

Interventions to Improve HPV Vaccine Uptake: A Systematic Review

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abstract

CONTEXT: The human papillomavirus (HPV) vaccine is a safe, effective cancer prevention method that is underutilized in the United States. Despite increased understanding of barriers to vaccination, rates remain low. Globally, developed and developing nations have achieved high rates of vaccination.

OBJECTIVE: Identification of effective strategies is necessary to optimize uptake of the HPV vaccine. We systematically reviewed the literature for national and international interventions that have successfully increased HPV vaccine uptake.

DATA SOURCES: We used a standardized protocol to search for articles published between January 1, 2006, and April 30, 2015, in 3 electronic databases: PubMed, Scopus, and Embase.

STUDY SELECTION: We identified interventions designed to increase HPV vaccine uptake among adolescents and young adults aged 11 to 26 years. All study designs were acceptable. Only articles that included postintervention vaccination rates were included.

DATA EXTRACTION: Two authors independently reviewed each article for data extraction and quality assessment. Interventions were classified according to the Community Preventive Service Task Force guide.

RESULTS: Results were reported according to the RE-AIM (Reach, Effectiveness, Adoption, Implementation, Maintenance) framework. Fifty-one articles met eligibility criteria: 2 informational interventions, 18 behavioral interventions, and 31 environmental interventions. Factors associated with HPV vaccine uptake were increased vaccine availability, decreased financial barriers, and interventions targeting both providers and patients.

LIMITATIONS: Lack of consistent RE-AIM metric reporting, limiting our ability to assess intervention validity and quality.

CONCLUSIONS: Population-based vaccination strategies that increased vaccine availability reached the greatest number of adolescents and were most successful in achieving high rates of vaccination.



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Human papillomavirus (HPV) leads to ~600 000 new cases annually of cervical and genitourinary cancer worldwide, 26 900 of which occur in the United States.^{1,2} A 3-dose quadrivalent recombinant HPV vaccine (HPV2) has been available globally since 2006, recommended by the World Health Organization and the Centers for Disease Control and Prevention^{3,4} for girls aged 9 to 26 and extended to boys in 2011. Worldwide vaccination uptake at a rate of 80% would prevent an estimated two-thirds of new cases of cervical cancer.³

Despite a nearly 10-year record of safety and efficacy,^{5,6} vaccination rates in the United States remain low. On average, 60% of girls 13 to 17 years of age initiate the series, and 39.7% receive all 3 doses; only 41.7% of boys initiate and 21.6% complete the series. Wide variation in coverage is observed both within and between states.⁷ Underuse of HPV2 is concerning: the majority of adolescents in the United States are missing an opportunity to prevent cancer later in life. Furthermore, a clear racial disparity associated with cervical cancer exists in the United States, African American women are more likely to be diagnosed at later disease stages and die at nearly twice the rate compared with non-Hispanic white women.⁸ This may be due to compromised access to secondary cancer screening and prevention services later in life,⁹ underscoring the necessity of primary prevention.

Multiple interventions to address poor vaccination rates have increased knowledge of HPV-related diseases and the HPV2.^{10–18} Although vaccination intent was increased, it was neither sustained nor translated into vaccination behavior. Furthermore, there has been speculation that parents from different ethnic and socioeconomic groups may face different barriers to vaccination and thus require different intervention strategies,^{17,19}

a critical point in the context of disparate HPV disease outcomes.

Recent systematic reviews examining interventions to increase HPV2 uptake have conflicting conclusions. Fu et al reviewed 33 articles describing educational interventions and concluded that no specific strategy merited recommendation.²⁰ However, the included studies did not consistently report postintervention vaccination rates, complicating interpretation of intervention success. Niccolai et al reviewed 14 community and clinic interventions and found several successes.²¹ The authors acknowledged that far greater numbers could be reached if interventions were implemented on a larger scale. Furthermore, the relative success of many of these interventions fell short of national averages and stated vaccination goals.

Other countries have considerably more success achieving high rates of HPV2 vaccination.¹ To gain insight from global efforts, we conducted a systematic review of the literature for national and international initiatives to increase HPV2 vaccination.

METHODS

This review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA; see Supplemental Table 6) guidelines,²² posing the question: “What interventions have successfully achieved high rates of HPV2 vaccination in men and women 11 to 26 years old?”

Inclusion and Exclusion Criteria

Eligibility criteria are outlined in Table 1. Only articles including postintervention HPV2 vaccination rates were included. Multiple articles describing the same intervention were excluded unless new data over a different time period was presented, allowing assessment of intervention sustainability.

TABLE 1 Eligibility Criteria

Inclusion
Study design: any
Participants: men and/or women 11–26 y old
Intervention: to increase HPV2 uptake
Outcome: postintervention HPV2 vaccination rate reported
Exclusion
Postintervention HPV2 vaccination rates not reported
No original data (exception made for articles describing government interventions)
Abstract or research communication report only
Population <11 or >26 y old
Study not available in English

Search Strategy

Search criteria were developed with the assistance of a medical librarian and conducted using 3 medical literature websites (PubMed, Scopus, and Embase) for articles published between January 1, 2006, and April 30, 2015 (Supplemental Information). One author (EW) scanned the bibliographies of included trials for articles missed by the original search, resulting in 51 eligible articles (Supplemental Figure 1).

