

# Human Papillomavirus Vaccination and Sexual Disinhibition in Females

## A Systematic Review



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**Context:** Some parents believe human papillomavirus (HPV) vaccination increases the chance of risky sexual behaviors among adolescents. This review summarizes the evidence available on adolescent girls and women engaging in risky sexual activity following HPV vaccination.

**Evidence acquisition:** Systematic review using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines was conducted in 2014 and updated in 2015. Literature was searched for articles published between 2004 and 2015 in MEDLINE, PsycInfo, CINAHL, Cochrane Database, Web of Science, and EMBASE without language limits. Studies were screened according to predefined inclusion and exclusion criteria. Methodologic quality of the included articles was assessed.

**Evidence synthesis:** The search resulted in 21 articles to be included in the review, with 527,475 participants. Included studies were conducted in 12 different countries using experimental and observational study designs. The review included data on girls aged as young as 11 years to women aged 40 years. Studies measured changes in sexual behaviors using a variety of outcomes, including age at sexual debut; risky sexual behaviors; use of condoms and contraception; and clinical indicators such as rates of sexually transmitted infections, HIV, and pregnancy terminations. Available data showed either no association between vaccination status and the outcomes of interest or a positive association between safer sexual behaviors, such as condom use and receipt of HPV vaccination. Methodologic quality of all but one study was moderate or weak.

**Conclusions:** This review did not find sufficient evidence to support compensatory sexual risk behaviors following HPV vaccination among adolescent girls or women.

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### Context

Recent studies have shown that prophylactic human papillomavirus (HPV) vaccination programs have resulted in significant reductions in vaccine-type infections.<sup>1</sup> Two studies from Australia and

New Zealand reported a steep decline, for instance, in genital warts following school-based HPV vaccination programs.<sup>2,3</sup> However, concerns about the effects of vaccination have slowed uptake in some countries.<sup>4,5,6</sup> These include fears that it may lead to premature sexual debut. There is some evidence that behavioral disinhibition is normative among young people and may be related to environmental exposures.<sup>7</sup> Some parents have expressed concerns that HPV vaccination could be interpreted as tacit approval of sexual activity or that young people may incorrectly assume that it provides protection against pregnancy and HIV.<sup>8,9,10</sup> Critics of HPV vaccination have also suggested that it may lead to an increased number of sex partners or a decrease in condom use, particularly among adolescents.<sup>11,12</sup>

Researchers have hypothesized that individuals accept a certain level of health risk in their daily activities.

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Accordingly, interventions reducing risk may lead to additional unsafe behaviors that bring the overall level of risk back to baseline levels; this has been referred to as “risk compensation.”<sup>13</sup> Other studies have also shown that environmental factors can influence sexual risk taking among young people.<sup>14,15</sup> Both hypotheses have been examined in numerous research studies on sexual risk in health interventions. Provision of free contraception was shown to have no effect on the number of sex partners and frequency of intercourse over time.<sup>16</sup> Similarly, studies of HIV prevention programs have shown no evidence that needle exchanges were associated with the time to HIV seroconversion, and researchers found that sexual risk behavior did not increase when participants were provided with pre-exposure prophylaxis to prevent HIV infection.<sup>17</sup> Findings around sexual disinhibition in medical male circumcision have been mixed. Kibira et al.<sup>18</sup> showed that sexually risky behavior was more common among circumcised men, whereas Westercamp and colleagues<sup>19</sup> reported no evidence of risk compensation in men following medical male circumcision.

Fewer studies have examined behavioral disinhibition associated with vaccination. Brewer et al.<sup>6</sup> examined the impact of vaccination against Lyme disease on protective behaviors and found some evidence of regression in protective behaviors after vaccination. Gray and colleagues<sup>20</sup> found that participation in an HIV vaccine efficacy trial did not increase sexual risk behavior as a result of receiving the vaccine.

Fears about the impact of HPV vaccination on sexual disinhibition and risk compensation are hampering vaccine programs; thus, summarizing the current literature is of public health importance.

