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Practice- and Community-Based Interventions to Increase Human Papillomavirus Vaccine Coverage:

A Systematic Review

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Abstract

IMPORTANCE—Vaccines against human papillomavirus (HPV) are recommended for routine use in adolescents aged 11 to 12 years in the United States, but uptake remains suboptimal. Educational interventions focused on parents and patients to increase coverage have not generally demonstrated effectiveness.

OBJECTIVE—To systematically review the literature on effectiveness of interventions conducted at the practice or community level to increase uptake of HPV vaccines in the United States.

EVIDENCE REVIEW—Keyword searches of the PubMed, Web of Science, and MEDLINE databases identified studies of adolescents that included the outcome of HPV vaccination published through July 2014. References of identified articles were also reviewed. A total of 366 records were screened, 38 full-text articles were reviewed, and 14 published studies were included. Results were summarized by different intervention approaches.

FINDINGS—Practice- and community-based intervention approaches included reminder and recall (n = 7), physician-focused interventions (eg, audit and feedback) (n = 6), school-based

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programs (n = 2), and social marketing (n = 2) (2 interventions tested multiple approaches). Seven studies used a randomized design, and 8 used quasiexperimental approaches (one used both). Thirteen studies included girls, and 2 studies included boys. Studies were conducted in a variety of populations and geographic locations. Twelve studies reported significant increases in at least one HPV vaccination outcome, one reported a nonsignificant increase, and one reported mixed effects.

CONCLUSIONS AND RELEVANCE—Most practice- and community-based interventions significantly increased HPV vaccination rates using varied approaches across diverse populations. This finding is in stark contrast to a recent review that did not find effects to warrant widespread implementation for any educational intervention. To address the current suboptimal rates of HPV vaccination in the United States, future efforts should focus on programs that can be implemented within health care settings, such as reminder and recall strategies and physician-focused efforts, as well as the use of alternative community-based locations, such as schools.

Human papillomavirus (HPV) is the most common sexually transmitted infection in the United States. There were an estimated 79 million prevalent cases in 2008, and up to 80% of individuals acquire HPV at some point during their lifetime, including 50% from their first sexual partner.¹⁻³ Human papillomavirus infections disproportionately affect younger compared with older women, with prevalence estimates of 27% to 45% among women aged 18 to 25 years.⁴⁻⁶ Many infections are asymptomatic and transient, but persistent infection can result in several cancers (cervical, anal, vaginal, vulvar, penile, and oropharyngeal) and genital warts.

Prevention of HPV infections and related diseases is now possible with 2 vaccines that are currently available in the United States. Both the bivalent HPV2 vaccine (Cervarix) and the quadrivalent HPV4 vaccine (Gardasil) prevent infection with HPV-16 and HPV-18, which cause 70% of invasive cervical cancers.^{7,8} The HPV4 vaccine also prevents infection with HPV-6 and HPV-11, which cause more than 90% of genital warts.⁸ Routine vaccination is recommended for adolescent girls and boys aged 11 to 12 years in a 3-dose series over 6 months, and catch-up vaccination is recommended through the age of 26 years for girls and the age of 21 years for boys.^{9,10} The HPV4 vaccine, used most frequently in the United States, has proven high safety and efficacy of 98% against high-grade cervical lesions associated with HPV-16 and HPV-18 when given before exposure,^{11,12} and a previous review¹³ found evidence of an early effect on HPV infections, warts, and cervical lesions. However, uptake remains suboptimal: in 2013, only 37.6% of girls and 13.9% of boys had received all 3 recommended doses; initiation with at least one dose was 57.3% for girls and 34.6% for boys.¹² Coverage is substantially lower than for other adolescent vaccines (85% for diphtheria and tetanus toxoids and a cellular pertussis [Tdap] and 74% for the meningococcal conjugate vaccine [MCV4])¹⁴ and lags behind other industrialized nations, such as Australia, Denmark, and England, which have all achieved greater than 70% coverage with 3 doses of HPV vaccine.¹⁵⁻¹⁷

A recent systematic review¹⁸ summarized the evidence that educational interventions increase HPV vaccination acceptance. A total of 33 studies with parents and adolescents or young adults were included. These interventions typically sought to improve parents' or adolescents' understanding of HPV vaccines to promote improved attitudes, intentions, and

behaviors related to HPV vaccination, but only a few of those observed improved HPV vaccine uptake. The authors concluded that well-designed and adequately powered studies were rare and generally did not demonstrate effectiveness. No clearly superior intervention was identified that could be recommended for widespread implementation at this time.

