

Overcoming Barriers to Adherence to HPV Vaccination Recommendations

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Abstract

Human papillomavirus (HPV) is a critical factor in the development of cervical cancer and can lead to genital warts and other clinical sequelae. Two vaccines against HPV have been developed recently that have shown to be safe and effective. The use of HPV vaccines holds promise for alleviating the burden of illness related to HPV infection. However, barriers specific to HPV vaccines, as well as barriers related to adolescent vaccination in general, may pose challenges to widespread implementation. Among these are: (1) lack of knowledge among the US population about HPV transmission and its relation to cervical cancer and other anogenital diseases; (2) parental concerns about vaccines in general and about vaccinating minors against sexually transmitted diseases; (3) financing by the government and private insurers for newly recommended vaccines; (4) challenges related to adolescents' healthcare-seeking behavior and health insurance coverage; and (5) barriers related to the dynamics of HPV infection (eg, protection against only certain types of HPV, duration of immunity, immunization schedules). Addressing these concerns will be critical in effective implementation of HPV vaccines and, potentially, vaccines against other sexually transmitted diseases.

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Vaccines are among the most cost-effective interventions in healthcare, but economic factors may interfere with their optimal delivery and utilization. This may be particularly true for vaccines against human papillomavirus (HPV), which have several unique characteristics that set them apart from other vaccines. This article discusses potential barriers to HPV vaccination related to public perceptions, vaccine economics, practice infrastructure, and the dynamics of HPV infection. To be successful, HPV vaccination efforts must address the concerns of healthcare providers, parents, and adolescent patients involved in the decision to be vaccinated against HPV.

Challenges to HPV Vaccination

It is now widely accepted that infection with HPV is a necessary, although not sufficient, etiologic agent in the development of virtually all cases of cervical cancer.¹ HPV infection can also lead to other significant clinical sequelae, including genital warts, precancerous cervical dysplasia, laryngeal papillomatosis, other anogenital cancers, and possibly some head and neck cancers.²

Two HPV vaccines have recently been developed and shown in large-scale clinical trials to be immunogenic, safe, and highly effective in preventing cervical dysplasia and (for 1 of the vaccines) genital warts.³⁻⁸ One of these vaccines was recently licensed by the US Food and Drug Administration for use in adolescent and young adult women,⁹ and approval may be expanded in the future to include males and older adults, as additional clinical trial data become available. If widely utilized, these vaccines could have a substantial impact on reducing the burden of HPV-associated illnesses within the population. However, barriers specific to HPV vaccines, as well as barriers related to adolescent vaccination in general, may pose challenges to their implementation.

Perceptions of HPV Infection

Studies consistently demonstrate that the US population generally has little awareness or knowledge of HPV, and that there is a pervasive lack of understanding that HPV is sexually transmitted, or that HPV infection is linked to anogenital diseases like cervical cancer or genital warts.¹⁰⁻¹⁵ For example, in a study of 321 college students, only one

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third had ever heard of HPV, only 17% correctly indicated that HPV was sexually transmitted, and only 2% identified HPV infection as a risk factor for cervical cancer.¹¹ Similar results have been found among adolescent and adult populations.^{10,12,13}

The general lack of knowledge about HPV may explain why the risk of acquiring HPV infection, or of developing HPV-related disease, is commonly underestimated, both at the individual and societal levels.¹¹ Such a low perception of risk is likely to impair community demand for HPV vaccination. As a consequence, significant and sustained public educational efforts designed to raise awareness about HPV and the benefits of HPV immunization will be necessary to ensure that these vaccines are widely utilized. Public education may be especially important if policies promoting HPV vaccination in males are adopted in the future, because the degree of clinical benefits afforded to males by HPV vaccination is likely to be less than that of females. Focusing additional attention on the indirect benefits provided to women by widespread HPV vaccination of men (“herd immunity”) may be useful for promoting the use of these vaccines among both sexes.

