

REVIEW

HPV vaccination: Population approaches for improving rates

Kristin Oliver, Alean Frawley, and Elizabeth Garland

Department of Preventive Medicine, Icahn School of Medicine at Mount Sinai, New York, NY, USA

ABSTRACT

Objective: To review the literature on interventions to increase HPV vaccinations and assess whether The Community Preventive Services Task Force recommendations are supported by current evidence. **Methods:** We used a PubMed search to identify studies that assessed interventions that looked at provider assessment and feedback, provider reminders, client reminder and recall, and clinic based education programs. **Results:** Of the 13 studies identified, 8 included client reminder and recall interventions, 4 included provider assessment and feedback and/or provider reminders and 2 included clinic based education. 11 of the 13 studies demonstrated a positive effect on HPV vaccine initiation or completion. Provider assessment and feedback studies were more likely to report a positive effect on HPV vaccine initiation than on series completion, while client reminder recall interventions more frequently produced an effect on series completion than on initiation. **Conclusions:** There is evidence to support the application of the Community Preventive Services Task Force recommendations specifically to HPV vaccination both for client reminder and recall programs and for provider assessment and feedback interventions. Multiple targeted approaches will be needed to substantially impact HPV vaccine rates.

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Introduction

Human papilloma virus (HPV) causes significant, preventable morbidity and mortality in the United States (US). Cervical cancer is the most common cancer caused by HPV. Approximately 11,000 women in the US are diagnosed with¹ and 4,000 women will die from cervical cancer each year.² HPV is also responsible for many cancers of the anus, penis, vagina, vulva and oropharynx. In particular, anal and oropharyngeal cancers have been rising over the past 3 decades and account for approximately 4,000 and 9,000 cancers per year respectively.¹

Three vaccines are currently available that can protect against the strains that cause most HPV related cancers: HPV2 (Cervarix), HPV4 (Gardasil) and HPV9 (Gardasil 9). These vaccines are recommended by the Advisory Committee on Immunization Practices (ACIP) for males (HPV4 and HPV9) and females (HPV2, HPV4, HPV9) beginning at 11–12 y of age.³ All HPV vaccines are given as a three dose series and can be administered at the same time as the other vaccines in the adolescent platform: tetanus-diphtheria-acellular pertussis (Tdap) and meningococcal conjugate (MenACWY) vaccine.⁴ Rates of HPV immunization have been rising since the vaccine was introduced in 2006. However, immunization rates continue to lag behind coverage for Tdap and MenACWY among adolescents age 13–17 y. As of 2014, 60% of females and 41% of males had initiated the HPV vaccine and 40% of females and 21% of males completed all 3 doses.⁵ In comparison, 88% of adolescents received Tdap and 79% received meningococcal vaccine.⁵ The reasons for this lag are multifactorial and involve both physician and patient factors. For HPV vaccine initiation, studies have shown that many primary care physicians do not

strongly recommend the HPV vaccine for their 11 to 12 year-old patients^{6,7} and those that do recommend it less strongly than the Tdap or meningococcal vaccine.⁸ Parents also view the vaccine differently than the other adolescent vaccines, believing it is not needed, particularly in 11–12 y of age, so far in advance of sexual activity.⁹ Series completion is complicated by the low percentage of adolescents that seek preventive care visits.¹⁰

The Community Preventive Services Task Force (Task Force), an expert panel established by the Department of Health and Human Services, conducts systematic reviews to identify proven, effective, population-based health interventions.¹¹ The Task Force recommends evidence-based strategies to increase vaccination rates and has identified some strategies for which there is insufficient evidence to recommend.¹¹ This article assesses the extent to which specific evidence for HPV vaccines supports the vaccination interventions recommended by the Guide to Community Preventive Services (Community Guide). We look at the categories of Provider Assessment and Feedback, Provider Reminders, Client Reminder and Recall, and Clinic Based Education.