## Evidence Acquisition

### Search Strategy

A protocol for this systematic review was registered through PROSPERO's database.<sup>21</sup> This review was conducted in 2014 (updated in 2015) and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.<sup>22</sup> MEDLINE, EMBASE, PsycINFO, CINAHL, Cochrane Central Register of Controlled Trials, and Web of Science were searched for papers published from 2004 through July 2015. A search strategy that included keywords, Medical Subject Headings, and exploded headings was first created for MEDLINE (Appendix, available online). The search algorithm was adapted for each database depending on search requirements. Authors also searched reference lists for all retrieved studies. No language restrictions were applied.

### Inclusion/Exclusion Criteria

Two authors performed the literature search with the assistance of a librarian. Titles and abstracts were screened for inclusion; when eligibility could not be ascertained, full-text articles were downloaded and screened. Disagreements were resolved by consensus.

To be included in the review, studies had to be quantitative research reporting data on individuals that had received HPV vaccination or interventions using an HPV vaccine that reported a comparison of change in sexual risk behaviors. Only peer-reviewed publications were included. All studies were required to report some measure of sexual disinhibition or risk compensation. Sexual disinhibition and risk compensation, for the purpose of the review, was defined as any behavior increasing the risk for acquisition of sexually transmitted infections (STIs) following HPV vaccination. Studies were excluded if they were qualitative in research design, conference abstracts, opinion pieces, narrative reviews, or gray literature. Additional requirements are described in Table 1.

### Data Extraction

Data were extracted using a standardized form that included the following variables: authors, publication year, location, study design, population, study setting, length of follow-up, intervention type, change in sexual risk behavior, and measures of effect.

### Risk of Bias Assessment

Methodologic quality was assessed independently by two reviewers using the quantitative research evaluation tool developed by the Effective Public Health Practice Project Group<sup>23</sup>; disagreements were resolved using adjudication by a third reviewer. Ratings were assigned to the following features: participant selection, study design, control of confounders, blinding, data collection methods, loss to follow-up, intervention integrity, and analyses. Cumulative scores were aggregated as: strong (no component rated weak), moderate (one component rated weak), and weak (two or more components rated weak).

## Evidence Synthesis

Figure 1 describes the literature search and is summarized here. The initial search of the databases resulted in 743 citations. From the manual search, an additional ten abstracts were identified, resulting in a total of 753 citations. Of these articles, 65 were duplicates. During the screening process, 593 records were excluded; the reasons for exclusion are included in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Chart (Figure 1). During the second screen, 95 full-text articles were retrieved and assessed for eligibility, of which 21 studies were identified to be included in the review. Table 2 provides a summary of characteristics of the reviewed studies. Of the 21 studies, 14 were cross-sectional,<sup>24–37</sup> three were retrospective cohort,<sup>38–40</sup> two were prospective cohort studies,<sup>41,42</sup> and two were experimental studies.<sup>43,44</sup> Nine studies were conducted in the U.S.,<sup>26,28,31,33,36,38,39,42,45</sup> three in the United Kingdom,<sup>34,37,41</sup> two in Sweden,<sup>25,30</sup> and one each in Australia,<sup>29</sup> Canada,<sup>44</sup> Colombia,<sup>32</sup> Denmark,<sup>25</sup> France,<sup>27</sup> Italy,<sup>35</sup> Norway,<sup>25</sup> Peru,<sup>6</sup> and Uganda.<sup>24</sup>

### Risk of Bias Within Studies

Of the 21 studies that met the eligibility criteria, 14 had a moderate rating (one component rated weak), and seven

