American Journal of
Preventive Medicine

REVIEW ARTICLE

Human Papillomavirus Vaccine Interventions in the U.S.: A Systematic Review and Meta-analysis

Ana M. Rodriguez, MD, MPH,[1,2] Thuy Quynh N. Do, PhD, MPH,[3] Michael Goodman, MD, MPH,[4] Kathleen M. Schmeler, MD,[5] Sapna Kaul, PhD,[3] Yong-Fang Kuo, PhD[3]

Context: Despite current recommendations, human papillomavirus vaccine uptake remains low. A systematic review and meta-analysis assessed the effectiveness of interventions targeting human papillomavirus vaccine initiation and completion among children, adolescents, and young adults aged 9–26 years.

Evidence acquisition: Three electronic databases (CINAHL, OVID, and Web of Science) were searched for articles published in English peer-reviewed journals between January 2006 and January 2017 of U.S. studies that evaluated intervention strategies and reported post-intervention human papillomavirus vaccine initiation or completion rates among individuals aged 9–26 years. Study characteristics and outcomes were extracted. Data were collected in 2016 and analyzed in 2017.

Evidence synthesis: Reviewers screened 983 unique titles and abstracts, read 241 full-text articles, and extracted data from 30 articles meeting the inclusion criteria (12 behavioral, ten environmental, four informational, and four combination strategies). Published EQUATOR (Enhancing the Quality and Transparency of Health Research) guidelines were used to assess study quality. Random effects meta-analyses were conducted. The meta-analyses included 17 RCTs and quasi-experiments involving 68,623 children, adolescents, and young adults. The pooled relative incidence estimates were 1.84 (95% CI=1.36, 2.48) for human papillomavirus vaccine initiation and 1.50 (95% CI=1.23, 1.83) for completion. Behavioral and informational interventions doubled human papillomavirus vaccine initiation (relative incidence estimate=2.04, 95% CI=1.36, 3.06 and relative incidence estimate=1.92, 95% CI=1.27, 2.91, respectively). Behavioral interventions increased completion by 68% (relative incidence estimate=1.68, 95% CI=1.25, 2.27).

Conclusions: Evidence supports behavioral interventions for increasing human papillomavirus vaccine initiation and completion. Future studies are needed to assess the effectiveness of interventions in reaching diverse populations and reducing missed opportunities for human papillomavirus vaccination.

Am J Prev Med 2019;56(4):591–602. *© 2018 American Journal of Preventive Medicine. Published by Elsevier Inc. All rights reserved.*

CONTEXT

Vaccinations are an effective primary prevention strategy for decreasing or eradicating infectious diseases. Human papillomavirus (HPV) is the most common sexually transmitted infection in the U.S.[1] and persistent HPV infection is strongly associated with the risk of HPV-related diseases. HPV infections can be prevented by completing the HPV vaccine series prior to sexual activity.[2–4] The vaccine is recommended for prevention of cervical, oropharyngeal, vulvar,

From the [1]Department of Obstetrics and Gynecology, University of Texas Medical Branch at Galveston, Galveston, Texas; [2]Sealy Institute for Vaccine Sciences, University of Texas Medical Branch at Galveston, Galveston, Texas; [3]Department of Preventive Medicine and Community Health, University of Texas Medical Branch at Galveston, Galveston, Texas; [4]Department of Epidemiology, Emory University, Atlanta, Georgia; and [5]Department of Gynecologic Oncology and Reproductive Medicine, University of Texas MD Anderson Cancer Center, Houston, Texas

Address correspondence to: Ana M. Rodriguez, MD, MPH, Department of Obstetrics and Gynecology, The University of Texas Medical Branch at Galveston, 301 University Boulevard, Galveston TX 77555.
E-mail: an3rodri@utmb.edu.

0749-3797/$36.00
https://doi.org/10.1016/j.amepre.2018.10.033

© 2018 American Journal of Preventive Medicine. Published by Elsevier Inc. All rights reserved.

vaginal, penile, and anal cancer, as well as anogenital warts.[5–13] The *Healthy People 2020* goal is to have 80% of adolescents aged 13–15 years fully vaccinated against HPV.[14] Despite these recommendations and its record of safety and efficacy,[15,16] HPV vaccine completion rates in 2016 for U.S. girls and boys aged 13–17 years were 43.0% and 31.5%, respectively.[17,18]

Current guidelines from the U.S. Centers for Disease Control and Prevention (CDC) recommend routine HPV vaccination for girls and boys aged 11 or 12 years. HPV vaccinations are recommended for females aged 9–26 years and males aged 9–21 years.[11,19] It is also recommended for males up to age 26 years who were not adequately vaccinated previously, as well as those who are gay, bisexual, other men who have sex with men, transgender, and immunocompromised (including those with HIV).[19] The HPV vaccine recommendation is supported by the American Academy of Pediatrics,[20] National Cancer Institute,[21] CDC,[11,19] the American College of Obstetricians and Gynecologists,[22] and the National Association of School Nurses.[23] Three different HPV vaccines are currently approved and recommended.[11] In October 2016, CDC reduced the recommended dosing schedule for those initiating before age 15 years to two doses given at least 6 months apart.[19] For those initiating on or after their 15th birthday and those with certain immunocompromising conditions, three doses are recommended.[19] Immunizing younger adolescents (aged 10–15 years) results in an increased immune response (higher anti-HPV-type-specific response) compared with individuals aged 16–23 years.[24] The vaccine is not effective against existing infection or precancerous lesions.[4]

Specific interventions have been designed to address poor HPV vaccination rates. Recent systematic reviews have shown mixed results.[15,25–27] Walling et al.[15] reviewed international and national interventions published between January 2006 and April 2015 that increased HPV vaccinations among those aged 11–26 years. Although informational interventions improved HPV vaccination rates during the active intervention period, the effect was not sustained.[15] Behavioral interventions demonstrated varying effectiveness, inconsistent results, and required significant effort, depending on the intervention.[15] Niccolai and colleagues[26] reviewed practice- and community-based interventions published through July 2014. Fu et al.[25] reviewed educational intervention studies and concluded that no specific intervention warranted widespread implementation. Because post-intervention vaccination rates were not consistently reported, improvements in HPV uptake are difficult to assess.[25,28] Other systematic reviews and meta-analyses have focused on factors affecting HPV vaccine uptake or acceptability (i.e., barriers and facilitators, knowledge, and parental attitudes).[29–35] Few studies have included males[36,37] and individuals of younger ages.[38–40] Currently, no superior intervention strategies have been identified for widespread implementation, nor has enough time passed to assess the October 2016 dosing recommendations.[25,26] This study's objective is to perform a systematic review and meta-analysis to assess the effectiveness of intervention strategies aimed at increasing HPV vaccine initiation and completion among U.S. children, adolescents, and young adults aged 9–26 years.

EVIDENCE ACQUISITION

Search Strategies

This review was conducted according to the PRISMA guidelines.[41] It addresses the broad research question: What interventions have successfully increased HPV vaccine initiation or completion in males and females aged 9–26 years? A systematic literature search was conducted by the lead author and a professional librarian using the CINAHL, Medline Ovid, and Web of Science databases to identify relevant articles published in English between January 1, 2006, and January 31, 2017. The earliest publication year was chosen to identify intervention studies that appeared in press after the HPV vaccine was licensed in 2006. The search used the following combination of terms: *human papillomavirus* OR *HPV* OR *human papillomavirus* AND (*vaccine* OR *vaccination* OR *immunization* OR *vaccinate)* including Medical Subject Headings (MeSH) terms whenever available. Titles, abstracts, and articles were independently reviewed by AMR and TQD for inclusion, and disagreements were settled by consensus. Bibliographies of selected articles were scanned for additional articles not captured by the electronic search.