Provider assessment and feedback

In 2000 the Task Force recommended the use of i) provider assessment and feedback and ii) provider reminders to increase vaccination rates.¹¹ Provider assessment and feedback includes interventions that give vaccination providers periodic data on their vaccination rates in their patient population. The feedback portion ranges from comparison of

rates between providers in a practice or geographic area to more extensive problem-solving and the development of strategies to improve rates.¹² CDC's Assessment, Feedback, Incentives, and eXchanges (AFIX) program is one highly validated, robust example.¹³

In their original systematic review, the Task Force's report included studies from 1980–1997 and found that assessment and feedback increased vaccination coverage 17% on average when used alone and 16% when used with other components. An update based on published evidence from 1997–2007 found an increase of 11% for assessment and feedback alone and 6% for assessment and feedback in conjunction with other components.¹² Fewer studies (7 study arms) evaluated assessment and feedback alone versus in conjunction with other components (13 study arms) which likely explains the smaller effect size of the former). None of the studies in either Task Force review focused on vaccines in the adolescent platform.

Provider reminders

The Task Force also recommends interventions that use provider reminders to increase vaccination rates for adults, children, and adolescents.¹¹ These reminders alert the providers when a specific patient is due for a vaccine. They may include notes on charts, electronic medical record alerts, or lists of patients overdue for vaccines for each day's schedule. The original report in 2000 identified an increase of 17% when reminders were used alone and 16% when combined with additional components. An updated review of the evidence from 1997–2007 found an increase of 12% when used alone and 10% when combined with additional interventions.¹⁴ Again, fewer studies examined reminders used alone, likely explaining the larger effect size.

Client reminder and recall systems

Client reminder and recall systems use various methods to alert patients that they are due (reminder) or overdue (recall) for specific vaccines. The Task Force recommends these interventions either alone or with other programs based on a review of evidence from 1997 to 2012. They found that used alone they increased immunization rates 6% on average and 12% when used in conjunction with other interventions. Their findings specifically mention the need for additional studies of these interventions in adolescent populations and with HPV vaccine.¹⁵

Clinic-based client education

In a systematic review in 2011 (updated with one study in 2012), the Task Force found insufficient evidence to determine the effectiveness of clinic-based education when implemented alone for increasing vaccination rates. The interventions studied included any approach delivered in advance of the client-provider visit. However, because these studies all involved pneumococcal polysaccharide vaccine uptake among older adults with very low baseline coverage, it is unclear what application these findings have to adolescent populations.¹¹

Results

We identified 13 studies that met our inclusion criteria. The majority of studies evaluated client reminder and recall systems, followed by provider assessment and feedback, provider reminders, and clinic-based education.

Client reminder and recall systems

We identified 8 studies that investigated the impact of client reminder recall systems on HPV vaccination. Only two studies included males in the study population.^{17,18} The study sites varied from urban to suburban and included both outpatient private practices and hospital-based practices. Interventions studied included letters, telephone calls, and text messages or a combination of these methods. All but one of the studies reported at least one positive effect of the interventions on HPV vaccination rates.

Of the studies using mailed letter reminders, one study sent patients quarterly reminder letters until HPV series completion. The result was a 10% absolute increase in HPV series completion compared to the control group.¹⁹ The other study that used mailed letters found a statistically significant increase in series completion but not initiation (hazard ratio of 1.5).²⁰

Four studies used telephone call reminders. One used a combination of parental education with an electronically prompted reminder call for HPV doses 2 and 3 and found a statistically significant increase in series completion compared to historical controls (OR 22).²¹ Another study compared the effects of telephone reminders for families with programs with provider assessment and feedback, education and provider reminders to a nonintervention group. They found the combined intervention increased both HPV initiation (9% relative increase) and series completion (13% relative increase), while the client based telephone reminder only interventions increased series completion (11%) but did not affect initiation.²² The third study, looked at only telephone reminder calls and likewise found a significant increase in completion but not initiation (HR 1.5).²⁰ One study used a combination of 2 phone calls and 2 letters for the adolescent platform vaccine reminders in the intervention group. HPV initiation rates in females increased 11% compared to those who did not get the reminders.²³