**Table 1.** Inclusion Criteria

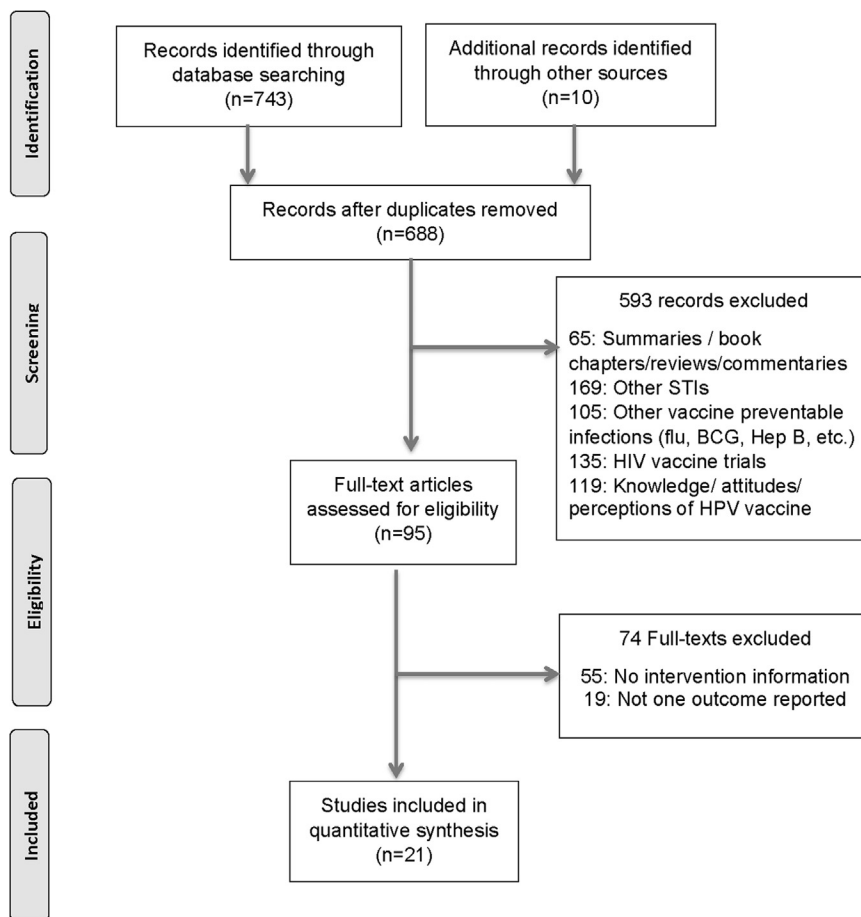
Variable	Criteria
Populations	Females
Interventions	Human papillomavirus vaccination
Comparisons	Standard of care, pre-intervention measures, and no-intervention control group
Outcomes	Biological or behavioral outcomes including sexually transmitted infection/HIV diagnosis or self-reported unprotected sexual intercourse; number of sex partners; sexual initiation; condom use; number of sex acts, contraceptive counseling, pregnancy, abortion, emergency contraception, and reported unprotected oral/anal sex

were assigned a weak rating (two or more components rated weak). There were no studies that could be rated as strong (no component rated weak). The most common risk of bias in all of the reviewed studies included selection and reporting bias.

**Human Papillomavirus Vaccination and Early Sexual Debut**

Three studies examined the impact of HPV vaccination on early sexual debut. Forster et al.<sup>41</sup> conducted a survey

among adolescent girls in seven schools in England examining whether HPV vaccination led to changes in sexual behavior. The change in the proportion of girls who were sexually active from baseline to follow-up was not significantly greater in the vaccinated group compared to the unvaccinated group (OR=0.80, 95% CI=0.40, 1.59). Hansen and colleagues<sup>25</sup> conducted a survey among 48,870 Nordic women aged 18–45 years randomly selected from population registries in Denmark, Norway, and Sweden. They reported no significant differences in the rates of sexual initiation for women



**Figure 1.** Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2009 flow diagram of selection of studies for the systematic review.