Clearly, alternative approaches to increase HPV vaccination are urgently needed. A smaller but increasing body of evidence is emerging about noneducational interventions to promote HPV vaccination. The purpose of this article is to systematically review this literature to assess the effectiveness of practice- and community-based interventions (as opposed to individual-level interventions) for increasing HPV vaccine coverage. Results can be used to identify priority areas for future programs and research that seek to increase and understand HPV vaccination among adolescents so that we may realize the full prevention potential of HPV vaccines.

At a Glance

- Human papillomavirus vaccine coverage in the United States remains suboptimal.
- There is insufficient evidence from educational interventions to warrant widespread implementation at this time.
- In contrast, most practice- and community-level programs, including reminder/recall, physician-focused interventions, school-based programs, and social marketing efforts, significantly increased human papillomavirus vaccination rates among adolescents.
- Although the scientific rigor of the interventions included in this review varies, the relative consistency of findings across diverse populations is promising.

Methods

Our primary search was conducted using the PubMed database and the following keywords in titles or abstracts: *HPV* or *human papillomavirus*, *vaccine* or *vaccination*, and *intervention* or *randomized*. We subsequently reviewed the references of retrieved and other relevant articles (eg, reviews). We used the same search terms in Web of Science and MEDLINE databases to identify any additional eligible articles. Databases were searched through July 2014. The inclusion criteria below were first applied to titles and abstracts and then to full-text articles to determine final inclusion status.

Inclusion criteria included the following: (1) conducted in the United States, (2) focused on adolescents 18 years and younger, (3) reported an outcome of actual HPV vaccination rates, and (4) included a comparison group. We included interventions that used both randomized and nonrandomized designs. Studies that examined only intentions or attitudes, only included young adults 18 years and older, were development or feasibility studies, or were only published as conference abstracts were excluded.

A standardized form was created to extract relevant study characteristics and used for all studies by both authors independently. Subsequent joint review by the authors was conducted to resolve discrepancies and achieve consensus regarding the accuracy of data extraction. Articles were described systematically, but formal meta-analysis was not performed because of heterogeneity across studies in outcomes measures. Outcomes that were considered were improved vaccine uptake using a variety of measures, including initiation, completion, being up to date, timeliness, and/or receiving at least one dose. Other outcomes, such as costs or process measures, are not described in this review.

Results

Our search resulted in the identification of 14 relevant articles that met our inclusion criteria (Figure 1).^{19–32} Characteristics are summarized in eTable 1 in the Supplement. Physician- and community-based interventions used a variety of approaches, including reminder and recall systems (n = 7), physician-focused interventions (n = 7), school-based programs (n = 2), and social marketing (n = 2). Four studies^{20–22,24} used more than one approach, and many studies^{19–22,24,25,31,32} (n = 8) used multiple strategies within or across approaches. Seven interventions^{19,23,25,28,30–32} were not specific for HPV vaccine and included other vaccines recommended for adolescents, including Tdap, MCV4, and/or influenza. Seven studies^{19, 23–25, 30–32} used a randomized design, and 8 studies^{19–22,26–29} used quasiexperimental designs (one used both designs for different components). Thirteen studies^{19–21,23–32} included girls, and 2 studies^{22,27} included boys; findings specific to boys were reported in 1 study.²² The ages of children in the studies ranged from 9 through 20 years and typically focused on 11- to 17-year-olds or students in fifth through eighth grades. Five studies^{20–23,25} focused exclusively or reported separately on younger adolescents (aged 13 years). Interventions were tested in a range of populations, including privately insured populations, publicly or underinsured populations, and a mix of patient demographics. A wide range of geographic locations was represented, including the Northeast (eg, New York), the Southeast (eg, North Carolina), and the Midwest (eg, Colorado and Illinois), and interventions in urban, suburban, and rural settings were each represented. A forest plot of intervention results is presented in Figure 2, and a summary of the specific intervention descriptions and findings is presented in eTable 2 in the Supplement.