Data Classification and Quality Assessment

The Community Guide’s Data Abstraction (CGDA) framework from the Community Preventive Services Task Force²³ was used to guide data extraction and synthesis (Table 2 and 3). The Task Force identifies successful health interventions by conducting systematic reviews and provides a framework to assess an intervention’s design and execution. One author (NB) created a modified version of the CGDA, and 2 authors independently extracted data from each article using this tool.

A modified RE-AIM (Reach, Effectiveness, Adoption, Implementation, Maintenance) model was used to evaluate quality and external validity.^{24–27} Metrics captured in this review are included in Table 4.

RESULTS

Results are reported according to the modified RE-AIM framework (Table 4, Supplemental Table 5).

Quality Assessment

Forty-nine articles described at least 1 element of all measured RE-AIM metrics. All articles described the intervention's reach. Twenty-two articles did not describe barriers to implementation.²⁸⁻⁴⁹ Two articles did not include maintenance metrics.^{32,33} Several articles commented on barriers specific to public perception of the HPV: lack of HPV knowledge,⁵⁰ negative media surrounding the HPV,⁵¹ and HPV safety concerns.⁵²⁻⁵⁴ Although not specific to intervention implementation, authors postulated these challenges likely compromised overall success of the intervention. Efficacy measures were heterogeneous, including rates of HPV initiation (receipt of dose 1), completion (receipt of 3 doses), receipt of any dose as well as hazard, and risk ratio of receiving the vaccine. Vaccination results were determined from record review,^{28,29,34-76} interview,^{31,33,77} and by survey or self-report of patients or parents.^{30,32,51,77,78}

Reach

There was considerable variation in the number of participants reached by an intervention. In general, environmental interventions had the largest scope, consistently reaching >100 000 adolescents, whereas behavioral interventions reached as few as 37 adolescents.⁶⁹ Provider and patient targeted interventions were an exception, often reaching several thousand^{34,39,40,62,74} and in 1 case >100 000 adolescents.³⁸ A county-wide information intervention reached ~19 842 adolescents.²⁹ Interventions overwhelmingly targeted girls; 9 targeted both genders,^{28,38,39,43,48,60,65,69,71,78} and 1 targeted only boys.²⁹ Four interventions targeted a specific

TABLE 2 CGDA Intervention Categories

Category	Intervention Definition
Informational	To increase knowledge of HPV, HPV-related disease, or the HPV
Behavioral	To change behavior by providing necessary skills to make a decision regarding the HPV. Subcategories by strategy: patient-targeted decision support (eg, message framing, health theory-based interventions), patient-targeted reminders, provider-targeted reminders, patient and provider interventions
Environmental	To change the social environment to facilitate vaccination, ie, decreased financial barriers, novel vaccination locations. Subcategory by policy level: small policy (organizational guidelines, no government involvement), large policy (formal laws, rules or regulations, national or local government involvement)

The authors determined the main category for interventions employing multiple strategies.

TABLE 3 CGDA Intensity Level

Intensity Level	Example
Active engagement by stakeholders targeted toward the individual	Patient or physician reminders
Active engagement by stakeholders targeted to population	School-based VP, educational classes
Passive engagement with significant effort	Educational media campaigns
Passive engagement with minimal effort	Notice on Web site

Interventions using multiple methods were classified according to the method of the highest intensity.

TABLE 4 RE-AIM Evaluation Dimensions

Reach: proportion of the target population that participated in the intervention. Setting, population density, HPV population, number of participants
Efficacy: success rate if implemented as in guidelines Postintervention HPV rates
Adoption: proportion of settings, practices, and plans that will adopt this intervention If applicable, described with implementation
Implementation: extent to which the intervention is implemented as intended Study design, barriers encountered
Maintenance: extent to which a program is sustained over time Sustainability and acceptability of the intervention

vulnerable population.^{45,50,75,78}

Only 12 studies reported participant rate: 11 in the United States^{29,31,34,36,39-42,62,65,71} 1 in South Africa.⁴³

Efficacy, Adoption/Implementation, and Maintenance

Informational Interventions (n = 2)

An intervention in the United States targeted low-income parents and provided HPV education, resulting in higher rates of series completion compared with preintervention (58% vs 42%).²⁸ A community-wide media information campaign in the United States targeting adolescent boys resulted in higher rates of HPV vaccination in the exposed community

during the media campaign compared with the control community (hazard ratio 1.34). The intervention was financially feasible, but there was no significant difference between case and control groups in the postintervention period.²⁹

Behavioral Interventions: Patient Targeted Decision Support (n = 5)

An intervention at an Australia university examined the effect of different informational material: a pamphlet emphasizing HPV cervical cancer and genital wart prevention versus a pamphlet emphasizing only HPV cervical cancer prevention. Two months postintervention, the women who received the pamphlet emphasizing both cervical cancer and

genital wart prevention had higher self-reported vaccination rates (42% vs 33%). However, response rate was low (54%), increasing the potential for bias.³⁰ Hopfer et al demonstrated that female university students in the United States shown an HPV education video narrated by a peer and an expert had significantly higher vaccination rates compared with the control group (21.8% vs 11.8%)³² An intervention based in US school health clinics tested health message framing. Although intent to vaccinate increased, no effect on actual behavior was observed at the 10-month follow-up.⁷¹ Similarly, Wegwarth et al found that students at a German school randomized to receive an evidence-based “balanced” leaflet versus those randomized to a sensationalist “unbalanced” leaflet had improved understanding of the HPV but no difference in vaccination behavior.³³ Finally, an intervention comparing the impact of using gain- or loss-framed messages among university students in the United States and found no effect on vaccine behavior.³¹