**Table 2.** Summary of Studies of the Association of HPV Vaccination and Sexual Disinhibition

First author (year)	Study design	Country	Study population	Study sample	Results
Observational studies					
Mattebo (2014) <sup>30</sup>	Cross-sectional	Sweden	17- to 21-year-old women	227 vaccinated, 121 unvaccinated	No differences between HPV-vaccinated and unvaccinated groups regarding condom use, STIs, and experiences of oral and anal sex, or “friends with benefit” relationships. However, having had sexual intercourse ( $p=0.005$ ) and “one-night stands” ( $p=0.046$ ) was more common in the vaccinated group.
Aujo (2014) <sup>24</sup>	Cross-sectional	Uganda	12- to 15-year-old girls	200 vaccinated, 200 unvaccinated	No significant difference in sexual behavior between vaccinated and unvaccinated girls.
Hansen (2014) <sup>25</sup>	Cross-sectional	Denmark, Norway, Sweden	18- to 45-year-old women	2,535 vaccinated, 37,481 unvaccinated	Number of sex partners and number of lifetime sex partners did not significantly differ among women vaccinated against HPV prior to sexual debut and matched unvaccinated women. Non-use of contraception during first intercourse was significantly less frequent among women who received the HPV vaccine before sexual debut than among matched unvaccinated women.
Liddon (2012) <sup>26</sup>	Cross-sectional	U.S.	18- to 24-year-old women	630 females aged 15–19 years, 613 females aged 20–24 years	Adolescents aged 15–19 years, compared with those who reported never using a condom, girls always using a condom were more likely to report receipt of HPV vaccine (AOR = 3.0; 95% CI 1.1, 7.9). None of the other sexual behavior variables were related to receipt of HPV vaccine. Among 20- to 24-year-olds, lifetime sex partners, consistent condom use in the past month and having received an STI service in the past year were unrelated to receipt of HPV vaccine.
Lutringer-Magnin (2013) <sup>27</sup>	Cross-sectional	France	14- to 23-year-old females	135 vaccinated, 181 unvaccinated	No difference was observed between vaccinated and non-vaccinated groups regarding requests for HIV serology, history of abortions, or emergency hormonal contraception.
Marchand (2013) <sup>28</sup>	Cross-sectional	U.S.	18- to 26-year-old women	42 vaccinated, 72 unvaccinated	Proportion of women who were sexually experienced did not differ by HPV vaccination status, by age at first intercourse, by number of sex partners in the past year, or by frequency of condom use.
Mather (2012) <sup>29</sup>	Cross-sectional	Australia	18- to 30-year-old women	119 vaccinated, 74 unvaccinated	Vaccinated women did not differ significantly from unvaccinated women on levels of perceived vulnerability to cervical cancer, intention to undergo cervical screening, uptake of cervical screening or likelihood of engaging in safe sexual behavior.
Ratanasiripong (2014) <sup>31</sup>	Cross-sectional	U.S.	18- to 26-year-old women	209 vaccinated, 175 unvaccinated	Mean numbers of lifetime sex partners were not significantly different between the two groups ( $F=0.75$ , $p=0.39$ ); mean numbers of sex partners in the past 12 months were not statistically significant ( $F=0.00$ , $p=0.98$ ); and difference in

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**Table 2.** Summary of Studies of the Association of HPV Vaccination and Sexual Disinhibition (*continued*)

First author (year)	Study design	Country	Study population	Study sample	Results
					condom use was not statistically significant ( $\chi^2=0.37$ , $p=0.54$ ). Difference in annual numbers of sex partners before and after vaccination among the vaccinated was not statistically significant ( $t=1.83$ , $df=51$ , $p=0.07$ ).
Ruiz-Sternberg (2014) <sup>32</sup>	Cross-sectional	Colombia	Females 26 years old and younger	506 vaccinated, 930 unvaccinated	Vaccination status was positively associated with consistent condom use (AOR = 1.49; 95% CI=1.11, 2.01); use of modern contraceptive methods (AOR=2.02; 95% CI=1.26, 3.22); routine Pap smear (AOR=2.35; 95% CI=1.69, 3.28). Vaccinated adult women more likely to have had sex as compared with unvaccinated women (AOR=1.89; 95% CI=1.42, 2.52). For women younger than 18 years, there was no association between vaccination status and sexual debut.
Rysavy (2014) <sup>33</sup>	Cross-sectional	U.S.	13- to 24-year-old females	153 vaccinated, 70 unvaccinated	A high percentage of both groups were found to engage in high-risk sexual behaviors, which was not significantly different between the two groups.
Sadler (2015) <sup>34</sup>	Cross-sectional	UK	14- to 20-year-old females	225 vaccinated, 111 unvaccinated	Having more than three sex partners in the last 6 months (AOR=2.12; 95% CI=1.08, 4.17), attending the clinic with symptoms (AOR=1.78; 95% CI=1.09, 2.92), having anal intercourse with their last sexual contact (AOR=4.34; 95% CI=1.23, 14.29), and receiving a positive chlamydia diagnosis (AOR=2.30; 95% CI=1.06, 5.00) were all positively associated with non-vaccination. Condom use at first intercourse (AOR=0.55; 95% CI=0.32, 0.96), however, was positively associated with receiving HPV vaccine.
Sopracordevole (2013) <sup>35</sup>	Cross-sectional	Italy	13- to 20-year-old females	286 vaccinated, 343 unvaccinated	No differences between vaccinated and unvaccinated girls in knowledge of HPV vaccine, diagnostic tests for HPV related lesions, post-vaccine prevention measures in terms of secondary prevention with Pap test and condom use during occasional intercourse.
Guo (2015) <sup>36</sup>	Cross-sectional	U.S.	20- to 26-year-old women	177 vaccinated, 701 unvaccinated	Vaccinated women had lower prevalence of HPV types covered by the vaccine than unvaccinated women. There was no significant difference in STI, lifetime sex partners between the two groups.
Jena (2015) <sup>42</sup>	Longitudinal database of insurance claims	U.S.	12- to 18-year-old girls	21,610 vaccinated, 186,501 unvaccinated	STI rate was 4.3 per 1,000 females in the year before vaccination among vaccinated females as compared to 2.8 per 1,000 females among matched unvaccinated females ( $p=0.007$ ). The difference-in-differences analysis that compared changes in STI rates over time between vaccinated and unvaccinated females found no evidence of an association between HPV vaccination and higher STI rates. The difference-in-differences estimate provided no evidence of increased risky sexual activity (OR=1.11; 95% CI=0.68, 1.81).