Inclusion and Exclusion Criteria

Studies were included if they (1) assessed vaccine outcomes for any individual or subgroups of individuals aged 9–26 years recommended to receive the HPV vaccine, (2) reported HPV vaccine initiation or completion rates after intervention, and (3) included an intervention strategy (behavioral, environmental, or informational) and a comparison group. The comparison group either received a different intervention, no intervention, or one of lower intensity, such as usual care. The definitions used for the intervention strategies were similar to those proposed by Walling and colleagues.[15] A behavioral strategy changes behavior by providing necessary skills to make a decision regarding initiation or completion of HPV vaccination.[15] Specifically, behavioral interventions target decision support (e.g., message framing, peer or expert education video, evidence-based pamphlet) and use healthcare system alerts or patient prompts (i.e., text messages, e-mail, mailed correspondence, and phone calls) as the intervention or a component of the intervention to change behavior. Behavioral interventions were categorized as decision support, reminders, or combination of reminders and decision support targeting individuals eligible for the vaccine (vaccine-eligible individuals), parents, or healthcare providers. An environmental strategy does not necessarily affect individual behavior, but rather changes the social environment to facilitate vaccination (e.g., via decreased financial barriers

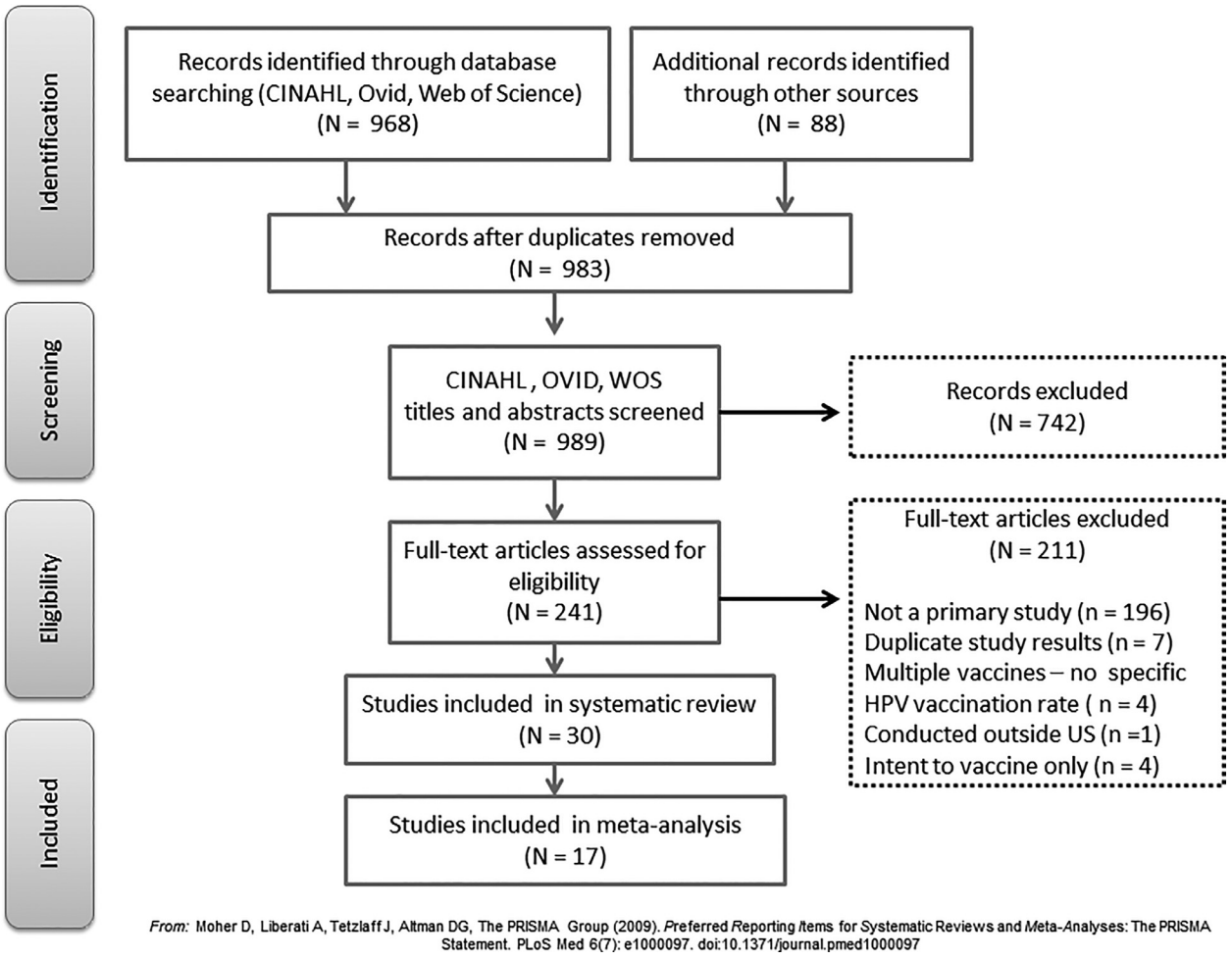

Figure 1. Selection of intervention studies for increasing HPV uptake based on the PRISMA flow diagram, 2006–2017.
Note: The search used the following combination of terms: *human papillomavirus* OR *HPV* OR *human papillomavirus* AND (*vaccine* OR *vaccination* OR *immunization* OR *vaccinate)*, including Medical Subject Headings terms (whenever available).
HPV, human papillomavirus.

[no cost/reduced cost vouchers] or novel vaccination sites [e.g., schools]). An informational strategy increased awareness and knowledge of HPV, HPV-related disease, or the HPV vaccine, but it does not specifically target decision making or influence social environment. It is important to point out that interventions not meeting the definition of a purely behavioral, environmental, or informational strategy were characterized as combined (i.e., incorporating more than two elements of different strategies).

Only peer-reviewed articles with post-intervention rates were included. Studies were excluded if they were (1) duplicated in the literature, (2) non-English articles, (3) conducted outside the U.S., (4) focused on intent to vaccinate, (5) without a vaccine strategy or complete evaluation of the HPV vaccine intervention (no post-intervention HPV vaccination rate), (6) not primary studies (i.e., literature reviews, systematic reviews, letters, guidelines, case reports, case series, dissertations or theses, editorials, or commentaries), and (7) abstract-only articles or conference presentations without full-text articles. If an article assessed multiple vaccinations and did not report the HPV vaccination rate separately, it was included.

The search in CINAHL, Medline Ovid, and Web of Science returned 1,056 items, of which 983 unique articles were screened (Figure 1). Among the 983 potentially relevant articles, 742 articles were excluded after screening titles and abstracts and applying the exclusion criteria. From the 241 full-text articles reviewed, 30 articles met the inclusion criteria (Figure 1).[36–40,42–66]

Data Collection and Quality Assessment

A standardized form was created to extract relevant study characteristics, including data source, first author, publication year, target population, level of evidence (Level I: RCT or quasi-experimental, or Level II: cohort study), study design, sample size, study period, location and setting, intervention, inclusion/exclusion criteria, potential confounders, and outcome (HPV vaccine initiation or completion). AMR and TQD independently extracted the data, and forms were reviewed jointly to achieve consensus. Article quality was independently evaluated by three reviewers using the EQUATOR (Enhancing the Quality and Transparency

of Health Research) reporting guidelines.[67] STROBE[68] and CONSORT[69] were used to assess a minimum set of information for reporting observational studies and randomized trials. STROBE, a 22-item checklist, was used to assess observational studies (case control and cohort), and CONSORT, a 25-item checklist, was used to assess clinical trials.