Three studies investigated the use of text messages reminders. One found a significant increase in on-time second and third doses of HPV when compared to both historical controls and a group who opted out of the texts (AOR 1.8 and 2 respectively).²⁴ A second study also found a significant difference in receipt of dose 2 and 3 and on-time receipt between intervention participants and patients who either opted-out of the text messages, did not complete the sign up or were not offered the reminders. The difference was significant in both males and females.¹⁸ Effects should be interpreted with caution because of the risk of bias in control groups for both of these studies: a third study that randomized participants to receive a text reminder for HPV vs. a general adolescent educational reminder found an effect on HPV vaccine receipt only after excluding participants who opted out after the first text message.¹⁷

Only three studies included a description of the costs associated with the reminders. One study reported the cost per reminder was similar between mail and telephone reminders (\$18.78 and \$16.68 respectively).²⁰ Another study found a combination of mailed letters and an autodialer phone reminder resulted in net revenue for the study practices.²³ None of the studies that used text messaging included cost data.

Provider assessment and feedback and provider reminders

We identified 4 studies that examined the use of provider assessment and feedback on HPV vaccination rates.^{22,25-28} None of these studies were completed at the time of the Task Force's systematic review. All of these studies included additional components combined with provider assessment and feedback. Three included an additional provider education component^{22,26,28} and 2 combined assessment and feedback with provider reminders.^{22,25,27} The studies were conducted in diverse practice settings and geographic locations including urban, suburban and rural settings and included patients with public and private insurance. Only 1 study included both males and females.²⁸ Three of the 4 studies reported at least one positive effect of the interventions.^{22,26-28}

One study specifically evaluated CDC's Assessment, Feedback, Incentives, and eXchanges (AFIX) program.²⁶ They found for 11–12 y old females that an in-person consultation produced a 1.5% increase of HPV initiation and a webinar produced a 1.9% increase, compared to the control group. HPV series completion rates were not affected by the AFIX program in this age group. However, in the 13–18 y old group, while there was no effect on HPV vaccine initiation rates, there was a slight increase (0.7 %) in series completion at sites that received the in person consultation. The effects described above were seen at the 5 month follow-up; at the 1 y follow-up there was no difference in coverage for initiation or completion in either age group.²⁶

Another study examined the AFIX approach in conjunction with academic detailing that included frequent, focused, education and feedback sessions with intervention practices, along with incentives (Maintenance of Certification credit).²⁸ During the active intervention period, initiation of the HPV series among 11–21 y old females was significantly higher in intervention practices (OR 1.6). This effect did not persist 6 months following the intervention period. The odds of HPV vaccine initiation among males was also significantly higher in the intervention practices (OR 11), and this effect was sustained in the 6 months post-intervention (OR 8.5).²⁸

Of the two studies that evaluated provider assessment and feedback in conjunction with provider reminders, one did not demonstrate an effect on HPV vaccine rates.²⁵ The other program was effective in increasing HPV initiation among females ages 11–17 (8 % increase) but did not affect series completion.²² A secondary analysis of this program that included only patients who had a visit during the study period found that the intervention increased both HPV initiation and completion. The effect was larger for initiation at preventive care visits and for series completion at acute visits (8.5% and 11.3% respectively).²⁷

In addition to the studies described above that combined assessment and feedback with provider reminders,^{22,25,27} 1 study investigated the effect of provider reminders alone.²⁹ This study found no effect of electronic health record provider prompts on HPV vaccine initiation or completion in females compared to a standard of care control group.

Clinic based education

We identified 2 studies that examined clinic-based education. Only 1 study addressed both adolescent boys and girls.³⁰ This study was unique in that it examined 2 interventions alone and in combination. Postcards were sent to the parents of adolescents who did not have a HPV vaccination claim on record. The postcard relayed information about HPV vaccine benefits, costs, side effects and safety and encouraged parents to discuss vaccination with their child's health care provider. In the clinic, these previously identified adolescents were offered a health information technology (HIT) program on a computer tablet. The program assessed the adolescent's interest in learning about the HPV vaccine and this information was passed on in real time to the provider. Adolescents who participated in the HIT and whose parents received the postcard had higher rates of HPV vaccine initiation than either arm alone, with girls responding better than boys in all arms.