Behavioral Interventions: Patient-Targeted Reminder Interventions (n = 7)

Four studies included randomization.^{34,35,62,74} Szilagyi et al described a tiered intervention escalating from telephone and letter reminders to home visits with the goal of increasing immunizations (including HPV) and preventative care visits. They found significantly higher rates of vaccine initiation (58.5% vs 42.9%) and completion (36.5% vs 24.1%) in the intervention versus the control group.³⁴ These researchers later examined an intervention that randomized patients to receive a letter, telephone call reminder, or standard of care. They found improved vaccination rates among those who received reminders but no significant difference based on modality.⁷⁴ Chao et al demonstrated increased HPV completion rates among

participants randomized to receive reminder letters versus standard of care (56.4% vs 46.6%).⁶² Both investigators identified a lack of reliable contact information as a barrier to implementation.^{62,74} Another trial randomized patients to receive telephone and mail reminders versus standard of care and showed significantly higher initiation (26.5% vs 15.3%) and completion rates (11.4% vs 4.4%) among the intervention group.³⁵ Two interventions used text message reminders; both showed significantly higher rates in the intervention group (51.6% vs 35%)⁶⁷ and (16% vs 5%).⁶⁹ Challenges included variable clinic adherence to intervention procedures⁶⁷ and participants forgetting to opt in to receive reminders, a barrier recognized and rectified early in the process.⁶⁹ Another text message reminder intervention failed to demonstrate a difference between intervention and control groups, which authors postulated was potentially due to inadequate follow-up time.³⁶ Several articles commented on the financial feasibility^{34,35,62,69,74} and acceptability by parents⁶⁹ of reminder interventions.

Behavioral Interventions: Provider-Targeted Interventions (n = 4)

Several interventions used a version of the Centers for Disease Control and Prevention–endorsed Assessment/Feedback/Incentive/Exchange (AFIX) approach.⁷⁹ Perkins et al compared HPV vaccination rates at clinics randomized to the AFIX approach versus control clinics and demonstrated significantly increased HPV uptake, most impressively among boys.³⁹ Gilkey et al randomized 91 clinics to 3 groups: in-person AFIX consultation, webinar AFIX consultation, or control. HPV completion rates were highest among clinics that received an in-person AFIX consult.³⁸ Both authors commented on the high level of acceptability of the intervention by

key stakeholders. Moss et al observed a small but statistically significant increase in series completion rates after a 1-time AFIX consultation over 1 month.³⁷ Lastly, an intervention including electronic medical record prompts of patients overdue for the HPV did not increase vaccination rates during the intervention period. Inaccurate vaccine tracking resulting in missed vaccination opportunities were cited as potential barriers to intervention success.⁵⁹

Behavioral Interventions: Patient- and Provider-Targeted Interventions (n = 2)

Fiks et al described a multifaceted intervention randomizing clinics to 1 of 4 arms: family-focused reminders, clinician-focused reminders and education, a combined approach, or control. The combined arm had the highest rates of vaccination initiation and completion (25% and 76%, respectively) compared with control (16% and 63%). Authors described financial feasibility of the 12-month intervention period.⁴⁰ An approach that included patient-focused education and telephone reminders with physician alerts and a script to address parents concerns resulted in 62.5% completion, representing a nearly 10-fold increase compared with the control group. Authors commented that implementation of the program was simple and parents welcomed the information.⁴¹

Environmental Interventions (n = 31)

Barriers to implementation at all policy levels included the following: obtaining vaccination consent,^{58,60,63,66} reaching adolescents not in school,^{58,72,76} and reaching underserved areas.^{75,77}

Environmental Interventions: Small Policy (n = 12)

Five school-based vaccination programs (VP) were identified. A feasibility trial for the upcoming government-funded program in England had high rates of HPV initiation after the first year (70.6%), despite challenges with vaccine

delivery and multiple missed appointments.⁵⁷ Programs in Brazil and South Africa included education campaigns and free vaccination, demonstrating uptake rates of 85%⁶⁴ (completion) and 58.6%⁵⁶ (at least 1 dose), respectively. Similar implementation challenges faced both programs: parents refusing to participate (up to 41%)⁵⁶ or not attending educational classes.⁵⁶ Two school-based VPs in the United States included free HPVV.^{66,73} One summoned students to the health center for vaccination and demonstrated an initiation rate similar to national averages (59%) but a dramatic improvement over the preintervention rate of 5%. However, none of the students received all 3 doses. Still, the intervention was found to be cost-effective and accepted among those who agreed to participate.⁶⁶ The second intervention included an HPVV education campaign and HPVV clinics at "host" schools, allowing students who attended control schools to receive vaccination at host schools. Researchers faced significant barriers including stipulations to vaccine administration, disparate implementation of the education campaign, and a low participation rate (2%). Low initiation and completion rates were observed at host schools (6% and 4.8%, respectively), but initiation rates were higher than control schools (1%). Authors noted that the intervention was financially feasible and parents who did participate were pleased with the intervention.⁷³