Data Analysis

The review was conducted in 2017. To determine the effectiveness of intervention strategies, HPV vaccine initiation and completion rates were calculated or abstracted from each article. Once the data were compiled, studies were categorized according to the outcome of interest (initiation or completion), target population (children aged 9–12 years, adolescents aged 13–17 years, young adults aged 18–26 years), and intervention strategy (behavioral, environmental, or informational). The meta-analysis included studies if (1) a control group was included and (2) they represented independent data (i.e., not derived from the same or overlapping cohorts). When two or more studies were based on the same cohort, the study with multiple interventions or target populations (i.e., males versus females) was selected. For the meta-analysis, the RR and 95% CIs were calculated for each study using OpenEpi online statistical software, version 3.01.[70] RR refers to the ratio of those who initiated or completed the HPV vaccine. The pooled relative incidence estimates (RIE) and the corresponding 95% CIs were calculated with random effects models. A random effects meta-analysis model assumes that observed estimates of the intervention effect vary across studies because of differences in the intervention effect in each study as well as sampling variability (chance).[71] Heterogeneity was assessed using I^2 and the Cochran Q statistic. Statistical tests for asymmetry were determined using funnel plots and accompanied by the Egger test. All meta-analyses were performed using Stata, version 11.2.

EVIDENCE SYNTHESIS

Description of the Literature

Table 1 provides a descriptive summary of the 30 systematic review articles.[36–40,42–66] Appendix Tables 1 and 2 (available online) provide detailed information on each article. Articles varied in study design, outcome, strategy, setting, geographic location, and target population. There were 14 RCTs,[36,39,40,42,48,50,52,53,55–57,59,62,66] 13 cohort studies,[37,38,43,44,46,47,49,54,58,61,63–65] and three quasi-experimental studies.[45,51,60] Most of the studies met the STROBE and CONSORT guidelines (Appendix Table 1, available online). Except for two studies that lacked method elements, most observational studies met the elements of the STROBE checklist. The RCTs were of excellent (nine studies with 20 or more of the 25 CONSORT elements) or very good quality (five studies with 17.5–19 of the elements).

The 30 articles included 12 behavioral,[37,39,40,46,50–53,55,56,59,60] ten environmental,[36,43,44,47–49,54,61,63,65] four informational,[38,42,58,62] and four combination strategies[45,57,64,66] (Table 1, Appendix Table 2, available online).

Table 1. Summary of Articles Included in the Systematic Review of HPV Vaccine Interventions, 2006–2017 (n=30)

Characteristic	Number of studies
Study design	
RCT[36,39,40,42,48,50,52,53,55–57,59,62,66]	14
Quasi-experimental[45,51,60]	3
Cohort[37,38,43,44,46,47,49,54,58,61,63-65]	13
Intervention strategy	
Behavioral[37,39,40,46,50–53,55,56,59,60]	12
Environmental[36,43,44,47–49,54,61,63,65]	10
Informational[38,42,58,62]	4
Combination[45,57,64,66]	4
Gender	
Male[36,37]	2
Female[38–40,42–45,47,50–56,58,61,63,65]	19
Male and female[46,48,49,57,59,60,62,64,66]	9
Age groups	
All ages (9–26 years)[39,40,43,57]	4
Children (9–12 years)[45]	1
Adolescents (13–17 years)[53,64]	2
Children and adolescents (9–17 years)[37,38,46,48–50,60–62,66]	10
Young adults (18–26 years)[36,42,44,47,51,52,54–56,58,59,63,65]	13
Outcome	
Initiation[37–39,44,46,48,51,52,55,60,61,63]	12
Completion[40,49,56,57,59,66]	6
Both[36,42,43,45,47,50,53,54,58,62,64,65]	12
Included other vaccines[48,66]	2
Intervention target	
Individuals[36,40,42–44,47–49,51–56,58–66]	23
Parents[37–39,45,53,62]	6
Providers[46]	1
Providers and family[50,57]	2
Sample size	
<250[36,37,45,49,51,53,54,58,63,65]	10
≥250[38–40,42–44,47,48,50,52,55–57,59–62,64,66]	19
Not provided[46]	1
Setting[a]	
Clinics[36,37,39,44–47,50,53–58,60,63,66]	17
University/college[36,42,47,52,54,55,59]	7
Schools[38,48,49,61,62,64]	6
Other[b] [40,43,51,65]	4

[a]Four studies recruited participants from both clinics and universities/colleges.
[b]Other includes postpartum unit, managed care, and community setting.
HPV, human papillomavirus.

Twelve articles examined both HPV vaccine initiation and completion,[36,42,43,45,47,50,53,54,58,62,64,65] and 18 examined either initiation (n=12)[37–39,44,46,48,51,52,55,60,61,63] or completion (n=6).[40,49,56,57,59,66] Two articles included other vaccines.[48,66] Most of the articles targeted individuals

(*n*=23),[36,40,42–44,47–49,51–56,58–66] included females only (*n*=19),[38–40,42–45,47,50–56,58,61,63,65] occurred in the clinic (*n*=17),[36,37,39,44–47,50,53–58,60,63,66] and had sample sizes of 250 or more people (*n*=19[38–40,42–44,47,48,50,52,55–57,59–62,64,66]; Table 1). Nine articles targeted males and females,[46,48,49,57,59,60,62,64,66] and two targeted males.[36,37] Four articles targeted all ages (9–26 years),[39,40,43,57] 13 targeted young adults,[36,42,44,47,51,52,54–56,58,59,63,65] and 13 targeted children and adolescents (mostly between ages 11 and 17 years[37,38,45,46,48–50,53,60–62,64,66]; Table 1).

Behavioral Strategies

Behavioral strategies[37,39,40,46,50–53,55,56,59,60] used reminder/recall systems or decision support to target vaccine-eligible individuals,[40,51–53,55,56,59,60] parents,[37,39,50,53] and providers.[46,50] There were eight RCTs,[39,40,50,52,53,55,56,59] two cohort studies,[37,46] and two quasi-experimental studies.[51,60] Interventions included postcards, reminder calls, texts, letters, postcards, in-clinic health information technology reminder or recall system, and decision support materials (educational messaging/video).

Behavioral interventions demonstrated varying effectiveness from increasing HPV uptake in seven studies[39,40,46,50–52,60] to little or no effect in five studies.[37,53,55,56,59] In a countywide intervention centered on immunization registry–driven recall and postcard reminders, the first dose improved for children aged 11–12 years for both boys (overall change, 14%–32%) and girls (27%–43%), but completion improved only for boys aged 13–18 years.[46] Compared with controls (no intervention), HPV vaccine initiation was the highest among children and adolescents aged 11–17 years who received the combined health information technology and postcard intervention (girls OR=2.4, boys OR=1.6) followed by the system-level postcard campaign (girls OR=1.6, boys OR=1.1 [not significant]) and the health information technology reminder system (girls OR=1.5, boys OR=1.4).[60] Vaccination rates were significantly higher among female university students who were shown peer- and expert-narrated HPV vaccine education videos (decision support) compared with controls (no video; 21.8% vs 11.8%).[52] Completion rates were higher among Kaiser Permanente members who received a reminder letter compared with controls (no reminder; 56% vs 47%).[40] Among adolescent girls whose parents opted to receive up to three text message reminders, on-time receipt of the next dose was higher than those who did not receive text reminders (52% vs 35%).[39] Another study included a reminder and recall component with physician- and family-focused arms (separately and combined), and a family-focused component (automated telephone reminders).[50] Those who received the combined intervention had higher vaccination rates compared with no intervention (Dose 1: 23% vs 16%, Dose 2: 73% vs 65%, and Dose 3: 76% vs 63%, respectively).[50]

Five studies showed little or no effect on HPV vaccination.[37,53,55,56,59] An intervention targeting boys aged 11–15 years tested messaging in a school-based health center and increased intent to vaccinate, but found little effect on vaccine behavior.[37] Rates were not significantly different for subsequent doses among those receiving text/e-mail appointment reminders and education messages compared with controls (no intervention; Dose 2: 53% vs 52%, Dose 3: 34% vs 32%).[59] Completion rates did not improve for participants who chose their preferred reminder (text, e-mail, phone, private Facebook message, or standard mail; 17.2% vs 18.9%) compared with routine follow-up.[56] HPV vaccine uptake was low (5.5%) among those randomized to receive HPV-specific education with a mailed reminder compared with standard care.[55] Joseph et al.[53] evaluated the impact of a client-centered behavioral intervention (Brief Negotiated Interviewing) on mothers' HPV vaccine knowledge and HPV vaccine initiation for their adolescent daughters, and found increased HPV knowledge among the intervention group than the controls, but nonsignificant differences in vaccination rates between groups.