The second article studied the impact of an educational brochure and telephone reminders on vaccine uptake and completion rates in a small private practice.²¹ The convenience sample had higher rates of HPV vaccine initiation and completion (OR 9 and 22 respectively) compared to historical controls, though most parents stated that it was the provider recommendation that contributed most to their decision-making. The effect of the education component could not be separated from the reminder calls.

Discussion

Our review found evidence to support the use of Community Preventive Services Task Force recommendations for client reminder and recall interventions, and provider assessment and feedback programs, alone and in conjunction with other components to improve HPV immunization rates. The evidence supported client reminder and recall systems most strongly, followed by provider assessment and feedback programs. While the Task Force also recommends provider reminder systems, our review found mixed evidence of the effectiveness of these interventions both alone and combined with other programs. Very few studies that met our inclusion criteria were available on clinic-based education used alone, which reflects the Task Force findings that there is currently insufficient evidence to recommend their wide-spread use.

HPV vaccine is unique in the adolescent vaccine platform in that it involves a 3-dose series, creating different challenges for initiation versus series completion that will likely require different approaches. We found that provider assessment and feedback studies were more likely to report a positive effect on HPV vaccine initiation than on series completion, while client reminder recall interventions more frequently found an effect on series completion than on initiation.

As has been reported elsewhere^{16,31} the effect size in many of the studies to increase HPV vaccination rates is lower than for childhood immunizations. We found a similar trend, with rates reported in the Community Guide higher than many rates in our review. Three studies compared intervention effects between Tdap, meningococcal, and HPV vaccine. One found a stronger effect on Tdap and meningococcal,²⁶ another found a similar effect size across the 3 vaccines,²⁹ and the third found a slightly higher effect size for HPV.²³

Our findings differed from the Community Guide in the area of provider reminders. This may be due to the limited number of studies that used provider reminders to improve HPV vaccine rates. In their report the Task Force noted that “a subset of the included evidence, however, suggests that standing orders may be more effective in improving vaccination rates in both inpatient and outpatient settings than a provider reminder system.”¹⁴ A brief PubMed search identified only one study on standing orders for HPV vaccines but the outcome investigated was perceived acceptability of standing orders, not vaccination rates and was conducted in the OBGYN office setting.³² This is an area that would benefit from additional investigation specifically for HPV vaccines.

Only 3 studies in our review included both males and females. For all 3 studies the effect was similar for males and females. While this is encouraging, more studies are needed to focus on interventions that will increase rates for males in particular as they continue to lag behind females.

While none of the studies in our review looked specifically at the effects of a strong provider recommendation, many included an additional provider education component that likely contributed to the effects observed.

Many of the studies in our review used quasi-experimental designs, historical controls, or control groups with a high risk of selection bias, which may limit the strength of their findings. However, the consistency of the findings across studies supports their validity.

Methods

We searched the PubMed database to identify studies on interventions that affected HPV vaccination rates. We used keywords (human papilloma virus, vaccine, intervention studies, randomized). In addition, references of retrieved papers and a recent systematic review¹⁶ were used to identify additional studies. We excluded articles written in languages other than English, studies that reported outcomes on vaccine intention rather than vaccination rates, studies that did not include a control group, studies on adults only, studies conducted in countries outside North America, Europe and Australia, and studies for which we were unable to obtain the full text. We extracted critical elements from the studies into a standardized data form. Some studies assessed multiple interventions – these interventions were considered both alone and, where possible, in combination based on the outcome data.

Conclusions

There is evidence to support the application of the Community Preventive Services Task Force recommendations specifically to

HPV vaccination both for client reminder and recall programs and for provider assessment and feedback interventions. The current studies point to better success with interventions that include multiple components, and indicate different approaches for HPV vaccine initiation vs. series completion may be necessary. Multiple targeted approaches are needed to substantially impact HPV vaccine rates.

Disclosure of potential conflicts of interest

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