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**Table 2.** Summary of Studies of the Association of HPV Vaccination and Sexual Disinhibition (*continued*)

First author (year)	Study design	Country	Study population	Study sample	Results
Bowyer (2014) <sup>37</sup>	Cross-sectional	UK	15- to 16-year-old girls	1,499 vaccinated, 413 unvaccinated/undervaccinated	There was no association between vaccine status and sexual experience.
Forster (2012) <sup>41</sup>	Prospective cohort	UK	16- to 17-year-old girls	433 offered vaccine, 620 not offered vaccine	Compared to the unvaccinated group, the vaccinated group did not have higher rate of sexual debut (OR=0.80; 95% CI=0.4, 1.59) or inconsistent condom use (OR=0.88; 95% CI=0.58, 1.33).
Romaih (2011) <sup>40</sup>	Retrospective cohort	U.S.	16-year-old girls	499 vaccinated	51.2% of the samples that had claimed to be sexually inactive at the start of vaccination series reported being sexually inactive at the end of 1 year; 2.8% of the sexually inactive females became sexually active by having at least one sex partner.
Bednarczyk (2012) <sup>38</sup>	Retrospective cohort	U.S.	11- to 12-year-old girls	493 vaccinated, 905 unvaccinated	Girls receiving HPV vaccine did not have a significantly higher IR of testing, diagnosis, or counseling (5.5/100 person years; aIRR=1.29; 95% CI=0.92, 1.80) compared with the unvaccinated group (3.9/100 person years; IRD 1.6/100 person years; 95% CI= -0.03, 3.24). No significantly increased IRRs estimated for individual outcomes comparing HPV vaccine exposed and unexposed girls.
Cummings (2012) <sup>39</sup>	Retrospective cohort	U.S.	14- to 17-year-old girls	75 vaccinated, 150 unvaccinated	Instances of vaginal intercourse without a condom were significantly lower in the vaccinated as compared to unvaccinated group ( $p < 0.001$ ). This was the only sexual behavior found to be different between cohorts. There was no difference in chlamydia and trichomoniasis detection rates between unvaccinated and vaccinated cohorts.
Experimental studies					
Brown (2013) <sup>43</sup>	Clinical trial	Peru	18- to 26-year-old females	200 vaccinated with two different schedules	Mean number of sex acts with new clients in the past 3 months decreased from baseline to follow-up ( $p < 0.001$ ).
Smith (2015) <sup>44</sup>	Quasi-experimental	Canada	13-year-old girls	260,493 with 4 birth cohorts of females born in 1992–1995 who had vaccination status available	No statistically significant increase in risk of the composite measure of indicators of sexual behavior in relation to HPV vaccination status was found (risk difference per 1,000 girls -0.61; 95% CI= -10.71, 9.49 and relative risk 0.96; 95% CI=0.81, 1.14).

aIRR, adjusted incidence rate ratio; HPV, human papillomavirus; IRD, incidence risk difference; IRR, incidence rate ratio; STI, sexually transmitted infection.

vaccinated before sexual debut and those that were not. This held true for both opportunistic vaccinators (adjusted hazard ratio=0.94; 95% CI=0.88, 1.02) and participants in organized vaccination programs (adjusted hazard ratio=0.88; 95% CI=0.76, 1.01). Ruiz-Sternberg and Pinzón-Rondón<sup>32</sup> carried out a cross-sectional study among a sample of 231 girls aged <18 years and 1,205 university students aged 18–26 years, attending three high schools and a university in Bogotá, Colombia. In their study, initiation of sexual intercourse before age 15 years was not associated with vaccination status after controlling for risk perception, age, educational level, and HPV knowledge.