Reminder and Recall Systems

The most common approach to increasing vaccination rates included reminder and recall systems that were evaluated in 7 studies,^{20,24,26,27,30–32} including 4 studies^{24,30–32} that used randomized designs. All 7 of these interventions revealed significant increases in at least one HPV vaccination outcome. Recall and reminder strategies included telephone calls, mailed letters, text messages, and/or outreach visits. In one study,³⁰ participants who were randomized to receive up to 2 mailed letters and 2 telephone calls had higher rates of initiation (11%) compared with usual care (4%). In another study,³¹ a tiered system that provided telephone, mail, and outreach with home visits revealed significantly higher rates of initiation compared with usual care (59% vs 43%). Another study³² revealed that both mail and telephone reminders resulted in significantly higher immunization rates for HPV vaccination initiation (27% for both) compared with usual care (21%). An additional

intervention that included a reminder and recall component tested physician-and family-focused arms (separately and combined), with the family-focused component including automated telephone reminders.²⁴ In this study, those who received the family-focused intervention only had higher rates of first, second, and third HPV doses (18%, 71%, and 73%, respectively) compared with no intervention (16%, 65%, and 63%, respectively), with the difference in receipt of each dose being statistically significant. The 3 quasiexperimental studies^{20,26,27} also revealed improvements in HPV vaccination: 2 through reminder text messages for the second and third doses after the first had been received and 1 through electronic alerts to prompt telephone calls.

Physician-Focused Interventions

Seven interventions included a focus on physicians and used various strategies, including education and training (n = 6),^{20–22,24,25,28} audit and feedback (n = 4),^{19,24,25,28} and/or electronic decision support or alerts (n = 2),^{19,24} with several studies^{19,24,25,28} using more than one strategy. Two programs evaluated the Centers for Disease Control and Prevention's AFIX (Assessment, Feedback, Incentives, and eXchange) approach.^{25,28} Three physician-focused interventions used a randomized design (one of these also included a quasi-experimental arm). In the combined physician- and family-focused intervention previously described, the physician intervention was multifaceted and included electronic decision support and alerts, audit and feedback, and education.²⁴ In this study, those who received the physician-focused intervention only had higher rates of first and third HPV doses among those eligible (24% and 67%, respectively) compared with no intervention (16% and 63%, respectively), with the difference in receipt of the first dose being statistically significant. Another randomized physician-focused intervention used the audit and feedback approach and found a nonsignificant increase in timeliness of HPV vaccination (27% increase).¹⁹ Finally, evaluation of the AFIX approach that provided in-person or webinar consultations to vaccine coordinators in primary care clinics revealed significant short-term gains in coverage for the HPV vaccine among 11- to 12-year-olds but not among 13- to 18-year-olds.²⁵ Of the 5 programs that used quasiexperimental designs (pre-post analysis), 3 found increases in HPV vaccination rates,^{20,22,28} 1 did not observe an increase,¹⁹ and 1 intervention had mixed results.²¹

School-Based Programs

The 2 programs^{23,29} that took place in schools evaluated vaccination clinics; one²³ was a randomized clinical trial. This intervention evaluated school-located adolescent vaccination clinics at 7 schools held on 3 days throughout the year that billed health insurance compared with 7 control schools.²³ Parental consent was required to participate. They reported significant increases in female students receiving at least one dose among sixth graders (34% vs 18%) and seventh and eighth graders (20% vs 7%). The nonrandomized study²⁹ evaluated extramural, school-located, HPV vaccination clinics offered in four 1-day sessions and was conducted in partnership with local health departments. Investigators reported a significant difference in female students initiating HPV vaccination in 6 host schools compared with 15 nonhost (satellite) schools (6% vs 1%).

Social Marketing Approaches

Two studies,^{21,22} both conducted in North Carolina, evaluated social marketing approaches using quasiexperimental designs; one study was targeted to girls²¹ and one to boys.²² Although similar to educational interventions in their goals to address parents' perceptions and awareness of benefits and barriers, these interventions were distinct in that their approach was targeted to communities and not delivered at the individual level. The first pilot intervention, initiated by county health departments and conducted in 2009, targeted mothers of adolescent girls in 4 primarily rural counties and included posters and brochures in local retail establishments, a web-site, a hotline, news releases during a 3-month period, and outreach to health care practices for provision of materials and guidance.²¹ The proportion of unvaccinated girls who initiated the series in the 6 months after the campaign was higher in 2 intervention counties (7% in both) and lower in 2 intervention counties (3% and 2%) compared with other counties in the region and the state (5.0% in both). A similar intervention focused on boys was initiated in 2012 and included public service announcements, a continuing medical education webinar, tip sheets for physicians, and a website.²² Vaccination rates increased by 34% in intervention counties compared with control counties.

