydia C2: Fact sheet about theenvironment	O: HPV vaccination intention A: Single item, (1 to 4, 4=very likely) assessed immediately post-intervention	174 boys and girls ages 13–16	Two grade schools in London	Post-licensure (date not specified)	I: 3.36 ±0.74 C1: 3.09±0.8 No significant difference I: 3.36 ±0.74 C2: 3.00 ±0.89 *P* = 0.02
Patel, 2012 J Am Coll Health[39]	Randomized controlled trial I: Fact sheet about HPV and vaccination given and contents reviewed with the study coordinator. Two weeks later, mailed copy of the fact sheet and reminder letter including how to schedule vaccination C: HPV vaccine briefly mentioned, different HPV vaccination fact sheet given and information on how to schedule vaccination given	O: Receipt of first dose of HPV vaccine A: Medical record review and if not available, self-report six months post intervention	256 female college students ages 18–26 White (67.2%), Asian (13.7%), African-American (9.0%), other (5.1%), more than one race (5.1%)	Gynecology clinic at University of Michigan	11/2007–01/2009 post-licensure	0.84 (0.31, 2.28)
Vanderpool, 2013 J Commun[37]	Randomized, controlled trial I:13-min educational video about HPV and vaccination, plus CDC HPV vaccine information sheet and a free t-shirt C: CDC HPV vaccine fact sheet and a free t-shirt	O: Completion of the 3-dose series A: Medical record review up to nine months after the initial HPV vaccine dose was administered	344 women ages 18–26 who received a free first dose of HPV vaccination from the study White non-Hispanic (94%) Some college education (48%)	Appalachian Kentucky: recruited from health departments, clinics, colleges, festivals, stores and homes	2010–2011 post-licensure	1.36 (1.03, 1.79)[c] Authors reported 43.3% of intervention group and 31.9% of control group completed the 3-dose series (*P* = 0.03)

[a] RR (95%CI) = relative risk (95% confidence intervals) where RR >1 indicates higher and RR< 1 indicates lower HPV vaccine acceptance. M ± SD = mean ± standard deviation.

[b] Reviewers calculated RR (95%CI) by combining the two control groups.

[c] Reviewers calculated RR (95%CI).

Table 4

HPV vaccination comparative message persuasiveness trials.

Author, year and journal	Intervention (I) and control (C)	Outcome (O) and assessment (A)	Population	Setting	Time frame	Results RR (95%CI) or M ± SD unless otherwise noted[a]
Cox, 2010 Health Psychol[41]	Randomized, controlled trial I: 4 groups all given 1-page fact sheet about HPV infection and vaccine of varying presentations of HPV risk statistics. Some were also asked rhetorical questions to gain commitment to cancer prevention and thus, HPV vaccination: I1: Graphic risk presentation I2: Graphic risk presentation + rhetorical questions 13. Non-graphic risk presentation 14. Non-graphic risk presentation + rhetorical questions C: 2 groups both given 1-page fact sheet about HPV infection and vaccine plus: C1: Rhetorical questions C2: No additional information	O: HPV vaccination intention for daughters A: Additive score of 3 survey items (1 = definitely would not get vaccinated, 5 = definitely would get vaccinated) assessed immediately post-intervention	471 mothers of children ages 11–16 White non-Hispanic (58.4%), Black (21%), Hispanic (20%) No high school diploma (4.9%), high school diploma (50.5%), Some college (22.2%), College graduate or more (16.3%) Trade school (5.8%)	Online participants from a US commercial sample vendor	Post-licensure. Date not specified	Graphic (I1 + I2): *M*= 12.96 Non-graphic (I3 + I4): *M* = 11.89 Control (C1 + C2): *M*= 11.88 *P* = 0.004 Rhetorical questions (I2 + I4 + C1): *M* = 12.60 No rhetorical questions (I1 + I3 +C2): *M*= 11.9 *P* = 0.033
Notes: N per cohort not reported. No standard deviations for means reported. Outcomes for each treatment group not reported separately. Authors report a significant interaction between rhetorical question and risk presentation format (*P* = 0.035) such that in the all intervention conditions (in which participants were given statistical risk information either graphic or non-graphic), there was minimal effect of the rhetorical question; whereas, in the control conditions (without statistical risk information),						