Four interventions set in clinics were identified. A feasibility trial in South Africa included an interview of parents and adolescents to assess HPVV acceptability and demonstrated a high completion rate (81.6%).⁴³ An intervention in Peru including cervical cancer screening of an older relative and free HPVV resulted in high rates of series completion (65%), despite recruitment challenges

and limited HPV knowledge.⁵⁰ Two interventions targeted specific vulnerable populations. Female sex workers in Cambodia received free HPVV, STD testing, reminders, and transportation to a health clinic, resulting in a series completion rate of 54%.⁴⁵ An intervention targeting rural, underserved women in the United States offered free HPVV and \$25 compensation for answering a questionnaire. Less than half (44.9%) of participants who signed consent received the first dose of the HPVV series. Implementation was challenged by inherent difficulties associated with reaching an underserved and undereducated population.⁷⁵

One intervention was set in both schools and clinics. A nationwide education campaign in Cameroon with reduced cost or free HPVV donated from the Merck patient assistance program resulted in an 84.6% completion rate. Authors commented that the success of this intervention offered further support that school-based VPs were the most efficient method for delivery of HPVV in Africa.⁴⁴

Two interventions offering free HPVV were set in US universities. One compensated participants \$10 for answering a questionnaire about HPV, resulting in vaccination rates similar to national averages (28.2% series completion).⁴² An intervention supported by the Merck patient assistance program targeted underinsured students and included up to 3 reminder telephone calls. Although 100% of participants initiated the vaccination series, only 48.3% received 3 doses.⁷⁸

Environmental Interventions: Big Policy, National Government Involvement (n = 12)

Australia was the first country to institute a national HPV program and observed high completion rates at 1 and 5 years (77% and 70%, respectively). In addition to a school-based VP for 11- and 12-year-olds with catch-up for older students, there

was early recognition of low rates of school attendance among indigenous populations, and efforts were made to increase HPVV availability in novel locations. Other challenges included HPVV safety concerns, obtaining parental consent, variable familiarity with school-based VPs, and variation in uptake across territories.^{52,58} Similarly, vaccination rates in Canada differed by province. Prince Edward Island had high rates after the sixth year of the school-based VP: 85% and 79% completion for girls and boys, respectively.⁴⁸ In Ontario, vaccination completion rates increased annually over 3 years (51%, 58%, and 59%). Implementation was challenged by a lack of a comprehensive vaccination strategy and several schools refused to participate.⁵¹ School-based VPs in Spain, Scotland, and Switzerland had high vaccination completion rates after 1 and 3 years of the ongoing programs (77.3%, 81.0%, and 61.4%, respectively).^{47,54,72} Notably, developing countries also had high vaccination rates. A partnership between the Program for Appropriate Technology in Health, a nonprofit global health organization, and the governments of 4 countries using an education campaign and free HPVV at schools and clinics resulted in high completion rates in India (87.8%), Peru (82.6%), Uganda (88.9%), and Vietnam (98.6%).⁷⁷ Likewise, a school-based VP in Rwanda had high rates of vaccine uptake after the first year of the program's implementation (93.2%).⁵⁵ A program in the Netherlands was an exception to the widespread success of national school-based VPs, reporting HPVV initiation rates at 49.9%. The authors questioned the quality of the education campaign and speculated that distrust of the HPVV among the local scientific community may have contributed to poor vaccination rates.⁵³

Two clinic based interventions offered free HPVV through national government programs. A program

in Italy included an education letter to parents and education of clinic staff. Dissatisfaction among parents and staff regarding the education was reported, and only 49.4% of the target population completed the HPV series.⁶¹ In Denmark, the HPV was incorporated into an existing vaccine program and accompanied by a nationwide education campaign, resulting in a completion rate of 62%.⁴⁶

Environmental Interventions: Big Policy, Local Government Involvement (n = 7)

High rates of completion were described in local governments of South Africa (97.8%),⁷⁰ Tanzania (78.7%),⁷⁶ and Brazil (73%).⁶⁸ All included an education campaign and free HPV. Three interventions were identified within the United States; 2 offered the HPV for free,^{60,65} and 1 billed to insurance.⁶³ All reported rates below national averages, challenged by low participation and difficulty obtaining consent and accurately tracking vaccine doses. However, students randomized to school-based VPs compared with control schools did demonstrate higher 3-dose completion rates (13.2% vs 2%).⁶³

A clinic-based intervention in a Japanese municipality included an official announcement by the mayor. High completion rates were observed among 14- and 15-year-olds (81%), whereas 11- and 12-year-olds had vaccination completion rates similar to the United States (32.4%). Success of this local intervention led to a national government-funded program.⁴⁹