Discussion

This review of 14 interventions conducted at the practice or community level to increase HPV vaccine coverage found statistically significant increases in at least one HPV vaccination outcome in 12 studies, a nonsignificant increase in 1 study, and mixed effects in 1 study. These results were achieved using a variety of approaches, including reminder and recall systems, physician-focused strategies (eg, audit and feedback), school-located programs, and social marketing. They were also observed across a broad range of populations, including lower- and higher-income participants, and in several different regions of the United States. These findings speak to the potential of these broader systems-based approaches that are based in practices or communities (rather than individually focused educational approaches¹⁸) to achieve higher coverage with safe and effective HPV vaccines. Although accurate knowledge and positive attitudes are likely to be important for uptake, they may not be sufficient. Practice and community programs that alter the structure of vaccination programs or the environments in which they are provided may be necessary to close the gap between current and optimal levels of HPV vaccination coverage.

Previous research has found that reminder and recall, audit and feedback, and school-located vaccination clinics have significantly improved immunization rates for other vaccines.^{33–35} Although it may not be surprising that these approaches also improve HPV immunization rates, it is important to note that HPV vaccine may be viewed differently from other recommended vaccines for adolescents. Although the Tdap and MCV4 vaccines are often required for school enrollment, this requirement is rarely the case for the HPV vaccine.³⁶ This difference may result in physicians presenting HPV vaccination as optional or of lower priority,³⁷ and parents may be more likely to opt out of vaccinating their children. Therefore, interventions that train and encourage physicians to present strong and consistent recommendations to all age-eligible patients will be important. The HPV vaccine also differs

from the Tdap and MCV4 vaccines in that it is recommended to be administered in 3 doses over 6 months. Although the first dose may be given at a well-child visit, additional health care visits needed to complete the series may be difficult for some families to arrange.³⁸ Reminder and recall and school-located programs are well suited to address associated challenges, including remembering to schedule or follow up HPV vaccination completion visits and access issues related to transportation and missing work or school.

Although the results of this review are encouraging about the possibilities of increasing HPV vaccine coverage, several challenges remain. Approaches vary in the resources that are required to implement them, and both absolute costs and cost-effectiveness are important considerations. Although vaccine cost is usually covered by private insurance or the federal Vaccines for Children program for low-income families, most interventions require additional resources. Programs included in this review that evaluated costs reported a range of \$6 to \$714 for vaccination administration per additional adolescent vaccinated with many programs in the lower end of that range.^{23,24,30–32} Certain strategies are inherently less expensive than others, such as webinars for physicians as opposed to in-person visits and text messages as an alternative to telephone or e-mail reminders, and could be implemented when resources are constrained. Challenges that are unique to school-based programs include the need for cooperation from school officials; concerns about potential fragmentation of care, including communication with parents and linking immunization records; and methods for billing.³⁹ One promising approach is to use school-based health centers that provide a range of primary care services. We are aware of one school-based health center program in the United States that used a reminder and recall approach to improve HPV immunization rates.⁴⁰ Although this study was not included in our review because it did not have a comparison group, the program was effective in vaccinating a substantial proportion (59%) of girls who needed at least one dose of HPV vaccine. A recent review⁴¹ identified school-based programs in 17 countries and concluded that they achieved high HPV vaccination coverage rates in young girls across different studies and locations. Requirements for HPV vaccination for school enrollment are another option, although few have been enacted to date.³⁶