### Human Papillomavirus Vaccination and Number of Sexual Partners

Ten studies examined whether HPV vaccination was associated with a greater number of sex partners. Hansen et al.<sup>25</sup> found that the number of sex partners was not significantly higher among women vaccinated prior to sexual debut compared to matched unvaccinated women. Using data from the 2007–2008 National Survey of Family Growth, Liddon and colleagues<sup>26</sup> found HPV vaccination was not associated with being sexually active or number of sex partners.

Two studies carried out anonymous web-based surveys among young female college students. Marchand et al.<sup>28</sup> found that the number of sex partners was not related to vaccine status. In the study by Ratanasiripong,<sup>31</sup> the adjusted means of the number of sex partners in a lifetime was 4.59 for vaccinees and 4.11 for non-vaccinees, and this was not significantly different between the two groups ( $p=0.39$ ).

Two studies examined sexual behaviors of clinic-based populations of young women. Rysavy and colleagues<sup>33</sup> found no significant difference between the number of lifetime sex partners and the mean number of sex partners for vaccinated versus unvaccinated clinic attendees (6.6 for both groups). Sadler et al.<sup>34</sup> showed that unvaccinated women were significantly more likely to have had three or more partners in the last 6 months compared with vaccinated females.

Two studies among adolescent girls in the U.S. examined HPV vaccination status and number of sex partners. Romaih and colleagues<sup>40</sup> found that among a sample of sexually active girls, 22.6% reported three or more partners in the prior year before vaccination; after a year, this had decreased to 22.4% and the difference was not statistically significant. Cummings et al.<sup>39</sup> compared a sample of vaccinated girls to an unvaccinated historic cohort and did not find a difference in the mean number of sex partners over the last year or mean number of sex partners in the prior 2 months.

Internationally, Brown and colleagues<sup>43</sup> showed that vaccination of Peruvian female sex workers resulted in a significant decrease in the number of clients, and the rates of sex with all clients were reduced by half (163.3 at baseline vs 70.68 at month 7,  $p<0.001$ ). Another study among Colombian women found no difference in the number of sex partners in the past year between the HPV vaccinated and unvaccinated groups (AOR=1.36, 95% CI=0.94, 1.99).<sup>32</sup>

### Human Papillomavirus Vaccination and Oral, Anal, and Group Sex

Two studies surveyed girls and women attending pediatric, adolescent, genitourinary, and general obstetrics and gynecology clinics to determine if HPV vaccination increased the number of episodes of oral, vaginal, or anal intercourse. Rysavy et al.<sup>33</sup> found no significant difference in the frequency of any of these sexual behaviors based on vaccination status. Sadler and colleagues<sup>34</sup> found that not being vaccinated against HPV increased risk for anal sex at the last sexual contact.

Three studies were carried out among school- or university-based populations. Aujo et al.<sup>24</sup> conducted a study in Uganda and found no significant difference in sexual behaviors between vaccinated and unvaccinated girls aged 12–15 years. Similarly, Mattebo and colleagues<sup>30</sup> found no difference between HPV vaccinated and unvaccinated Swedish high school students in having anal, oral, or group sex, or ever having had a “friend with benefits” relationship. In a survey of female students at the University of Sydney, Mather et al.<sup>29</sup> showed that HPV vaccination was not a significant predictor of self-reported sexual behavior.

### Use of Condoms and Other Contraception

Two studies examined condom use among young women in a community setting. Mattebo and colleagues<sup>30</sup> found no significant difference in use of condoms at either first sexual intercourse or at last intercourse between vaccinated and unvaccinated girls. Liddon et al.<sup>26</sup> found that among sexually active participants, vaccinated girls aged 15–19 years were more likely to report always using a condom compared with unvaccinated girls (AOR=3.0, 95% CI=1.1, 7.9).