Environmental Strategies

Environmental strategies[36,43,44,47–49,54,61,63,65] took place in health clinics,[36,44,47,54,63] postpartum units,[43,65] schools,[48,49,61,63] and universities/community colleges.[36,47,54] Although convenient (i.e., location, no cost, timing), uptake was relatively low among some of the studies (≅40%).[44,47,54] Two studies offered the HPV vaccine post partum (shortly after delivery) and scheduled vaccinations with postpartum visits.[43,65] One study reported 41.3% (62/150) received Dose 1 post partum and 30.7% (46/150) completed the series.[65] Another study reported 661 patients receiving vaccines post partum (Dose 1: 575, Dose 2 or 3: 86).[43] Location was important among college-aged females, with higher uptake among the clinic recruits than the community college (45% vs 7%, respectively).[44] Uptake of the next dose was also greatest for women recruited from clinics than colleges.[47] A college setting was effective in vaccinating young adult males, with completion higher using an alternative dosing schedule than standard dosing schedule (0, 2, 12 months vs 0, 6, 12 months).[36]

School-based HPV immunization programs may be a viable approach to improving vaccination initiation and completion rates among children/adolescents.[48,49,61,63,64] The programs often involve a partnership between a

local school system and the health department.[49,61,64] At school-located vaccination clinics in Denver, Colorado (intervention), more females received at least one dose (OR=2.56, 95% CI=1.34, 4.88) than controls (no school-located vaccination clinics).[48] During a "vaccine blitz" at a Michigan middle school, 67 doses were provided by a team of medical students, public health students, and school-based health center staff after a brief educational exercise, distribution of educational materials, and written/verbal consent.[49] More females initiated vaccination at host schools (middle schools hosting four 1-day clinics) than satellite schools (schools whose students could receive the HPV vaccine at host school clinics) (6% vs 1%).[61] Through a school-based vaccination program, 70% of HPV vaccine-naïve high school students initiated and 62% completed the three-dose series (88% who initiated successfully completed the series).[64]

Informational Strategies

Four studies used informational strategies[38,42,58,62] comprising two RCTs[42,62] and two cohort studies.[38,58] The strategies included education (e.g., exercises, audit and feedback, video intervention, peer/medical narrative), educational websites tailored to baseline knowledge, and brochures/factsheets to increase awareness and knowledge of HPV vaccine and HPV. Informational strategies produced mixed results in increasing HPV uptake. Effects on HPV-related knowledge, intention to vaccinate, and HPV vaccine initiation were similar among females receiving a non-tailored CDC factsheet (control) and females randomized to an online educational tool (intervention: website individually tailored to baseline survey responses).[42] Two studies increased vaccine uptake by targeting HPV knowledge and beliefs and using constructs from the Health Belief Model,[38,58] which posits that messages achieve optimal behavior change if perceived barriers, benefits, self-efficacy, and threats are successfully targeted.[72] In a three-arm RCT, two educational interventions were used to increase vaccination for four recommended vaccines: tetanus, diphtheria, acellular pertussis; measles-containing vaccine-4; HPV; and influenza.[62] Parents in the two intervention arms who received educational materials to improve their knowledge and attitude toward HPV vaccination were less likely to report HPV vaccination compared with the control group who received no educational materials.[62] Positive attitude and beliefs about the HPV vaccine were consistent predictors for receipt of the HPV vaccine.[38,58,62]

Combination of Intervention Strategies

Studies using a combination of intervention strategies with active feedback were effective in improving HPV vaccine uptake.[45,57,64,66] In a quasi-experimental study, parents of eligible girls aged 11–12 years who received an educational brochure based on predictors of parental acceptance and Health Belief Model constructs (informational strategy) and telephone reminders (behavioral strategy) were more likely to initiate and complete the HPV vaccine compared with historical controls not receiving the intervention (OR=9.4 and OR=22.5, respectively).[45] Another intervention targeted providers and used repeated contacts, education, individualized feedback, and strong quality improvement incentives to increase HPV uptake.[57] Boys and girls at the intervention health centers were more likely to initiate and complete their next HPV dose than control practices (girls OR=1.6, boys OR=11 vs girls OR=1.4, boys OR=23, respectively).[57] Improvements in HPV uptake were sustained in the post-intervention/maintenance period (girls OR=1.6, boys OR=25, respectively).[57] Guided by evidence- and practice-based strategies, one study involved multiple components (educational materials, informational booth, reminder calls, and school-based vaccination program) to improve HPV vaccination and reduce known barriers (70% initiated, 62% completed).[64] Compared with standard care (telephone and phone reminders), a tiered patient immunization intervention escalating from phone and letter reminders to home visits and preventive care visits significantly increased HPV initiation (59% vs 43%) and completion (37% vs 24%) among girls aged 11–15 years.[66]

Meta-analysis

Table 2 presents the meta-analysis results (15 RCTs and two quasi-experimental studies) involving 68,623 children, adolescents, and young adults.[36,39,40,42,45,48,50,52,53,55–57,59,60,62,63,66] Figures 2A and 2B are forest plots of estimates for HPV vaccine initiation and completion studies. A subset analysis for high-quality RCTs (articles with quality score >20) was 1.73 (95% CI=1.02, 2.94) for HPV vaccine initiation and 1.77 (95% CI=0.99, 3.16) for HPV vaccine completion. The pooled effect of the high-quality RCTs estimates that the mean initiation rate in the intervention group increased by 73% and 77% for completion.

For HPV vaccine initiation, the meta-analysis included 11 studies (nine RCTs and two quasi-experimental studies) with 14 RIEs.[36,42,45,48,50,52,53,55,57,60,62] Three articles had two RIEs because of multiple intervention groups (i.e., females/males[57,60] or female adolescents/parents).[62] The overall pooled RIE for HPV vaccine initiation was 1.84 (95% CI=1.36, 2.48; Table 2 and Figure 2A). The mean initiation increased by 84% for the intervention. There was a high level of between-study heterogeneity with an I^2 of 90.9% and Cochran Q test $p<0.0001$. The funnel plot (Appendix Figure 1,

Table 2. Summary of Meta-analysis Performed to Increase HPV Uptake Among Children, Adolescents, and Young Adults, 2006–2017