DISCUSSION

We systematically reviewed national and international interventions to increase HPV uptake over the 9-year period since the first HPV was approved. We compared the relative efficacy of these interventions, broadly classified as informational, behavioral, and environmental. Informational interventions using

both individualized and community-wide education campaigns improved vaccination uptake during the active intervention period. However, there was no evidence to suggest the effect was sustained, indicating that this is not a sufficient modality when used alone. Furthermore, if not applied at a population level, the intervention's reach was limited. Behavioral interventions demonstrated a range of effectiveness, required significant effort, and had inconsistent outcomes. There was a consistent lack of reporting implementation barriers common to all decision support interventions, information that would be useful to guide future interventions. Still, important lessons can be learned from the described efforts. Hopfer et al illustrated the importance of peer group endorsement for behavior among young women, a factor that outweighed expert endorsement.³² Juraskova et al demonstrated that vaccination intent was associated with knowing someone with cervical cancer, but behavior was associated with perceived susceptibility to HPV. Perceived benefit of vaccination was associated with both intent and behavior.³⁰ These results imply that future interventions should emphasize the high prevalence of HPV and the safety and efficacy of the HPV. Additionally, evidence is mounting that while health belief models may influence intent to vaccinate, the effect on behavior is minimal.^{30,71,80}

Reminder strategies were largely successful. An interesting theme that emerged was that provider targeted interventions appeared to be most successful for HPV series initiation while patient targeted interventions appeared to be most successful for series completion, indicating that providers pose a more significant barrier to vaccine series initiation, while patient or family barriers are a greater hindrance to series completion. This was demonstrated by the success of interventions targeting both the provider and the patient.^{40,41}

Environmental interventions, particularly school-based VP, had 2 major advantages that contributed to their success: increased access to the HPV and ability to reach a large, diverse population, regardless of individual access to health care. Important themes emerged from descriptions of international school-based VP, which were widely accepted and welcomed by key stakeholders, including school personnel and parents. Location of HPV vaccination varied by age group; younger adolescents were more likely to receive vaccines at school, whereas older adolescents were more likely to go to their health care provider.^{47,68,72} Similarly, adolescents with poor school attendance had lower vaccination rates than those in school, underscoring the importance of convenience in modifying behavior.⁷² Finally, the success of environmental interventions in developing countries through school- and clinic-based vaccination programs illustrated that high vaccination coverage is not limited to high-income populations.^{43-45,55,56,70,76,77}

School-based VPs in the United States offered additional insight. An intervention in Colorado comparing schools with vaccination clinics to control schools demonstrated a higher risk ratio of receiving the HPV vaccine than the risk of receiving the other 2 adolescent vaccines offered, highlighting the importance of increased access and convenience needed to achieve HPV coverage.⁶³ In support of this conclusion, an important observation by Stubbs et al was higher rates of initiation in "host" schools where vaccine clinics were located compared with "satellite" schools, again demonstrating the importance of increased availability. Additionally, although a small percentage of adolescents initiated the vaccine series, the majority of those who received the first dose of HPV completed the series.⁷³ This implies that with greater participation,

school-based VPs in the United States could achieve high HPVV completion rates and provide health care access for underserved populations. However, community support is vital for school-based VP to be successful. This may in part explain the low participation in school-based VP in the United States compared with those abroad. The relative novelty of school-based VP and differences in health care structures likely contribute to the disparate success.

Finally, it is worthwhile to note that cervical cancer does not carry the same widespread burden of morbidity and mortality in the United States as it does in developing countries. Worldwide, cervical cancer is the second most common cancer among women, and an overwhelming majority of deaths due to cervical cancer take place in developing countries.³ Perhaps these countries have a better appreciation of HPV-related disease and a greater sense of urgency to take advantage of the vaccine. These factors may contribute to greater uptake of HPVV internationally.

This study was strengthened by the wide scope of interventions and number of countries represented. This is simultaneously a limitation because the ability to generalize strategies to the United States may be compromised by local health care policy. The heterogeneity of the interventions affected our ability to assess quality. We initially planned to use the CGDA framework to assess quality; however, we ultimately determined that RE-AIM metrics were a better marker for intervention feasibility and sustainability. It became clear that traditional metrics of quality assessment captured by the CGDA, bias measures in particular, simply did not apply. For example, <2% of articles reported a participation rate, and only 1 study reported the attrition rate. Moreover, for nationwide vaccination strategies, participation and attrition rates were not applicable. The heterogeneous reporting of

outcomes complicated interpretation of success, making direct comparison difficult. Five interventions had self-reported results, likely introducing a reporting bias. Series completion rate was frequently reported based on the proportion of those who initiated the HPVV series, rather than using the total targeted population as reference. Preintervention vaccination rates were rarely included. This was less problematic in analysis of national government interventions because the intervention represented national access to the HPVV. Many studies lacked a control group, making it impossible to tell if observed changes in vaccination rates would have occurred over time in the absence of the intervention. Finally, omission of implementation barriers and maintenance metrics was unfortunate because these details are key to replicating or improving an intervention.

One consistent deficiency in nearly all studies was the lack of data on race/ethnicity and socioeconomic status reporting, making it difficult to elucidate trends to support the theory that participants from different backgrounds respond preferentially to certain interventions. Given the significant disparity in outcomes of HPV related diseases, it is imperative we develop a better understanding of the relationship between demographics and vaccination behavior. As demonstrated in this review, environmental interventions targeting underserved populations can be successful and should be employed to protect the most vulnerable adolescents.^{45,50,75,78}

CONCLUSIONS

A concerted effort is necessary to optimize uptake of the HPVV among adolescents in the United States. Overall, this review supports the use of environmental interventions such as school-based VP. Environmental

approaches consistently reached the greatest number of participants and achieved the highest vaccination rates. The remarkable success internationally of government-initiated HPVV programs should be used to inform and guide US policy. When population-based vaccination strategies are not feasible, we support multipronged interventions that target both the provider and the patient.