Author, year and journal	Intervention (I) and control (C)	Outcome (O) and assessment (A)	Population	Setting	Time frame	Results RR (95%CI) or M ± SD unless otherwise noted[a]
there was a strongly positive effect of the rhetorical questions						
DiClemente, 2011 Int J STD AIDS[42]	Randomized trial I: 3 groups all viewed HPV vaccine slide presentation of varying focus: I1: Cervical cancer prevention for women I2: Genital warts prevention for men I3: Head and neck cancer protection for men C: No control condition	O: "Because the HPV vaccine is now available for use in men, how likely would you get the HPV vaccine within the next year?" A: Single item (1 = very unlikely to 6 = very likely) assessed pre- and immediately post-intervention	150 male college students ages 18–24 Black (53.3%), White (19.3%), Asian or Pacific Islander (21.3%), other (6.1%)	2 universities in Southern US	10/09–12/09 post-licensure	Comparison of post-test scores for the 3 groups *P* = 0.56 (scores not specified) Pre-intervention (I1 + I2 + I3): 3.19 ± 1.33 Post-intervention (I1 + I2 + I3): 3.91 ± 1.34 *P* = 0.0001
Notes: N per cohort not reported. Results also reported as comparison pre- to post-intervention						
Dunlop, 2010 Commun Monogr[43]	Randomized, controlled trial I: 3 groups all listened to radio advertisement of varying format and some given 5-min discussion time afterwards: I1: Narrative ad (woman describes her cervical cancer treatment) + discussion I2: Informational ad (facts about HPV and cervical cancer) + discussion I3:Narrative ad only (no discussion) C: Informational ad only (no discussion)	O: HPV vaccination intention A: Average score of 3 items, (1 =disagree strongly to 7 = agree strongly) assessed immediately post-intervention	69 female college students ages 18–26 (in friendship dyads)	Australian University	Post-licensure Date not specified	No significant main effects of message format and discussion condition I1: 4.83 ±0.93 I2: 5.62± 1.16 I3: 5.8 ±0.73 C: 5.02± 1.31
Notes: Authors report a significant interaction between message format and discussion time ($P < 0.05$) such that in the narrative condition, there was a negative effect of discussion time; whereas in the informational condition, there was no significant effect of discussion time						

Author, year and journal	Intervention (I) and control (C)	Outcome (O) and assessment (A)	Population	Setting	Time frame	Results RR (95%CI) or M ± SD unless otherwise noted[a]
Fahy, 2010 Irish J Med Sci[44]	Randomized trial I: 2 groups both given 1-page fact sheet about HPV infection and vaccine of varying message frame: I1: Gain I2: Loss C: No control condition	O: HPV vaccination intention for daughters A: Average score of 3 items, (1 =very unlikely or strongly disagree to 7 = very likely or strongly agree) assessed immediately post-intervention	72 mothers of girls ages 8–16	North County Kildare, Ireland	Post-licensure Date not specified.	I1:5.9 ±1.3 I2:5.62±1.4 *P* = 0.397
Gainforth, 2012 J Health Psychol[45] *Notes:* N per cohort not reported. How the HPV vaccination intention measure was scored was not specified. Authors also reported outcomes (not significant) for interactions among gain/loss, risk framing and history of Pap smear (not shown here)	Randomized trial I: 4 groups presented with an online message of varying gain/loss and risk frames: I1: Gain, high-risk I2: Gain, low-risk I3: Loss, high-risk I4: Loss, low-risk C:No control condition	O: HPV vaccination intention A: 3 items, each a 7 point scale (scale response categories not specified) assessed immediately post-intervention	286 female college students with average age 22 White (80%)	Canadian university	Post-licensure Date not specified.	Main effects: High-risk (I1 + I3): 20.00 ± 11.23 Low risk message (I2 +I4): 22.27±11.37 *P* = 0.04–0.05* (text and table report different *P* values) Gain (I1 + I2): 21.40 ± 11.59 Loss (I3 + I4): 20.81 ± 11.03 *P* = 0.81
Gainforth, 2012 Public Health Nursing[46]	Randomized trial I: 6 groups presented with an online message based on the Ontario government's about HPV vaccine for parents of varying gain, loss or mixed frame: I1: Gain for parents of girls I2: Loss for parents of girls I3: Mixed for parents of girls	O: HPV vaccination intention for child within the next 3 years A: Single survey item (1 = strongly disagree to 7 = strongly agree) assessed immediately post-intervention	367 parents of children in grades 5–7 ages 10–12	Child-centered community and sporting events in Ontario, Canada	10/09–3/10 post-licensure for girls (but pre-licensure for boys until 2/10)	No significant main effect of message frame on intention (scores and significance level not specified) N per cohort not reported