Variable	Number of studies/ number of RIEs	Test for overall effect		Heterogeneity, I^2, %
		RIE (95% CI)	*p*-value	
HPV vaccine initiation[36,42,45,48,50,52,53,55,57,60,62]	**11/14**	**1.84 (1.36, 2.48)**	**0.0001**	**90.9**
Intervention strategy				
Behavioral	10/10	2.04 (1.36, 3.06)	**0.001**	90.0
Environmental	2/2	1.48 (0.56, 3.92)	0.432	88.2
Informational	3/4	1.92 (1.27, 2.91)	**0.002**	78.9
Gender				
Both	2/2	2.10 (1.83, 2.40)	**0.0001**	0.0
Female	9/9	1.60 (1.23, 2.08)	**0.001**	70.6
Male	3/3	2.48 (0.61, 10.05)	0.204	98.0
Age groups				
All	2/2	2.52 (0.63, 10.12)	0.192	97.0
Children/adolescents	6/8	1.88 (1.49, 2.37)	**0.0001**	73.2
Young adults	3/3	1.09 (0.74, 1.63)	0.163	44.8
Study type and quality				
High-quality RCT (>20)	6/7	1.73 (1.02, 2.94)	**0.043**	94.4
HPV vaccine completion[36,39,40,42,45,50,53,56,57,59,62,63,66]	**13/15**	**1.50 (1.23, 1.83)**	**0.0001**	**93.4**
Intervention strategy				
Behavioral	10/11	1.68 (1.25, 2.27)	**0.001**	93.9
Environmental	2/2	1.03 (0.82, 1.30)	0.792	78.7
Informational	3/4	1.65 (0.90, 3.02)	0.103	69.8
Gender				
Both	3/3	1.25 (0.94, 1.66)	0.132	84.5
Female	9/9	1.30 (1.08, 1.56)	**0.006**	73.2
Male	2/2	4.51 (0.19, 108.33)	0.354	99.3
Age groups				
All	2/2	1.14 (1.08, 1.20)	**0.0001**	0.0
Preadolescents/adolescents	8/10	1.94 (1.40, 2.68)	**0.0001**	94.3
Young adults	3/3	0.92 (0.78, 1.09)	0.863	0.0
Study type and quality				
High-quality RCT (>20)	6/7	1.77 (0.99, 3.16)	0.054	96.2

Note: Boldface indicates statistical significance ($p<0.05$).
HPV, human papillomavirus; RIE, relative incidence estimate.

available online) demonstrated the results were generally symmetric with one evident outlier. When removing the outlier (results not shown), the pooled RIE decreased to 1.60 (95% CI=1.27, 2.01) and I^2 decreased to 70.5%. The subgroup analyses show behavioral and informational intervention strategies were effective in increasing HPV vaccine initiation with RIE of 2.04 (95% CI=1.36, 3.06) and 1.92 (95% CI=1.27, 2.91), respectively (Table 2).

For HPV vaccine completion, the meta-analysis included 13 articles (11 RCTs, one quasi-experimental, and one cohort) providing 15 RIEs.[36,39,40,42,45,50,53,56,57,59,62,63,66] Two articles had two RIEs because of multiple intervention groups (i.e., females/males[57] or female adolescents/parents).[62] The overall pooled RIE for HPV vaccine completion was 1.50 (95% CI=1.23, 1.83), an increase of 50% (Table 2 and Figure 2B). There was a high level of between-study heterogeneity with an I^2 of 93.4% and Cochran Q test $p<0.0001$. The funnel plot (Appendix Figure 2, available online) demonstrated the results were generally symmetric with one evident outlier. When removing the outlier (results not shown), the effect was lowered (RIE=1.19, 95% CI=1.04, 1.35) and the I^2 decreased to 78.6%. When limiting to studies involving informational and behavioral interventions for HPV vaccine completion, RIE was similar (1.65 vs 1.68; Table 2).

DISCUSSION

This systematic review summarizes 30 published studies over the 11-year period since the HPV vaccine was

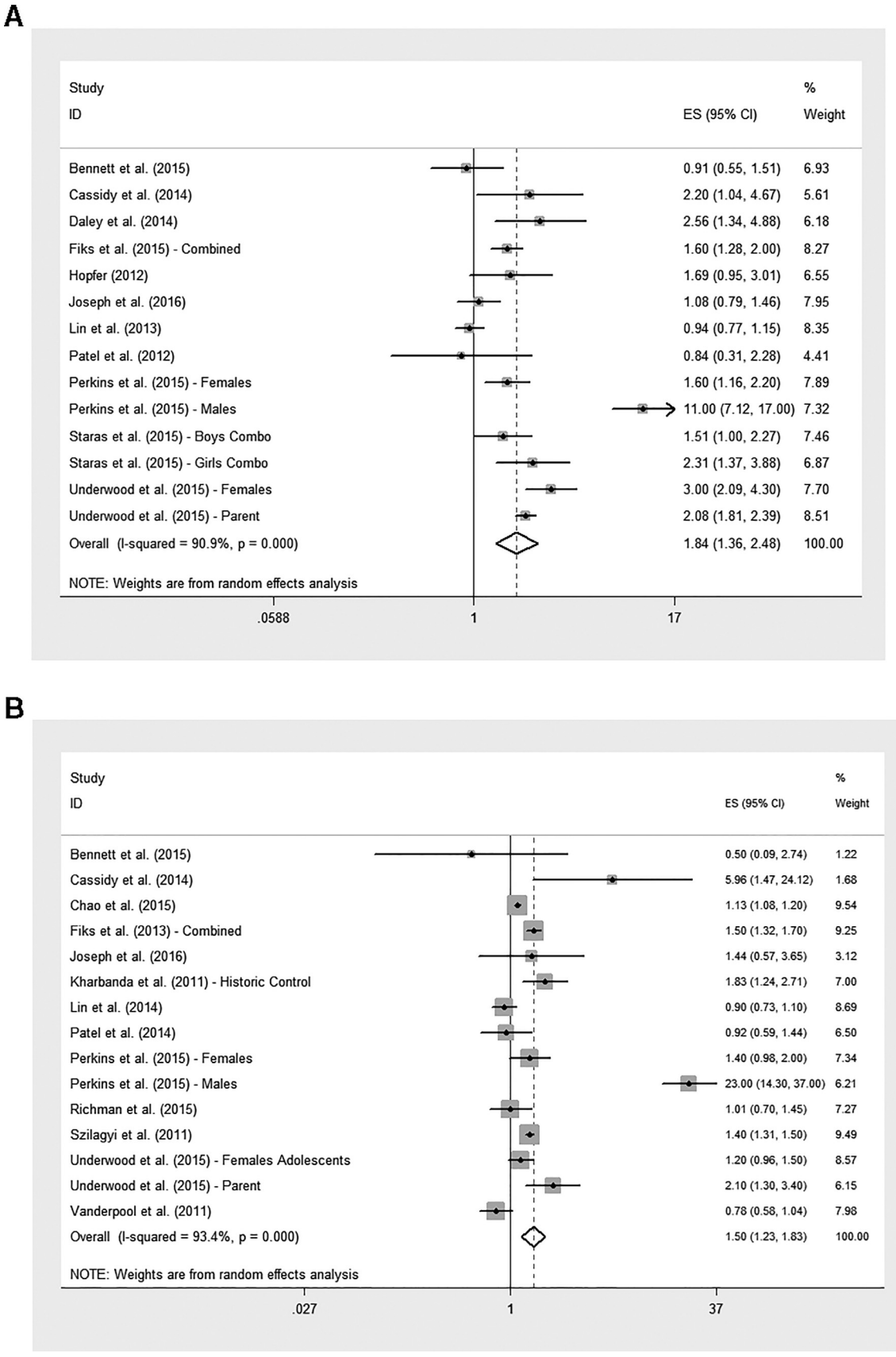

Figure 2. Forest plot of relative risks for HPV vaccination (2A) initiation and (2B) completion among children, adolescents, and young adults.
HPV, human papillomavirus.

approved.[36–40,42–66] It provides evidence supporting specific interventions to increase HPV uptake among targeted groups. Various approaches were used, including reminder/recall systems, informational videos, targeted population strategies, and novel sites (schools, universities, and postpartum units). This review adds to the literature, incorporating more recent articles,[42,43,46,49,51,53,59,60,62,64] articles not previously included,[36,38,44,55,58,65] novel sites (post partum,[43,65] schools,[48,49,61,63] universities/community colleges.[36,47,54]), all ages (9–26 years including younger than 11 years[38–40]), and both sexes.[46,48,49,57,59,60,64,66] Previous reviews assessed educational interventions,[25] community and practice setting interventions,[26] and older ages (11–26 years),[15,25,26] and included international studies,[15] which may not be applicable in the U.S. Consistent with Walling and colleagues,[15] this study included all intervention types (behavioral, environmental, informational, and combined).