In addition to these challenges, several important questions also remain. First, although most interventions reveal statistically significant increases in HPV vaccination coverage for at least one out-come, some effects sizes were modest, some increases were not sustained over time, and some HPV vaccination outcomes did not improve.^{24,25,28,32} Therefore, although change is possible, the clinical relevance of some of these results may be less certain. Increasing our understanding of which intervention components work, for which outcomes, and in what settings and target populations will be important in future research. Furthermore, small effects in research studies may have large effects at the population level if programs are widely and effectively disseminated, so this focus is an important future direction. Second, although many programs included technological components, such as automated decision support, text reminders for parents, or webinars, other technological innovations remain untested. For example, the use of social media, mHealth (eg, applications for mobile devices), and text reminders for teens could be effective and useful interventions to include and evaluate in future programs. Third, only 2 interventions included boys, and few focused on younger adolescents at the target ages for routine vaccination (11 and 12

years of age). Limited focus to date on vaccinating boys could be due to the later recommendations for routine vaccination in boys (in 2011) than for girls (in 2006). It is less clear why limited attention has been directed to younger adolescents. Although low rates among the 11- to 12-year-old population necessitate important efforts to vaccinate in the catch-up age ranges, it is also important to emphasize and promote vaccination at the recommended ages to increase the likelihood that vaccination will precede exposure. Other vaccines that are routinely recommended for this age group further support focusing on this age group. Identifying approaches that are most effective for the target population of 11- to 12-year-old boys and girls will be particularly important.

Unfortunately, the existing published intervention studies did not allow for a quantitative meta-analysis. Another consideration in the interpretation of this review is the variable quality of the included studies. To be as comprehensive as possible and aid in the wide dissemination of findings, we did not exclude any study on the basis of quality. As can be seen in eTable 2 in the Supplement, study designs and sample sizes varied considerably. Although many studies were scientifically rigorous (eg, randomized designs and large sample sizes), a number of studies also used nonrandomized designs,^{19–22,26–29} historical controls,^{20,26,27} or a small number of participants in the intervention group.^{19,20,26} Original sources may be consulted to consider the strength of the evidence in planning for future interventions, programs, and research. Despite these limitations, each article contributed unique evidence and knowledge to our understanding of the potential usefulness of various interventions.

Conclusions

This review indicates that interventions at the practice and community levels can be implemented successfully and increase HPV immunization rates. The choice of a particular strategy may depend on considerations, such as financial and logistical challenges. Future research should explore how best to widely disseminate and sustain programs that work and evaluate the effectiveness of alternative untested strategies using rigorous and high-quality research methods.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Satterwhite CL, Torrone E, Meites E, et al. Sexually transmitted infections among US women and men: prevalence and incidence estimates, 2008. *Sex Transm Dis.* 2013; 40(3):187–193. [PubMed: 23403598]
2. Syrjänen K, Hakama M, Saarikoski S, et al. Prevalence, incidence, and estimated life-time risk of cervical human papillomavirus infections in a nonselected Finnish female population. *Sex Transm Dis.* 1990; 17(1):15–19. [PubMed: 2154865]