Finally, a known barrier to successful vaccination is the 3-dose requirement. Early evidence indicates that fewer than 3 doses may be protective.⁸¹ Adolescents in the United States may not be as undervaccinated as indicated by the current rate of HPVV completion; an estimated 50% of girls and 31% of boys have received 2 doses.⁸² Until further research validates this finding, we should continue to adhere to international and national recommendations.

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ABBREVIATIONS

AFIX: Assessment/Feedback/
Incentive/Exchange
CGDA: Community Guide Data
Abstraction
HPV: human papillomavirus
HPVV: human papillomavirus
vaccine
PRISMA: Preferred Reporting
Items for Systematic
Reviews and
Meta-Analysis
RE-AIM: Reach, Effectiveness,
Adoption, Implementa-
tion, Maintenance
VP: vaccination programs

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REFERENCES

1. Rimer BK, Harper H, Witte ON; President's Cancer Panel. Accelerating HPV Vaccine Uptake: Urgency for Action to Prevent Cancer. Available at: http://deainfo.nci.nih.gov/advisory/pcp/annualReports/HPV/PDF/PCP_Annual_Report_2012-2013.pdf. Accessed April 24, 2016
2. Cancer of the Cervix Uteri—SEER Stat Fact Sheets. <http://seer.cancer.gov/statfacts/html/cervix.html>. Accessed August 28, 2015
3. World Health Organization. Human papillomavirus (HPV) and cervical cancer. Available at: www.who.int/mediacentre/factsheets/fs380/en/. Accessed August 28, 2015
4. Vaccines: VPD-VAC/HPV/Vaccine FAQ. Available at: www.cdc.gov/vaccines/vpd-vac/hpv/vac-faqs.htm#vaccine. Accessed August 28, 2015
5. Dillner J, Kjaer SK, Wheeler CM, et al; 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
6. Giuliano AR, Palefsky JM, Goldstone S, et al. Efficacy of quadrivalent HPV vaccine against HPV infection and disease in males. *N Engl J Med*. 2011;364(5):401–411
7. 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
8. Browse the SEER Cancer Statistics Review 1975–2012. Available at: http://seer.cancer.gov/csr/1975_2012/browse_csr.php?sectionSEL=5&pageSEL=sect_05_table.11.html. Accessed September 8, 2015
9. Sheppard C, El-Zein M, Ramanakumar AV, Ferenczy A, Franco EL. Assessment of mediators of racial disparities in cervical cancer survival in the United States. *Int J Cancer*. January 2016;138(11):2622–2630
10. Mehta P, Sharma M, Lee RC. Designing and evaluating a health belief model-based intervention to increase intent of HPV vaccination among college males. *Int Q Community Health Educ*. 2013–2014;34(1):101–117
11. Paiva AL, Lipschitz JM, Fernandez AC, Redding CA, Prochaska JO. Evaluation of the acceptability and feasibility of a computer-tailored intervention to increase human papillomavirus vaccination among young adult women. *J Am Coll Health*. 2014;62(1):32–38
12. Reiter PL, Stubbs B, Panozzo CA, Whitesell D, Brewer NT. HPV and HPV vaccine education intervention: effects on parents, healthcare staff, and school staff. *Cancer Epidemiol Biomarkers Prev*. 2011;20(11):2354–2361
13. Kester LM, Shedd-Steele RB, Dotson-Roberts CA, Smith J, Zimet GD. The effects of a brief educational intervention on human papillomavirus knowledge and intention to initiate HPV vaccination in 18-26 year old young adults. *Gynecol Oncol*. 2014;132(suppl 1):S9–S12
14. Perkins RB, Clark JA. What affects human papillomavirus vaccination rates? A qualitative analysis of providers' perceptions. *Womens Health Issues*. 2012;22(4):e379–e386
15. Rosenthal SL, Weiss TW, Zimet GD, Ma L, Good MB, Vichnin MD. Predictors of HPV vaccine uptake among women aged 19-26: importance of a physician's recommendation. *Vaccine*. 2011;29(5):890–895
16. Sussman AL, Helitzer D, Sanders M, Urquieta B, Salvador M, Ndiaye K. HPV and cervical cancer prevention counseling with younger adolescents: implications for primary care. *Ann Fam Med*. 2007;5(4):298–304
17. Thompson VLS, Arnold LD, Notaro SR. African American parents' attitudes toward HPV vaccination. *Ethn Dis*. 2011;21(3):335–341
18. Gottvall M, Tydén T, Höglund AT, Larsson M. Knowledge of human papillomavirus among high school students can be increased by an educational intervention. *Int J STD AIDS*. 2010;21(8):558–562
19. Holman DM, Benard V, Roland KB, Watson M, Liddon N, Stokley S. Barriers to human papillomavirus vaccination among US adolescents: a systematic review of the literature. *JAMA Pediatr*. 2014;168(1):76–82
20. 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
21. 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