The meta-analyses indicated that behavioral (RIE=2.04, 95% CI=1.36, 3.06) and informational strategies (RIE=1.92, 95% CI=1.27, 2.91) were effective for HPV vaccine initiation. Behavioral strategies effectively increased completion by 68% (RIE=1.68, 95% CI=1.25, 2.27). Research has shown that accurate knowledge and positive attitudes and beliefs towards the HPV vaccine are important predictors for acceptance and receipt of the HPV vaccine.[38,42,58,62] Informational strategies may influence the intent to vaccinate by increasing HPV-related knowledge and awareness, but the effect on HPV vaccine behavior is minimal.[37,53] The most effective strategy to change vaccination behavior is multifaceted[26,39,40,46,50–52,60,64–66]—create positive attitudes and beliefs about the HPV vaccine and its benefits,[38,42,58,62] improve access, and use prompts/reminders.

Consistent with Walling et al.,[15] behavioral interventions demonstrated varying effectiveness and inconsistent results. This review shows reminders without active feedback were not effective and revealed similar results to those receiving usual care (fact sheet).[37,53,55,56,59] HPV vaccination rates improved if reminders were used in combination with recall systems, incentives, or education.[26,39,40,46,50–52,60,64–66] Provider-focused interventions were effective for increasing provider recommendation and support for initiation, whereas family-focused interventions increased support for completion.[38,50] Peer endorsement was important for changing vaccine behavior among young women.[52] School-based vaccination clinics improved HPV vaccine uptake[48,49,61,63] by improving access to the HPV vaccine, convenience, and the ability to reach a large, diverse population. Initiation was higher among students attending schools hosting vaccine clinics (host schools) than students from surrounding schools (satellite schools).[61] Adolescents initiating the vaccine in host schools were more likely to complete the series than those from surrounding schools. Adolescents in surrounding schools dealt with extra travel distance, unfamiliarity with host schools, and lack of visibility of the vaccination clinics.[61]

Limitations

Although the results are encouraging, several challenges remain in assessing interventions. First, findings are limited by shortcomings of the available literature. At the time of this review, new studies/publications have not been published to assess the impact of the new two-dose schedule. This schedule reduces the number of doses needed for completion for children younger than 15 years. Although all ages and sexes were included in the search (especially those younger than 11 years and males), the number of studies was limited. Most studies included adults (18–26 years) and focused on females. Second, the included studies varied in design and quality. Although a meta-analysis was originally proposed to combine findings from several studies to produce an overall summary estimate, interpretation of this estimate presents a challenge because of heterogeneity of methods and results. Despite these concerns, this meta-analysis may still offer useful information about patterns of reported results depending on the types of research questions and study methods.[73–75] Next, not many studies used environmental and informational strategies, resulting in low precision of meta-estimates. Last, no cultural appropriateness was assessed. Most studies did not include race/ethnicity and SES data, making it difficult to explain how specific populations respond to certain interventions. Given the disparities in HPV-related diseases, it is important to understand the relationship between demographics and vaccine behavior. Despite these limitations, each article contributed unique evidence and knowledge about the potential usefulness of various interventions.

CONCLUSIONS

Continued efforts are needed to improve HPV vaccine uptake among U.S. adolescents. The findings of this review support behavioral and informational interventions for HPV vaccine initiation and behavioral interventions for completion. Given the association between individual knowledge, attitudes, and beliefs, and HPV acceptance and initiation, future studies should focus on culturally appropriate interventions to reach a more diverse population. To reduce HPV-associated morbidity and mortality, more effective interventions should target diverse populations (especially males), younger

ages, and under-immunized populations (Hispanics), as well as overlooked opportunities for HPV vaccination.

ACKNOWLEDGMENTS

We would like to thank the medical librarian at the University of Texas Medical Branch, Tara Atkins, for her assistance developing the search criteria and identifying articles for review. We would also like to thank Iris Tijerina and Carolyn Martin for helping with the quality assessment.

The content is solely the responsibility of the authors and does not necessarily represent the official views of NIH or the Cancer Prevention Institute of Texas.

This study was conducted with the support of the Institute for Translational Sciences at the University of Texas Medical Branch, supported in part by a Clinical and Translational Science Award (UL1 TR001439) from the National Center for Advancing Translational Sciences, NIH. In addition, AMR also received grant funding from The Cancer Prevention Research Institute of Texas (CPRIT; grant number PP160097). Neither NIH nor CPRIT have roles in the development of this article (i.e., in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the paper for publication).

All authors (AMR, TQD, MG, KMS, SK, and YFK) participated in the concept and design, writing, interpretation of results, revisions, and gave final approval of the manuscript. AMR and TQD conducted the systematic review and meta-analysis and completed the data extraction. AMR, TQD, MG, and YFK conducted the data analysis.

No financial disclosures were reported by the authors of this paper.

SUPPLEMENTAL MATERIAL

Supplemental materials associated with this article can be found in the online version at https://doi.org/10.1016/j.amepre.2018.10.033.