3. Winer RL, Lee SK, Hughes JP, Adam DE, Kiviat NB, Koutsky LA. Genital human papillomavirus infection: incidence and risk factors in a cohort of female university students. *Am J Epidemiol*. 2003; 157(3):218–226. [PubMed: 12543621]
4. Dunne EF, Unger ER, Sternberg M, et al. Prevalence of HPV infection among females in the United States. *JAMA*. 2007; 297(8):813–819. [PubMed: 17327523]
5. Manhart LE, Holmes KK, Koutsky LA, et al. Human papillomavirus infection among sexually active young women in the United States: Implications for developing a vaccination strategy. *Sex Transm Dis*. 2006; 33(8):502–508. [PubMed: 16572039]
6. Hariri S, Unger ER, Sternberg M, et al. Prevalence of genital human papillomavirus among females in the United States, the National Health and Nutrition Examination Survey, 2003–2006. *J Infect Dis*. 2011; 204(4):566–573. [PubMed: 21791659]
7. Muñoz N, Bosch FX, de Sanjosé S, et al. International Agency for Research on Cancer Multicenter Cervical Cancer Study Group. Epidemiologic classification of human papillomavirus types associated with cervical cancer. *N Engl J Med*. 2003; 348(6):518–527. [PubMed: 12571259]
8. Forman D, de Martel C, Lacey CJ, et al. Global burden of human papillomavirus and related diseases. *Vaccine*. 2012; 30(suppl 5):F12–F23. [PubMed: 23199955]
9. Centers for Disease Control and Prevention (CDC). FDA licensure of bivalent human papillomavirus vaccine (HPV2, Cervarix) for use in females and updated HPV vaccination recommendations from the Advisory Committee on Immunization Practices (ACIP). *MMWR Morb Mortal Wkly Rep*. 2010; 59(20):626–629. [PubMed: 20508593]
10. Centers for Disease Control and Prevention (CDC). Recommendations on the use of quadrivalent human papillomavirus vaccine in males—Advisory Committee on Immunization Practices (ACIP), 2011. *MMWR Morb Mortal Wkly Rep*. 2011; 60(50):1705–1708. [PubMed: 22189893]
11. Schiller JT, Castellsagué X, Garland SM. A review of clinical trials of human papillomavirus prophylactic vaccines. *Vaccine*. 2012; 30(suppl 5):F123–F138. [PubMed: 23199956]
12. Stokley S, Jeyarajah J, Yankey D, et al. Immunization Services Division, National Center for Immunization and Respiratory Diseases, CDC; Centers for Disease Control and Prevention (CDC). Human papillomavirus vaccination coverage among adolescents, 2007–2013, and postlicensure vaccine safety monitoring, 2006–2014—United States. *MMWR Morb Mortal Wkly Rep*. 2014; 63(29):620–624. [PubMed: 25055185]
13. Hariri S, Markowitz LE, Dunne EF, Unger ER. Population impact of HPV vaccines: summary of early evidence. *J Adolesc Health*. 2013; 53(6):679–682. [PubMed: 24263069]
14. Centers for Disease Control and Prevention (CDC). National and state vaccination coverage among adolescents aged 13–17 years—United States, 2012. *MMWR Morb Mortal Wkly Rep*. 2013; 62(34):685–693. [PubMed: 23985496]
15. Gertig DM, Brotherton JM, Saville M. Measuring human papillomavirus (HPV) vaccination coverage and the role of the National HPV Vaccination Program Register, Australia. *Sex Health*. 2011; 8(2):171–178. [PubMed: 21592430]
16. Baandrup L, Blomberg M, Dehlendorff C, Sand C, Andersen KK, Kjaer SK. Significant decrease in the incidence of genital warts in young Danish women after implementation of a national human papillomavirus vaccination program. *Sex Transm Dis*. 2013; 40(2):130–135. [PubMed: 23324976]
17. Public Health England. [Accessed January 11, 2014] Annual HPV vaccine coverage in England: 2012–13. http://www.gov.uk/government/uploads/system/uploads/attachment_data/file/266207/HPV_AnnualDataTable2012_13_AT_acc5.pdf
18. Fu LY, Bonhomme L-A, Cooper SC, Joseph JG, Zimet GD. Educational interventions to increase HPV vaccination acceptance: a systematic review. *Vaccine*. 2014; 32(17):1901–1920. [PubMed: 24530401]
19. Bundy DG, Persing NM, Solomon BS, et al. Improving immunization delivery using an electronic health record: the ImmProve project. *Acad Pediatr*. 2013; 13(5):458–465. [PubMed: 23726754]
20. Cassidy B, Braxter B, Charron-Prochownik D, Schlenk EA. A quality improvement initiative to increase HPV vaccine rates using an educational and reminder strategy with parents of preteen girls. *J Pediatr Health Care*. 2014; 28(2):155–164. [PubMed: 23522561]