22. Moher D, Shamseer L, Clarke M, et al; PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev*. 2015;4:1
23. The Guide to Community Preventive Services (The Community Guide). Available at: www.thecommunityguide.org/index.html. Accessed September 3, 2015
24. Glasgow RE, Klesges LM, Dziewaltowski DA, Estabrooks PA, Vogt TM. Evaluating the impact of health promotion programs: using the RE-AIM framework to form summary measures for decision making involving complex issues. *Health Educ Res*. 2006;21(5):688–694
25. Jauregui E, Pacheco AM, Soltero EG, et al. Using the RE-AIM framework to evaluate physical activity public health programs in México. *BMC Public Health*. 2015;15:162
26. Folta SC, Lichtenstein AH, Seguin RA, et al. The StrongWomen-Healthy Hearts program in Pennsylvania: RE-AIM analysis. *Transl Behav Med*. 2015;5(1):94–102
27. Paez DC, Reis RS, Parra DC, et al. Bridging the gap between research and practice: an assessment of external validity of community-based physical activity programs in Bogotá, Colombia, and Recife, Brazil. *Transl Behav Med*. 2015;5(1):1–11
28. Suryadevara M, Bonville CA, Ferraioli F, Domachowske JB. Community-centered education improves vaccination rates in children from low-income households. *Pediatrics*. 2013;132(2):319–325
29. 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
30. Juraskova I, Bari RA, O'Brien MT, McCaffery KJ. HPV vaccine promotion: does referring to both cervical cancer and genital warts affect intended and actual vaccination behavior? *Women's Health Issues*. 2011;21(1):71–79
31. Gerend MA, Shepherd JE. Predicting human papillomavirus vaccine uptake in young adult women: comparing the health belief model and theory of planned behavior. *Ann Behav Med*. 2012;44(2):171–180
32. 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
33. Wegwarth O, Kurzenhäuser-Carstens S, Gigerenzer G. Overcoming the knowledge-behavior gap: The effect of evidence-based HPV vaccination leaflets on understanding, intention, and actual vaccination decision. *Vaccine*. 2014;32(12):1388–1393
34. Szilágyi 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
35. Suh CA, Saville A, Daley MF, et al. Effectiveness and net cost of reminder/recall for adolescent immunizations. *Pediatrics*. 2012;129(6). Available at: www.pediatrics.org/cgi/content/full/129/6/e1437
36. 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
37. 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
38. Gilkey MB, Dayton AM, Moss JL, et al. Increasing provision of adolescent vaccines in primary care: a randomized controlled trial. *Pediatrics*. 2014;134(2). Available at: www.pediatrics.org/cgi/content/full/134/2/e346
39. 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
40. 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
41. 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
42. 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
43. Katz IT, Nkala B, Dietrich J, et al. A qualitative analysis of factors influencing HPV vaccine uptake in Soweto, South Africa among adolescents and their caregivers. *PLoS One*. 2013;8(8):e72094
44. Ogembo JG, Manga S, Nulah K, et al. Achieving high uptake of human papillomavirus vaccine in Cameroon: lessons learned in overcoming challenges. *Vaccine*. 2014;32(35):4399–4403
45. Wadhwa P, Evans JL, Stein E, et al. Human papillomavirus knowledge, vaccine acceptance, and vaccine series completion among female entertainment and sex workers in Phnom Penh, Cambodia: the Young Women's Health Study. *Int J STD AIDS*. 2015;26(12):893–902
46. Widgren K, Simonsen J, Valentiner-Branth P, Mølbak K. Uptake of the human papillomavirus-vaccination within the free-of-charge childhood vaccination programme in Denmark. *Vaccine*. 2011;29(52):9663–9667
47. Jeannot E, Sudre P, Chastonay P. HPV vaccination coverage within 3 years of program launching (2008–2011) at Geneva State, Switzerland. *Int J Public Health*. 2012;57(3):629–632
48. McClure CA, MacSwain M-A, Morrison H, Sanford CJ. Human papillomavirus vaccine uptake in boys and girls in a school-based vaccine delivery program in Prince Edward Island, Canada. *Vaccine*. 2015;33(15):1786–1790
49. Hayashi Y, Shimizu Y, Netsu S, Hanley S, Konno R. High HPV vaccination