Three studies examined sexual behavior and HPV vaccination status among college women. Ratanasiripong<sup>31</sup> examined condom use during sex in the prior 30 days and found that 51.2% of the vaccinated and 50% of the non-vaccinated women reported using condoms >75% of the time and this was not statistically significant. Ruiz-Sternberg and colleagues<sup>32</sup> found consistent condom (OR=1.49, 95% CI=1.11, 2.01) or other contraceptive use (OR=2.02, 95% CI=1.26, 3.22) was positively

associated with HPV vaccination. Marchand et al.<sup>28</sup> showed lower condom use was associated with older age, lower income, and committed relationship status, but not with HPV vaccination status.

Cummings and colleagues<sup>39</sup> found that instances of vaginal intercourse without a condom in the prior 60 days were significantly lower in the vaccinated group compared with unvaccinated controls ( $p < 0.001$ ). Lutringer-Magnin et al.<sup>27</sup> surveyed French girls and women aged 14–23 years and found no association between HPV vaccination and reduced condom use during a participant's first sexual intercourse, most recent intercourse, or use of emergency contraception. Rysavy and colleagues<sup>33</sup> reported no significant difference in condom use between vaccinated and unvaccinated female patients aged 13–24 years attending an obstetrics gynecology and pediatric clinic. Finally, Sadler et al.<sup>34</sup> found unvaccinated girls at a genitourinary clinic were significantly less likely to have used a condom at first sexual intercourse ( $p = 0.036$ ), but use of a condom at the last intercourse or emergency contraception was not associated with HPV status. Hansen and colleagues<sup>25</sup> examined contraception during first intercourse among Nordic women and found that it was significantly more common among those attending organized HPV vaccination campaigns (AOR=0.27, 95% CI=0.15, 0.48) and those that were opportunistically vaccinated (AOR=0.69, 95% CI=0.52, 0.93) compared with unvaccinated women.

### Human Papillomavirus Vaccination and Sexually Transmitted Infections, Pregnancy, or Abortions

Three large retrospective studies examined medical claims from administrative, insurance, or managed care databases to examine the temporal relationship between HPV vaccination and rates of STIs or abortions. Jena et al.,<sup>42</sup> in their analysis of female dependents of employees in 41 large employers across the U.S., compared medical claims for treatment of chlamydia, gonorrhea, herpes, HIV, or syphilis among HPV vaccinated and unvaccinated girls and women aged 12–18 years. They found that although HPV vaccinated women had higher STI rates compared with matched controls, these differences existed before vaccination; a difference-in-difference analysis found no evidence of an association between higher HPV vaccination and higher rates of STI. Bednarczyk and colleagues<sup>38</sup> conducted a similar examination using a large managed care database to examine rates of STI testing, diagnosis, or counseling and also found no relationship to HPV vaccine status. Finally, Smith et al.,<sup>44</sup> examined Canada administrative health databases for associations between HPV vaccination status and clinical indicators of sexual behavior among

eighth grade adolescent girls before and after the implementation of HPV vaccination in school-based clinics. An analysis of medical records for 260,493 girls could find no evidence that vaccination increased the risk for a composite outcome that included pregnancy and STI.

Four studies examined HPV vaccination and pregnancy or STIs among girls and women in clinic-based populations. In the study of young women aged 13–24 years who attended Obstetrics Gynecology and Pediatrics clinics, Rysavy and colleagues<sup>33</sup> found no significant difference between vaccinated and unvaccinated attendees in the rates of pregnancy or diagnosis of STIs, including HIV and HPV. Lutringer-Magnin et al.<sup>27</sup> found no differences between vaccinated and unvaccinated groups in requests for HIV serology or history of abortions. In their study of urban adolescents attending a primary care clinic, Cummings and colleagues<sup>39</sup> found that unvaccinated controls had 9.5 greater odds of vaccine-specific HPV infections, but there was no difference in the rate of diagnosis of chlamydia or trichomoniasis between vaccinated and unvaccinated girls. In a study of genitourinary clinic attendees in England, Sadler et al.<sup>34</sup> found no difference between vaccinated and unvaccinated women in the rate of terminations, STI diagnosis, or treatment. However, they did find that not being vaccinated against HPV was associated with a more than doubling of odds (AOR=2.30, 95% CI=1.06, 5.00) for a positive *Chlamydia trachomatis* test result and symptomatic attendance at the clinic visit.