21. Cates JR, Shafer A, Diehl SJ, Deal AM. Evaluating a county-sponsored social marketing campaign to increase mothers' initiation of HPV vaccine for their pre-teen daughters in a primarily rural area. *Soc Mar Q.* 2011; 17(1):4–26. [PubMed: 21804767]
22. Cates JR, Diehl SJ, Crandell JL, Coyne-Beasley T. Intervention effects from a social marketing campaign to promote HPV vaccination in preteen boys. *Vaccine.* 2014; 32(33):4171–4178. [PubMed: 24886960]
23. Daley MF, Kempe A, Pyrzanowski J, et al. School-located vaccination of adolescents with insurance billing: cost, reimbursement, and vaccination outcomes. *J Adolesc Health.* 2014; 54(3): 282–288. [PubMed: 24560036]
24. Fiks AG, Grundmeier RW, Mayne S, et al. Effectiveness of decision support for families, clinicians, or both on HPV vaccine receipt. *Pediatrics.* 2013; 131(6):1114–1124. [PubMed: 23650297]
25. Gilkey MB, Dayton AM, Moss JL, et al. Increasing provision of adolescent vaccines in primary care: a randomized controlled trial. *Pediatrics.* 2014; 134(2):e346–e353. [PubMed: 25002671]
26. Kharbanda EO, Stockwell MS, Fox HW, Andres R, Lara M, Rickert VI. Text message reminders to promote human papillomavirus vaccination. *Vaccine.* 2011; 29(14):2537–2541. [PubMed: 21300094]
27. Matheson EC, Derouin A, Gagliano M, Thompson JA, Blood-Siegfried J. Increasing HPV vaccination series completion rates via text message reminders. *J Pediatr Health Care.* 2014; 28(4):e35–e39. [PubMed: 24200295]
28. Moss JL, Reiter PL, Dayton A, Brewer NT. Increasing adolescent immunization by webinar: a brief provider intervention at federally qualified health centers. *Vaccine.* 2012; 30(33):4960–4963. [PubMed: 22652406]
29. Stubbs BW, Panozzo CA, Moss JL, Reiter PL, Whitesell DH, Brewer NT. Evaluation of an intervention providing HPV vaccine in schools. *Am J Health Behav.* 2014; 38(1):92–102. [PubMed: 24034684]
30. Suh CA, Saville A, Daley MF, et al. Effectiveness and net cost of reminder/recall for adolescent immunizations. *Pediatrics.* 2012; 129(6):e1437–e1445. [PubMed: 22566415]
31. Szilagyi PG, Humiston SG, Gallivan S, Albertin C, Sandler M, Blumkin A. Effectiveness of a citywide patient immunization navigator program on improving adolescent immunizations and preventive care visit rates. *Arch Pediatr Adolesc Med.* 2011; 165(6):547–553. [PubMed: 21646588]
32. Szilagyi PG, Albertin C, Humiston SG, et al. A randomized trial of the effect of centralized reminder/recall on immunizations and preventive care visits for adolescents. *Acad Pediatr.* 2013; 13(3):204–213. [PubMed: 23510607]
33. Szilagyi PG, Bordley C, Vann JC, et al. Effect of patient reminder/recall interventions on immunization rates: a review. *JAMA.* 2000; 284(14):1820–1827. [PubMed: 11025835]
34. Bordley WC, Chelminski A, Margolis PA, Kraus R, Szilagyi PG, Vann JJ. The effect of audit and feedback on immunization delivery: a systematic review. *Am J Prev Med.* 2000; 18(4):343–350. [PubMed: 10788739]
35. Pannaraj PS, Wang H-L, Rivas H, et al. School-located influenza vaccination decreases laboratory-confirmed influenza and improves school attendance. *Clin Infect Dis.* 2014; 59(3):325–332. [PubMed: 24829215]
36. National Conference of States Legislatures. [Accessed September 3, 2014] HPV vaccine policies: introduced legislation. 2013–2014. <http://www.ncsl.org/research/health/hpv-vaccine-state-legislation-and-statutes.aspx#2013-2014>
37. Perkins RB, Clark JA, Apte G, et al. Missed opportunities for HPV vaccination in adolescent girls: a qualitative study. *Pediatrics.* 2014; 134(3):e666–e674. [PubMed: 25136036]
38. Rand CM, Szilagyi PG, Albertin C, Auinger P. Additional health care visits needed among adolescents for human papillomavirus vaccine delivery within medical homes: a national study. *Pediatrics.* 2007; 120(3):461–466. [PubMed: 17766516]
39. Caskey RN, Macario E, Johnson DC, Hamlish T, Alexander KA. A school-located vaccination adolescent pilot initiative in Chicago: lessons learned. *J Pediatr Infect Dis Soc.* 2013; 2(3):198–204.

40. Kempe A, Barrow J, Stokley S, et al. Effectiveness and cost of immunization recall at school-based health centers. *Pediatrics*. 2012; 129(6):e1446–e1452. [PubMed: 22566414]
41. Paul P, Fabio A. Literature review of HPV vaccine delivery strategies: considerations for school- and non-school based immunization program. *Vaccine*. 2014; 32(3):320–326. [PubMed: 24295804]

Figure 1.