- uptake rates for adolescent girls after regional governmental funding in Shiki City, Japan. *Vaccine*. 2012;30(37):5547–5550
50. Abuelo CE, Levinson KL, Salmeron J, Sologuren CV, Fernandez MJV, Belinson JL. The Peru Cervical Cancer Screening Study (PERCAPS): the design and implementation of a mother/daughter screen, treat, and vaccinate program in the Peruvian jungle. *J Community Health*. 2014;39(3):409–415
 51. Wilson SE, Harris T, Sethi P, Fediurek J, Macdonald L, Deeks SL. Coverage from Ontario, Canada's school-based HPV vaccine program: the first three years. *Vaccine*. 2013;31(5):757–762
 52. Brotherton JML, Deeks SL, Campbell-Lloyd S, et al. Interim estimates of human papillomavirus vaccination coverage in the school-based program in Australia. *Commun Dis Intell Q Rep*. 2008;32(4):457–461
 53. Rondy M, van Lier A, van de Kasstelee J, Rust L, de Melker H. Determinants for HPV vaccine uptake in the Netherlands: a multilevel study. *Vaccine*. 2010;28(9):2070–2075
 54. Limia A, Pachón I. Coverage of human papillomavirus vaccination during the first year of its introduction in Spain. *Euro Surveill*. 2011;16(21):19873
 55. Binagwaho A, Wagner CM, Gatera M, Karema C, Nutt CT, Ngabo F. Achieving high coverage in Rwanda's national human papillomavirus vaccination programme. *Bull World Health Organ*. 2012;90(8):623–628
 56. Botha MH, van der Merwe FH, Snyman LC, Dreyer G. The vaccine and cervical cancer screen (VACCS) project: acceptance of human papillomavirus vaccination in a school-based programme in two provinces of South Africa. *S Afr Med J*. 2015;105(1):40–43
 57. Brabin L, Roberts SA, Stretch R, et al. Uptake of first two doses of human papillomavirus vaccine by adolescent schoolgirls in Manchester: prospective cohort study. *BMJ*. 2008;336(7652):1056–1058
 58. Brotherton JML, Murray SL, Hall MA, et al. Human papillomavirus vaccine coverage among female Australian adolescents: success of the school-based approach. *Med J Aust*. 2013;199(9):614–617
 59. 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
 60. Caskey RN, Macario E, Johnson DC, Hamlisch T, Alexander KA. A school-located vaccination adolescent pilot initiative in Chicago: lessons learned. *J Pediatric Infect Dis Soc*. 2013;2(3):198–204
 61. Chadenier GMC, Colzani E, Faccini M, Borriello CR, Bonazzi C. Assessment of the first HPV vaccination campaign in two northern Italian health districts. *Vaccine*. 2011;29(26):4405–4408
 62. 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
 63. 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
 64. Fregnani JHTG, Carvalho AL, Eluf-Neto J, et al. A school-based human papillomavirus vaccination program in Barretos, Brazil: final results of a demonstrative study. *PLoS One*. 2013;8(4):e62647
 65. Gold R, Naleway AL, Jenkins LL, et al. Completion and timing of the three-dose human papillomavirus vaccine series among adolescents attending school-based health centers in Oregon. *Prev Med*. 2011;52(6):456–458
 66. Kempe A, Barrow J, Stokley S, et al. Effectiveness and cost of immunization recall at school-based health centers. *Pediatrics*. 2012;129(6). Available at: www.pediatrics.org/cgi/content/full/129/6/e1446
 67. 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
 68. Kury C, Kury M, Silva R, et al. Implementation of the quadrivalent vaccine against HPV in the Municipality of Campos dos Goytacazes, Brazil—a combination of strategies to increase immunization coverage and early reduction of genital warts. *Trials Vaccinol*. 2013;2:19–24
 69. 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
 70. Moodley I, Tathiah N, Mubaiwa V, Denny L. High uptake of Gardasil vaccine among 9–12-year-old schoolgirls participating in an HPV vaccination demonstration project in KwaZulu-Natal, South Africa. *S Afr Med J*. 2013;103(5):318–321
 71. Rickert VI, Auslander BA, Cox DS, Rosenthal SL, Rupp RE, Zimet GD. School-based HPV immunization of young adolescents: effects of two brief health interventions. *Hum Vaccin Immunother*. 2015;11(2):315–321
 72. Sinka K, Kavanagh K, Gordon R, et al. Achieving high and equitable coverage of adolescent HPV vaccine in Scotland. *J Epidemiol Community Health*. 2014;68(1):57–63
 73. 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
 74. 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
 75. 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
 76. Watson-Jones D, Baisley K, Ponsiano R, et al. HPV vaccination in Tanzanian schoolgirls: cluster-randomised trial comparing two vaccine delivery strategies. *J Infect Dis*. 2012;206(5):678–686
 77. LaMontagne DS, Barge S, Le NT, et al. Human papillomavirus vaccine delivery strategies that achieved high

- coverage in low- and middle-income countries. *Bull World Health Organ.* 2011;89(11):821–830B
78. Navarrete J, Padilla M, Castro L, Rivera J. Development of a community pharmacy human papillomavirus vaccine program for under-insured university students along the United States/Mexico border. *J Am Pharm Assoc (2003)*. 2014;54(6):642–647
79. Centers for Disease Control and Prevention. Overview of AFIX. Available at: www.cdc.gov/vaccines/programs/afix/about/overview.html. Accessed September 5, 2015
80. Cox DS, Cox AD, Sturm L, Zimet G. Behavioral interventions to increase HPV vaccination acceptability among mothers of young girls. *Health Psychol.* 2010;29(1):29–39
81. Kreimer AR, Struyf F, Del Rosario-Raymundo MR, et al; Costa Rica Vaccine Trial Study Group Authors; PATRICIA Study Group Authors; HPV PATRICIA Principal Investigators/Co-Principal Investigator Collaborators; GSK Vaccines Clinical Study Support Group. Efficacy of fewer than three doses of an HPV-16/18 AS04-adjuvanted vaccine: combined analysis of data from the Costa Rica Vaccine and PATRICIA Trials. *Lancet Oncol.* 2015;16(7):775–786
82. Centers for Disease Control and Prevention. 2014 NIS Teen Vaccination Coverage Table Data. Available at: www.cdc.gov/vaccines/imz-managers/coverage/nis/teen/data/tables-2014.html#overall. Accessed September 12, 2015

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