Author, year and journal	Intervention (I) and control (C)	Outcome (O) and assessment (A)	Population	Setting	Time frame	Results RR (95%CI) or M ± SD unless otherwise noted[a]
	I4: Gain for parents of boys I4: Gain for parents of boys I5: Loss for parents of boys I6: Mixed for parents of boys C:No control condition					
Notes: Authors also reported results for outcome of HPV vaccination attitudes (not shown here). No significant 3-way interaction among parent's gender, child's gender and message frame (P = 0.17–0.19)						
Gerend, 2007 Health Psychol[48]	Randomized trial I: 2 groups both given 2-page fact sheet about HPV vaccine of varying message frame: I1: Gain I2: Loss C: No control condition	O: HPV vaccination intention A: Average score of 5 items, (1 = very unlikely to 6 = very likely) assessed immediately post-intervention	121 female college students White (85%), Black (10%), other(5%) Hispanic (12%)	Florida State University	Pre- licensure Date not specified.	No significant main effect of message frame on intention (scores and significance level not specified)
Notes: N per cohort not reported. Authors report a significant interaction between message frame and number of lifetime partners (P = 0.035) as well as message frame and frequency of condom use (P = 0.002) in a regression model that included message frame, number of partners and condom use, and these two interaction terms. Authors also report a significant interaction between message frame and avoidance motivation (P = 0.043) in a regression model that included message frame, avoidance motivation, approach motivation and the interaction terms message frame × avoidance motivation and message frame × approach motivation						
Gerend, 2008 Ann Behav Med[49]	Randomized trial I: 4 groups all given 2-page fact sheet of varying message frame and	O: HPV vaccination intention A: Average score of 5 items, (1 =very	243 female college students White (76%), Black (13%),	University in Southern US	11/2005 pre-licensure	I1:3.96 ± 1.54 I2:3.74 ± 1.72 P = 0.45 I3: 3.60 ± 1.55

Author, year and journal	Intervention (I) and control (C)	Outcome (O) and assessment (A)	Population	Setting	Time frame	Results RR (95%CI) or M ± SD unless otherwise noted[a]
	hypothetical number of HPV doses they would receive hypothetical number of HPV doses they would receive I1: Gain, 6-shot series I2: Loss, 6-shot series I3: Gain, single shot I4: Loss, single shot C: No control condition	unlikely to 6 = very likely) assessed immediately post-intervention	Asian/Pacific Islander (2%), other (8%) Hispanic (8%)			I4: 4.65 ± 1.32 *P* < 0.001
Notes: N per cohort not reported						
Gerend, 2009 J Exp Soc Psychol[50]	Randomized trial I: 4 groups all given 2-page fact sheet about HPV infection and vaccine of varying message frame and color- threat priming: I1: Gain, red text box I2: Loss, red text box I3: Gain, gray text box I4: Loss, gray text box C: No control condition	O: HPV vaccination intention A: Average score of 5 items (1 = very unlikely to 6 = very likely) assessed immediately post-intervention	126 male college students	Florida State University	01/2007–03/2007 pre-licensure for men	I1:3.62 ±0.259 I2: 4.41 ±0.237 *P* < 0.05 I3: 3.86±0.251 I4: 3.67 ±0.250 *P* > 0.5
Notes: N per cohort not reported. Authors report a significant interaction between frame and color observed (*P* < 0.05) in regression model that included existence of a current sexual partner, message frame, color and the interaction term						
Gerend, 2009 Sex Transm Dis[47]	Randomized trial I: 2 groups both given 2-page fact sheet about HPV infection and vaccine with varying additional content about: I1: Consequences for men I2: Consequences for men +women C: No control condition	O: HPV vaccination intention A: Average score of 5 items, (1 = very unlikely to 6 = very likely) assessed immediately post-intervention	356 heterosexual male college students White (84%), Black (4%), other/not reported (12%) Hispanic (14%)	Florida State University	Pre-licensure for men (date not specified)	I1: 3.93 ± 1.40 I2: 3.78± 1.52 *P* > 0.15
Notes: N per cohort not reported						
Hopfer, 2012 Prev Sci[51]	Randomized, controlled trial I: 3 groups shown brief video about HPV vaccine in a narrative format delivered by varying source types:	O: Receipt of first HPV vaccine dose A: Single survey item (yes/no) assessed 2 months post-intervention	404 female college students ages 18–26 White (72%), Black (10%), Asian-American	Pennsylvania State University	2008, Post-licensure	I1:17.8% vaccinated I2: 6.0% vaccinated I3: 21.8% vaccinated C: 11.8% vaccinated