REFERENCES

1. Braaten KP, Laufer MR. Human papillomavirus (HPV), HPV-related disease, and the HPV vaccine. *Rev Obstet Gynecol.* 2008;1(1):2–10.
2. Hilton S, Hunt K, Bedford H, Petticrew M. School nurses' experiences of delivering the UK HPV vaccination programme in its first year. *BMC Infect Dis.* 2011;11:226. https://doi.org/10.1186/1471-2334-11-226.
3. Bosch X, Harper D. Prevention strategies of cervical cancer in the HPV vaccine era. *Gynecol Oncol.* 2006;103(1):21–24. https://doi.org/10.1016/j.ygyno.2006.07.019.
4. CDC. HPV Vaccine Information for Young Women. www.cdc.gov/std/hpv/stdfact-hpv-vaccine-young-women.htm. Published January 3, 2017. Accessed 2017.
5. Dochez C, Bogers JJ, Verhelst R, Rees H. HPV vaccines to prevent cervical cancer and genital warts: an update. *Vaccine.* 2014;32(14):1595–1601. https://doi.org/10.1016/j.vaccine.2013.10.081.
6. Schiffman M, Wentzensen N, Wacholder S, Kinney W, Gage JC, Castle PE. Human papillomavirus testing in the prevention of cervical cancer. *J Natl Cancer Inst.* 2011;103(5):368–383. https://doi.org/10.1093/jnci/djq562.
7. Thomas TL, Strickland O, Diclemente R, Higgins M. An opportunity for cancer prevention during preadolescence and adolescence: stopping human papillomavirus (HPV)-related cancer through HPV vaccination. *J Adolesc Health.* 2013;52(5 suppl):S60–S68. https://doi.org/10.1016/j.jadohealth.2012.08.011.
8. Walboomers JM, Jacobs MV, Manos MM, et al. Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. *J Pathol.* 1999;189(1):12–19. https://doi.org/10.1002/(SICI)1096-9896(199909)189:1≤12::AID-PATH431≥3.0.CO;2-F.
9. CDC. Basic Information about HPV-associated cancers. www.cdc.gov/cancer/hpv/basic_info. Published September 5, 2013. Accessed August 24, 2014.
10. CDC. HPV-Associated Cancers Statistics. www.cdc.gov/cancer/hpv/statistics/index.htm. Published 2014. Accessed April 2, 2018.
11. Petrosky E, Bocchini JA Jr., Hariri S, et al. Use of 9-valent human papillomavirus (HPV) vaccine: updated HPV vaccination recommendations of the Advisory Committee on Immunization Practices. *MMWR Morb Mortal Wkly Rep.* 2015;64(11):300–304.
12. Markowitz LE, Dunne EF, Saraiya M, et al. Human papillomavirus vaccination: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2014;63(RR-05):1–30.
13. Shah PD, Gilkey MB, Pepper JK, Gottlieb SL, Brewer NT. Promising alternative settings for HPV vaccination of U.S. adolescents. *Expert Rev Vaccines.* 2014;13(2):235–246. https://doi.org/10.1586/14760584.2013.871204.
14. Office of Disease Prevention and Health Promotion, Immunization and Infectious Diseases. *Healthy People 2020.* www.healthypeople.gov/2020/topics-objectives/topic/immunization-and-infectious-diseases/objectives. Accessed April 24, 2018.
15. Walling EB, Benzoni N, Dornfeld J, et al. Interventions to improve HPV vaccine uptake: a systematic review. *Pediatrics.* 2016;138(1):e20153863. https://doi.org/10.1542/peds.2015-3863.
16. The FUTURE I/II Study Group. Four year efficacy of prophylactic human papillomavirus quadrivalent vaccine against low grade cervical, vulvar, and vaginal intraepithelial neoplasia and anogenital warts: randomised controlled trial. *BMJ.* 2010;341:c3493. https://doi.org/10.1136/bmj.c3493.
17. Reagan-Steiner S, Yankey D, Jeyarajah J, et al. National, regional, state, and selected local area vaccination coverage among adolescents aged 13–17 years—United States, 2014. *MMWR Morb Mortal Wkly Rep.* 2015;64(29):784–792. https://doi.org/10.15585/mmwr.mm6429a3.
18. HHS. Accelerating HPV Vaccine Uptake: Urgency for Action to Prevent Cancer. Washington, DC: HHS, 2014.
19. CDC. Clinician FAQ: CDC Recommendations for HPV Vaccine 2-Dose Schedules. www.cdc.gov/hpv/downloads/hcvg15-ptt-hpv-2dose.pdf. Published November 30, 2016. Accessed 2018.
20. Committee on Infectious Diseases. HPV vaccine recommendations. *Pediatrics.* 2012;129(3):602–605. https://doi.org/10.1542/peds.2011-3865.
21. National Cancer Institute. Preventing cervical cancer: the development of HPV vaccines. www.cancer.gov/research/progress/discovery/hpv-vaccines. Published December 2, 2016. Accessed 2018.
22. American College of Obstetrics and Gynecologists' Committee on Adolescent Health Care. Committee Opinion No. 641: Human Papillomavirus Vaccination. *Obstet Gynecol.* 2015;126(3):e38–e43. https://doi.org/10.1097/AOG.0000000000001052.
23. National Association of School Nurses. NASN position statement: immunizations. *NASN Sch Nurse.* 2011;26(2):121–122. https://doi.org/10.1177/1942602X10398003.
24. Block SL, Nolan T, Sattler C, et al. Comparison of the immunogenicity and reactogenicity of a prophylactic quadrivalent human papillomavirus (types 6, 11, 16, and 18) L1 virus-like particle vaccine in male and female adolescents and young adult women. *Pediatrics.* 2006;118(5):2135–2145. https://doi.org/10.1542/peds.2006-0461.

25. Fu LY, Bonhomme LA, Cooper SC, Joseph JG, Zimet GD. Educational interventions to increase HPV vaccination acceptance: a systematic review. *Vaccine.* 2014;32(17):1901–1920. https://doi.org/10.1016/j.vaccine.2014.01.091.
26. Niccolai LM, Hansen CE. Practice- and community-based interventions to increase human papillomavirus vaccine coverage: a systematic review. *JAMA Pediatr.* 2015;169(7):686–692. https://doi.org/10.1001/jamapediatrics.2015.0310.
27. Kessels SJ, Marshall HS, Watson M, Braunack-Mayer AJ, Reuzel R, Tooher RL. Factors associated with HPV vaccine uptake in teenage girls: a systematic review. *Vaccine.* 2012;30(24):3546–3556. https://doi.org/10.1016/j.vaccine.2012.03.063.
28. Priest HM, Knowlden AP. Systematic review of primary prevention human papillomavirus interventions targeting college students. *Int J Sex Health.* 2015;27(2):125–144. https://doi.org/10.1080/19317611.2014.945631.
29. Bartlett JA, Peterson JA. The uptake of human papillomavirus (HPV) vaccine among adolescent females in the United States: a review of the literature. *J Sch Nurs.* 2011;27(6):434–446. https://doi.org/10.1177/1059840511415861.
30. Holman DM, Benard V, Roland KB, Watson M, Liddon N, Stokley S. Barriers to human papillomavirus vaccination among U.S. adolescents: a systematic review of the literature. *JAMA Pediatr.* 2014;168(1):76–82. https://doi.org/10.1001/jamapediatrics.2013.2752.
31. Allen JD, Coronado GD, Williams RS, et al. A systematic review of measures used in studies of human papillomavirus (HPV) vaccine acceptability. *Vaccine.* 2010;28(24):4027–4037. https://doi.org/10.1016/j.vaccine.2010.03.063.
32. Brewer NT, Fazekas KI. Predictors of HPV vaccine acceptability: a theory-informed, systematic review. *Prev Med.* 2007;45(2–3):107–114. https://doi.org/10.1016/j.ypmed.2007.05.013.
33. Cassidy B, Schlenk EA. Uptake of the human papillomavirus vaccine: a review of the literature and report of a quality assurance project. *J Pediatr Health Care.* 2012;26(2):92–101. https://doi.org/10.1016/j.pedhc.2010.06.015.
34. Chan ZC, Chan TS, Ng KK, Wong ML. A systematic review of literature about women's knowledge and attitudes toward human papillomavirus (HPV) vaccination. *Public Health Nurs.* 2012;29(6):481–489. https://doi.org/10.1111/j.1525-1446.2012.01022.x.
35. Fisher H, Trotter CL, Audrey S, MacDonald-Wallis K, Hickman M. Inequalities in the uptake of human papillomavirus vaccination: a systematic review and meta-analysis. *Int J Epidemiol.* 2013;42(3):896–908. https://doi.org/10.1093/ije/dyt049.
36. Lin CJ, Zimmerman RK, Nowalk MP, Huang HH, Raviotta JM. Randomized controlled trial of two dosing schedules for human papillomavirus vaccination among college age males. *Vaccine.* 2014;32(6):693–699. https://doi.org/10.1016/j.vaccine.2013.11.098.
37. Rickert VI, Auslander BA, Cox DS, et al. School-based vaccination of young U.S. males: impact of health beliefs on intent and first dose acceptance. *Vaccine.* 2014;32(17):1982–1987. https://doi.org/10.1016/j.vaccine.2014.01.049.
38. Brewer NT, Gottlieb SL, Reiter PL, et al. Longitudinal predictors of human papillomavirus vaccine initiation among adolescent girls in a high-risk geographic area. *Sex Transm Dis.* 2011;38(3):197–204. https://doi.org/10.1097/OLQ.0b013e3181f12dbf.
39. 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. https://doi.org/10.1016/j.vaccine.2011.01.065.
40. Chao C, Preciado M, Slezak J, Xu L. A randomized intervention of reminder letter for human papillomavirus vaccine series completion. *J Adolesc Health.* 2015;56(1):85–90. https://doi.org/10.1016/j.jadohealth.2014.08.014.
41. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med.* 2009;6(7):e1000097. https://doi.org/10.1371/journal.pmed.1000097.
42. Bennett AT, Patel DA, Carlos RC, et al. Human papillomavirus vaccine uptake after a tailored, online educational intervention for female university students: a randomized controlled trial. *J Womens Health (Larchmt).* 2015;24(11):950–957. https://doi.org/10.1089/jwh.2015.5251.
43. Berenson AB, Rahman M, Hirth JM, Rupp RE, Sarpong KO. A human papillomavirus vaccination program for low-income postpartum women. *Am J Obstet Gynecol.* 2016;215(3)318.e1–318.e9. https://doi.org/10.1016/j.ajog.2016.02.032.
44. Casey BR, Crosby RA, Vanderpool RC, Dignan M, Bates W. Predictors of initial uptake of human papillomavirus vaccine uptake among rural Appalachian young women. *J Prim Prev.* 2013;34(1–2):71–80. https://doi.org/10.1007/s10935-013-0295-2.
45. 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. https://doi.org/10.1016/j.pedhc.2013.01.002.
46. Chung RJ, Walter EB, Kemper AR, Dayton A. Keen on teen vaccines: improvement of adolescent vaccine coverage in rural North Carolina. *J Adolesc Health.* 2015;56(5 suppl):S14–S16. https://doi.org/10.1016/j.jadohealth.2014.10.272.
47. Crosby RA, Casey BR, Vanderpool R, Collins T, Moore GR. Uptake of free HPV vaccination among young women: a comparison of rural versus urban rates. *J Rural Health.* 2011;27(4):380–384. https://doi.org/10.1111/j.1748-0361.2010.00354.x.
48. 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. https://doi.org/10.1016/j.jadohealth.2013.12.011.
49. Eldred SV, Hamid HS, Snider JC, et al. A medical student-driven "vaccine blitz" at a school-based health center as an effective way to improve adolescent vaccination rates. *Fam Med.* 2015;47(7):546–548.
50. 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. https://doi.org/10.1542/peds.2012-3122.
51. Lee HY, Koopmeiners JS, McHugh J, Raveis VH, Ahluwalia JS. mHealth pilot study: text messaging intervention to promote HPV vaccination. *Am J Health Behav.* 2016;40(1):67–76. https://doi.org/10.5993/AJHB.40.1.8.
52. Hopfer S. Effects of a narrative HPV vaccination intervention aimed at reaching college women: a randomized controlled trial. *Prev Sci.* 2012;13(2):173–182. https://doi.org/10.1007/s11121-011-0254-1.
53. Joseph NP, Bernstein J, Pelton S, et al. Brief client-centered motivational and behavioral intervention to promote HPV vaccination in a hard-to-reach population: a pilot randomized controlled trial. *Clin Pediatr (Phila).* 2016;55(9):851–859. https://doi.org/10.1177/0009922815616244.
54. Moore GR, Crosby RA, Young A, Charnigo R. Low rates of free human papillomavirus vaccine uptake among young women. *Sex Health.* 2010;7(3):287–290. https://doi.org/10.1071/SH09136.
55. Patel DA, Zochowski M, Peterman S, Dempsey AF, Ernst S, Dalton VK. Human papillomavirus vaccine intent and uptake among female college students. *J Am Coll Health.* 2012;60(2):151–161. https://doi.org/10.1080/07448481.2011.580028.
56. Patel A, Stern L, Unger Z, et al. Staying on track: a cluster randomized controlled trial of automated reminders aimed at increasing human papillomavirus vaccine completion. *Vaccine.* 2014;32(21):2428–2433. https://doi.org/10.1016/j.vaccine.2014.02.095.
57. Perkins RB, Zisblatt L, Legler A, Trucks E, Hanchate A, Gorin SS. Effectiveness of a provider-focused intervention to improve HPV vaccination rates in boys and girls. *Vaccine.* 2015;33(9):1223–1229. https://doi.org/10.1016/j.vaccine.2014.11.021.