Of the remaining three studies, two were conducted internationally, and the third was an analysis of data on a nationally representative sample of adolescents and young adults from a population-based study in the U.S. In a study among Colombian women, Ruiz-Sternberg and colleagues<sup>32</sup> found sexual risk behaviors were not associated with HPV vaccination status. Mattebo et al.<sup>30</sup> found no significant differences in STIs between vaccinated and unvaccinated groups of Swedish high school students, although chlamydia, condylomata acuminata, and genital herpes were reported in both groups. Finally, when Liddon and colleagues<sup>26</sup> analyzed responses from the National Survey of Family Growth, they found no significant differences in reported rates of obtaining in the last year a service related to an STI between women with and without HPV vaccination.

### Discussion

This review found that there is no evidence that female HPV vaccination is associated with sexual risk compensation or disinhibition in the U.S. or other countries where studies have been conducted. The evidence comes



from a variety of populations including girls and women in schools and universities, healthcare facilities, population-based studies, and large medical and insurance databases. It also includes data on girls ranging in age from as young as 11 years to women aged 40 years. Importantly, the studies have also measured changes in sexual behaviors using a variety of outcomes, including age at sexual debut; risky sexual behaviors; use of condoms and contraception; and clinical indicators such as rates of STIs, HIV, and terminations. The data from the 21 included studies showed either no association between vaccination status and the outcomes of interest, or indicated a positive association between safer sexual behaviors and receipt of HPV vaccination.

Except for one study,<sup>41</sup> none of the research was designed to explicitly assess sexual risk compensation and HPV vaccination. Most studies showed no influence of HPV vaccine on sexual risk behaviors, including condom use and number of sex partners. Studies were either neutral or supportive of the hypothesis that HPV vaccination is not associated with risk compensation or sexual disinhibition.

### Strengths and Limitations

One of the strengths of this review is that it examined biomedical and behavioral outcomes. It is also one of the few reviews summarizing current risk compensation evidence following HPV vaccination. This review was not without limitations. Despite the extensive search, some potentially eligible studies may have been left out. It also did not include qualitative studies or conference abstracts. Additionally, owing to non-comparable measurements and various study designs, desired conclusions and inferences could not be drawn. Furthermore, studies were highly heterogeneous, with most of the evidence derived from cross-sectional studies. Because most studies used self-reports, they may be prone to recall and social desirability bias. However, if that were the case, it would affect both groups, which might bias the effect towards null. It is possible that some of the studies may have had issues related to “confounding by indication,” as it is likely that sexually active girls may potentially be more likely to seek HPV vaccine. There was considerable variation in the age groups examined among studies. For instance, some studies restricted analysis to younger girls who were less likely to already have been sexually active. Other studies failed to specify whether there were age differences between vaccinated and unvaccinated groups. In addition, the review was restricted to include only female participants and did not examine this question among male participants. The studies included in the review varied in terms of demographic characteristics

(i.e., school, university students, female adolescents, and adults), thus results should not be generalized to all populations. Finally, it is possible that some studies with non-significant findings may not have been accepted for publication, which might lead to publication bias, as data from those studies may not be available for review.

### Conclusions

This systematic review did not find evidence to support the hypothesis that HPV vaccination is associated with risk compensation or sexual disinhibition. Given this, the positive benefits of vaccinating young girls against HPV infection are clear and compelling. The availability of HPV vaccines provides an opportunity to decrease the burden of cervical and anogenital cancers and their precursors. The evidence that HPV immunization will not lead to increased risk behavior is overwhelming; it is important to consider increasing efforts in how to best deliver the vaccine in the most effective manner by having a communication strategy that is more focused on HPV vaccination as a cancer prevention vaccine and highlighting the benefits and possible risks associated with it.

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PM had full access to all the data in the review and takes responsibility for the integrity of the data and the accuracy of the review. PM and DP-V were responsible for study concept and design. KK, DP-V, and PM drafted the manuscript. All authors were responsible for acquisition, analysis, or interpretation of data; administrative, technical, or material support; and final approval of the manuscript.

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## Appendix

### Supplementary data

Supplementary data associated with this article can be found at <http://dx.doi.org/10.1016/j.amepre.2016.03.015>.