Author, year and journal	Intervention (I) and control (C)	Outcome (O) and assessment (A)	Population	Setting	Time frame	Results RR (95%CI) or M ± SD unless otherwise noted[a]
	I1: peers I2: medical experts I3: peers and medical experts C: 3 groups shown varying video content: C1: HPV informational video without narrative C2: Campus website with information about HPV and the vaccine C3: No-message control		(11%), Hispanic (5%), other (1%)			I1 vs. control (C1 + C2 + C3): 1.61 (0.80,3.28) 12 vs. control (C1 +C2 + C3): 0.48 (0.13,1.69) 13 vs. control (C1 +C2 + C3): 2.07 (1.05, 4.10)
Notes: N per cohort not reported. Authors also reported outcomes for HPV vaccination intention (not shown here)						
Juraskova, 2011 Womens Health Issues[52]	Randomized trial I: 2 groups both given fact sheet about HPV disease and vaccine with framing paragraphs of varying focus: I1. Cervical cancer prevention I2. Cervical cancer + genital warts prevention C: No control condition	O: Receipt of first HPV vaccine dose A: Single survey item (yes/no) assessed 2 months post-intervention	75 female first-year college students age <27	University of Sydney for course credit	6/2007–8/2007 post-licensure	I1:33.3% vaccinated I2: 41.7% vaccinated (P = 0.61) 0.2 (−0.44, 0.56)
Notes: Authors presented vaccination outcomes as proportion immunized. Reviewers calculated P value and RR (95%CI). Authors also reported results for outcome of HPV vaccination intention and attitudes (not shown here)						
Krieger, 2013 Health Commun[53]	Randomized trial I: 2 groups both given 1-page HPV vaccine fact sheet of varying focus: I1: Genital warts prevention I2: Cervical cancer prevention C: No control condition	O: Intention to talk to doctor (daughters) or encourage daughter to talk to doctor (mothers) about HPV vaccination A: Average score of 3 items, (5-point Likert-type scale, higher score indicating higher intention) assessed	188 female college students and 115 corresponding mothers Students: White (76%), Black (12%), Asian (8%), other (5%) Mothers: White (85%), Black (9%), Asian (5%), other (1%)	US Midwestern university	Post-licensure. Date not specified	No significant direct effect of message focus on daughters' or mothers' intentions