58. Pierre Joseph N, Clark JA, Mercilus G, Wilbur M, Figaro J, Perkins R. Racial and ethnic differences in HPV knowledge, attitudes, and vaccination rates among low-income African-American, Haitian, Latina, and Caucasian young adult women. *J Pediatr Adolesc Gynecol.* 2014;27(2):83–92. https://doi.org/10.1016/j.jpag.2013.08.011.
59. Richman AR, Maddy L, Torres E, Goldberg EJ. A randomized intervention study to evaluate whether electronic messaging can increase human papillomavirus vaccine completion and knowledge among college students. *J Am Coll Health.* 2016;64(4):269–278. https://doi.org/10.1080/07448481.2015.1117466.
60. Staras SAS, Vadaparampil ST, Livingston MD, Thompson LA, Sanders AH, Shenkman EA. Increasing human papillomavirus vaccine initiation among publicly insured Florida adolescents. *J Adolesc Health.* 2015;56(5):S40–S46. https://doi.org/10.1016/j.jadohealth.2014.11.024.
61. 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. https://doi.org/10.5993/AJHB.38.1.10.
62. Underwood NL, Weiss P, Gargano LM, et al. Human papillomavirus vaccination among adolescents in Georgia. *Hum Vaccin Immunother.* 2015;11(7):1703–1708. https://doi.org/10.1080/21645515.2015.1035848.
63. Vanderpool RC, Casey BR, Crosby RA. HPV-related risk perceptions and HPV vaccine uptake among a sample of young rural women. *J Community Health.* 2011;36(6):903–909. https://doi.org/10.1007/s10900-010-9345-3.
64. Vanderpool RC, Breheny PJ, Tiller PA, et al. Implementation and evaluation of a school-based human papillomavirus vaccination program in rural Kentucky. *Am J Prev Med.* 2015;49(2):317–323. https://doi.org/10.1016/j.amepre.2015.05.001.
65. Wright JD, Govindappagari S, Pawar N, et al. Acceptance and compliance with postpartum human papillomavirus vaccination. *Obstet Gynecol.* 2012;120(4):771–782. https://doi.org/10.1097/AOG.0b013e31826afb56.
66. 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. https://doi.org/10.1001/archpediatrics.2011.73.
67. Centre for Statistics in Medicine, University of Oxford. Enhancing the QUAlity and Transparency Of health Research (EQUATOR) reporting guidelines. www.equator-network.org/reporting-guidelines/. Accessed April 26, 2017.
68. Vandenbroucke JP, von Elm E, Altman DG, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. *Epidemiology.* 2007;18(6):805–835. https://doi.org/10.1097/EDE.0b013e3181577511.
69. CONSORT Transparent Reporting of Trials. Consolidated Standards of Reporting Trials (CONSORT) Statement. www.consort-statement.org/. Published 2010. Accessed April 6, 2017.
70. Sullivan KM, Dean A, Soe MM. OpenEpi: a web-based epidemiologic and statistical calculator for public health. *Public Health Rep.* 2009;124(3):471–474. https://doi.org/10.1177/003335490912400320.
71. Riley RD, Higgins JP, Deeks JJ. Interpretation of random effects meta-analyses. *BMJ.* 2011;342:d549. https://doi.org/10.1136/bmj.d549.
72. Jones CL, Jensen JD, Scherr CL, Brown NR, Christy K, Weaver J. The health belief model as an explanatory framework in communication research: exploring parallel, serial, and moderated mediation. *Health Commun.* 2015;30(6):566–576. https://doi.org/10.1080/10410236.2013.873363.
73. Davey Smith G, Egger M, Phillips AN. Meta-analysis. Beyond the grand mean. *BMJ.* 1997;315(7122):1610–1614. https://doi.org/10.1136/bmj.315.7122.1610.
74. Egger M, Smith GD. Meta-analysis: potentials and promise. *BMJ.* 1997;315(7119):1371–1374. https://doi.org/10.1136/bmj.315.7119.1371.
75. Greenland S. Can meta-analysis be salvaged? *Am J Epidemiol.* 1994;140(9):783–787. https://doi.org/10.1093/oxfordjournals.aje.a117326.