Flow Diagram (Preferred Reporting Items for Systematic Review and Meta-Analyses) of Articles Considered for Inclusion

HPV indicates human papillomavirus.

Randomized designs

Bundy et al¹⁹ (audit/feedback)^a
 Daley et al²³ (HPV-1, sixth graders)
 Daley et al²³ (HPV-1, seventh and eighth graders)
 Daley et al²³ (HPV-3, sixth graders)^{b,c}
 Daley et al²³ (HPV-3, seventh and eighth graders)
 Fiks et al²⁴ (HPV-1)^d
 Fiks et al²⁴ (HPV-2)^d
 Fiks et al²⁴ (HPV-3)^d
 Gilkey et al^{25,e}
 Suh et al³⁰ (HPV-3 for HPV-0 at baseline)^b
 Suh et al³⁰ (HPV 1/2 at baseline)^b
 Szilagyi et al³¹ (HPV-1)
 Szilagyi et al³¹ (HPV-2)
 Szilagyi et al³¹ (HPV-3)
 Szilagyi et al³² (HPV-1, mail)
 Szilagyi et al³² (HPV-2, mail)
 Szilagyi et al³² (HPV-3, mail)
 Szilagyi et al³² (HPV-1, phone)
 Szilagyi et al³² (HPV-2, phone)
 Szilagyi et al³² (HPV-3, phone)

Nonrandomized designs

Bundy et al¹⁹ (CDS)^a
 Cassidy et al²⁰ (HPV-1)^f
 Cassidy et al²⁰ (HPV-3)^f
 Cates et al²¹ (county 1)^{b,g}
 Cates et al²¹ (county 2)^{b,g}
 Cates et al²¹ (county 3)^{b,g}
 Cates et al²¹ (county 4)^{b,g}
 Cates et al²² (9-13 years)^b
 Cates et al²² (11-12 years)^b
 Kharbands et al²⁶ (on-time receipt)^h
 Kharbands et al²⁶ (within 4 months)^{b,h}
 Matheson et al²⁷ (HPV-2)^{b,i}
 Matheson et al²⁷ (HPV-3)^{b,i}
 Moss et al²⁸ (HPV-1)^b
 Moss et al²⁸ (HPV-2)^b
 Moss et al²⁸ (HPV-3)^b
 Stubbs et al²⁹ ^j

Figure 2.

Forest Plot of Intervention Results

The text, eTable 1 and eTable 2 in the Supplement, and original sources provide additional study details. Blue squares are estimates presented in the original source article; orange squares are estimates calculated by review authors based on data presented in the original source article. Size of squares is proportional to the study sample size: small squares, fewer than 250 patients; medium squares, 250 through 999 patients; and large squares, 1000 or more patients. Multiple estimates presented from single studies are noted by author name. Error bars indicate 95% CIs. CDS indicates clinical decision support.

^aSample size is not reported. Estimates for nonrandomized clinical trials are not reported but are described as “did not improve” for 13-year-olds and “rate of increase slowed” among 14-year-olds, and both were nonsignificant.

^bEstimate is significant at $P < .05$ when no 95% CIs were reported.

^cEffect estimate is reported as 6.6 and is not represented on the graph because it is beyond the range used for graphic presentation ($n = 1000$).

^dEstimates for combined intervention (physician and family) compared with the control condition.

^eEstimates in the article are presented as difference (not ratio) measures and are not included on the plot. Differences for human papillomavirus 1 (HPV-1) were significant at $P < .05$ for the 11- to 12-year-old group but not the 13- to 18-year-old group, and differences in HPV-3 were significant at $P < .05$ for the 13- to 18-year-old group but not the 11- to 12-year-old group.

^fEffect estimates of 9.4 (95% CI, 2.6–33.1) for HPV-1 and 22.5 (95% CI, 4.3–118.0) are not represented on the graph because they are beyond the range used for graphic presentation (n = 250).

^gComparison group is regional counties (not state).

^hComparison group is opt-out condition.

ⁱComparison group is standard of care condition.

^jEffect estimate is reported as 6.56 (95% CI, 3.99–10.78) and is not represented on the graph because it is beyond the range used for graphic presentation (n = 1000).