Author, year and journal	Intervention (I) and control (C)	Outcome (O) and assessment (A)	Population	Setting	Time frame	Results RR (95%CI) or M ± SD unless otherwise noted[a]
		immediately post-intervention immediately post-intervention				
Notes: No means or standard deviations provided. Authors also reported that self-efficacy and response efficacy sequentially mediated the positive indirect influence of the genital warts prevention message on HPV vaccination intention						
Leader, 2009 J Womens Health[54]	Randomized trial I:3 groups all viewed online paragraph about HPV disease and vaccine with framing paragraphs of varying focus: I1. Cervical cancer prevention I2. Cervical cancer + sexually transmitted illness (STI) prevention I3. Cervical cancer + sexually transmitted illness (STI) prevention + suggestion that HPV vaccination may lead to sexual promiscuity C: No control condition	O: HPV vaccination intention at little or no cost (women: for self and parents: for daughters) A:1 item, (1 = very unlikely to 5 = very likely) assessed immediately post-intervention	635 adults White non-Hispanic (75%), Black non-Hispanic (11.4%), Hispanic (9.0%) More than high school graduation (55.7%) Income of > 50,000 (43.6%)	Online participants from a US commercial sample vendor	June 2006 pre-licensure	Parents with daughters ages 9–17 only (n = 70): I1: 3.77 ± 1.45 I2: 3.21 ± 1.47 I3: 3.40 ± 1.23 P = 0.360
Notes: Authors also reported separate analyses for HPV vaccination intention with out-of-pocket cost and for parents with daughters ages 0–8 and 18–26 and for women of any age (not shown here)						
Lechuga, 2011 Ann Behav Med[55]	Randomized trial I: 2 groups, both given gain and loss-framed brochures about HPV virus and the vaccine in varying order: I1: Gain before loss I2:Loss before gain C:No control condition	O: HPV vaccination intention A: Average score of 5 items, (1 =definitely no to 7 = definitely yes) assessed pre-intervention, after reading 1 brochure, and after reading 2 brochures	150 mothers of daughters ages 9–17 White non-Hispanic (33.3%), Black (33.3%), Hispanic (33.3%) High school or less (59.3%), Some college (23.3%), College graduate (9.3%), Technical school (6.0%)	4 Women, Infants and Children (WIC) supplemental nutrition clinics in Wisconsin	Post-licensure (date not specified)	No results reported for comparison of the two message framing orders (I1 vs. I2) overall ethnicities Pre-intervention: 5.13 ± 1.63 Post-intervention, after reading loss-framed message only: 6.51 ± 1.13 P < 0.05

Author, year and journal	Intervention (I) and control (C)	Outcome (O) and assessment (A)	Population	Setting	Time frame	Results RR (95%CI) or M ± SD unless otherwise noted[a]
						Pre-intervention: 5.13 ± 1.63 Pre-intervention: 5.13 ± 1.63 Post-intervention, after reading gain-framed message only: 6.22 ± 1.28 $P < 0.01$
Notes: Authors also reported separate analyses by racial/ethnic group (not shown here). Authors also reported marginally significant ($P = 0.06$) interaction between framing order and ethnic group such that both gain-and loss-framed messaged messages were equally effective in non-Hispanic white mothers; whereas, the loss-framed message was more effective in non-Hispanic African-American and Hispanic mothers						
Nan, 2012 Health Commun[56]	Randomized trial I: 2 groups, both viewed online informational pamphlet about HPV infection and a section about HPV vaccine with varying message frame: I1: Gain I2: Loss C: No control condition	O: HPV vaccination intention at no cost A: Average score of 3 items (1 = extremely unlikely to 7 = extremely likely) assessed immediately post-intervention	229 male and female college students ages 18–26 White (61.1%), Black (11.4%), Asian (15.7%), other (7.4%) Hispanic (4.4%)	University for course credit	Post-licensure (date not specified)	No main effect of message framing on intention $P = 0.65$
Notes: N per cohort not reported. Author also reported separate analyses for HPV vaccination intention with out-of-pocket cost (not shown here). Authors also reported a significant interaction between message framing and motivation ($P < 0.05$) such that the loss-framed message was more effective for avoidance-oriented participants; whereas, both frames were equally effective for approach-oriented participants						
Nan, 2012 Hum Commun Res[57]	Randomized trial	O: HPV vaccination intention at no cost	282 male and female college	Northeast university for course credit	Post-licensure (date not specified)	No significant main effect of message

Author, year and journal	Intervention (I) and control (C)	Outcome (O) and assessment (A)	Population	Setting	Time frame	Results RR (95%CI) or M ± SD unless otherwise noted[a]
	I: 2 groups, both viewed online information pamphlet about HPV infection and a section about HPV vaccine with varying message frame: I: 2 groups, both viewed online information pamphlet about HPV infection and a section about HPV vaccine with varying message frame: I: 2 groups, both viewed online information pamphlet about HPV infection and a section about HPV vaccine with varying message frame: I: 2 groups, both viewed online information pamphlet about HPV infection and a section about HPV vaccine with varying message frame: I: 2 groups, both viewed online information pamphlet about HPV infection and a section about HPV vaccine with varying message frame: I: 2 groups, both viewed online information pamphlet about HPV infection and a section about HPV vaccine with varying message frame: I1: Gain I2: Loss C: No control condition	A: Average score of 3 items (1 =extremely unlikely to 7 = extremely likely) assessed immediately post-intervention	students HPV infection 26 White (65.8%), Black (9.9%), Asian (12.8%), Hispanic (5.5%), other (6%)			framing on intentions 0.05 ≤ *P*< 0.1
Notes: N per cohort not reported. Author also reported separate analyses for HPV vaccination intention with out-of-pocket cost (not shown here). Author also reported a significant interaction between message framing and time orientation ($P < 0.05$) such that the loss-framed message was more effective for present-minded participants; whereas, both frames were equally persuasive for future-minded participants						
Nan and Madden, 2012 Health Commun[58]	Randomized trial I: 2 groups, both viewed online blog with varying levels of support for HPV vaccine: I1: Positive blog (vaccine is “effective and safe”) I2: Negative blog (vaccine is “not effective and potentially dangerous”) C: No blog	O: HPV vaccination intention at no cost A: Average score of 3 items (1 =extremely unlikely to 7 = extremely likely) assessed immediately post-intervention	176 male and female college students White (63.9%), Black (10.9%), Asian (16.7%), Hispanic (4.4%), other (4.1%)	Northeast university for course credit	Post-licensure Date not specified.	I1:4.872 ± 0.0205 (standard error) I2: 3.97 ±0.242 (standard error) $P < 0.05$ I1:4.872 ± 0.0205 (standard error) C: 4.781 ±0.214 (standard error) $P < 0.05$ I2 vs. C $P \geq 0.05$
Notes: N per cohort not reported. Author also reported separate analyses for HPV vaccination intention with out-of-pocket cost (not shown here)						

[a] RR (95%CI) = relative risk (95% confidence intervals) where RR > 1 indicates higher and RR < 1 indicates lower HPV vaccine acceptance. *M* ± SD = mean ± standard deviation.

Table 5

Ways in which HPV vaccination messages were varied and tested between treatment conditions in each included study 1.

Author, year and journal	Content focus on cervical cancer/STI	Other content focus	Presentation or delivery format	Gain/loss	Other
Cox, 2010 Health Psychol[41]			×		
Diclemente, 2011 Int J STD AIDS[42]	×				
Dunlop, 2010 Commun. Monogr[43]			×		
Fahy, 2010 Ir J Med Sci[44]				×	
Gainforth, 2012 J Health Psychol[45]				×	× (high/low risk)
Gainforth, 2012 Public Health Nurs[46]				×	
Gerend, 2007 Health Psychol[48]				×	
Gerend, 2008 Ann Behav Med[49]				×	× (number of shots)
Gerend, 2009 J Exp Soc Psychol[50]			×	×	
Gerend, 2009 Sex Transm Dis[47]	×	×			
Hopfer 2012 PrevSci[51]			×		
Juraskova, 2011 Womens Health Issues[52]	×				
Krieger, 2013 Health Commun[53]	×				
Leader, 2009 J Womens Health[54]	×				
Lechuga, 2011 Ann Behav Med[55]				×	
Nan, 2012 Health Commun[56]				×	
Nan, 2012 Hum Commun Res[57]				×	
Nan and Madden, 2012		×			

Author, year and journal	Content focus on cervical cancer/STI	Other content focus	Presentation or delivery format	Gain/loss	Other
Health Commun[58]					