The perceptions of parents about HPV vaccines will also be critical to HPV vaccination success, because parental consent will be required to administer HPV vaccines to minor children. Significant lay media attention has focused on the possibility that the sexual nature of HPV transmission may significantly hinder parental acceptance of these vaccines, which could, in turn, lead to their underutilization. For example, one oft-cited concern is that parental consent to HPV vaccination may be misconstrued by adolescent children as condoning early sexual activity. Another is that parents (or physicians) will find it insurmountably difficult to explain to young adolescent children the need for vaccination against a sexually transmitted infection (STI).

Despite the extensive media attention given to these types of concerns, research on parental attitudes about vaccines actually suggests that opposition to vaccination against STIs in general, or to HPV vaccination in particular, is not widespread.¹⁶⁻²²

Studies indicate that the majority of parents favor HPV vaccination, with 65% to 84% indicating that they would want their child immunized against HPV if the vaccine were available.^{16,17,20} Furthermore, in a qualitative study that explored in depth the parental attitudes about vaccination against STIs, including HPV, the perception that their children were at low risk for contracting the infection or a lack of understanding that vaccination is most beneficial if performed before the onset of sexual activity were found as the primary reasons for rejecting vaccination, as opposed to concerns about promoting sexual activity.¹⁸ Moreover, in another study that evaluated the relative contribution of 4 different vaccine characteristics on parental vaccine acceptability—disease transmissibility (STI vs non-STI), severity of infection prevented by vaccination, vaccine efficacy, and availability of behavioral methods to prevent infection—there was little difference between STI and non-STI vaccines.¹⁹ Factors such as disease severity and vaccine efficacy were comparatively much more influential for parents.

Taken together, these results suggest that the sexual transmissibility of HPV may not be a significant barrier to parental consent for HPV vaccination for their children, and indicate that educational efforts may be better directed toward other issues, such as describing vaccine efficacy or the high prevalence of HPV infection among adolescents. In addition, the concerns of other groups with interest in adolescent health, such as teachers, schools, and religious organizations, will also need to be addressed.

In addition to concerns related specifically to HPV vaccines, misperceptions about the safety of vaccination in general may pose additional barriers to the use of these vaccines. For example, although serious adverse events related to vaccination are exceedingly rare,²³ they garner a disproportionately high level of media attention, leading many parents and patients to be suspicious of new vaccines that do not yet have a long-standing track record of safety.²⁴ A litany of other misperceptions about vaccine safety add to the fear of vaccination, such as concerns that administering too many vaccines during childhood can “overwhelm the system,” lead-

ing to a weakened immune state^{25,26}; that vaccines may actually cause the disease they are designed to prevent²⁷; or that vaccination may cause other health problems, such as autism or allergies.^{27,28} The large number of studies that allay these concerns may not be enough to substantially impact public opinion about the safety of vaccination.²⁹⁻³¹

Vaccine Financing for Adolescents

As the number of recommended childhood and adolescent vaccines increases and vaccines become increasingly expensive,^{32,33} financing for newly recommended vaccines grows as a potential barrier. At an announced retail price of \$120 per dose (\$360 per series) for the quadrivalent HPV vaccine,³⁴ the adolescent HPV vaccination series will be the most expensive series ever universally recommended by the Advisory Committee on Immunization Practice (ACIP) of the Centers for Disease Control and Prevention.

In the private insurance market, parents and their adolescents will face the question of whether their plans cover all or part of the vaccine cost. Other costly vaccines that have recently been recommended (such as the pneumococcal conjugate vaccine, which was the most expensive vaccine series ever universally recommended at its introduction in spring 2000) have been covered by most, but not all, private health plans within a year of their recommendation by ACIP.³⁵

Lack of health plan coverage leaves parents with a variety of options for their children: (1) pay out of pocket for the vaccine series; (2) appeal to their health plan medical director and hope that the appeal succeeds and coverage for a vaccine is approved as a benefit; (3) wait to vaccinate, in hopes that the health plan will approve coverage in the future; (4) seek financing for the vaccines through public programs financed at the federal or state level. These options will be discussed further below.

Of note, a recent national study found that 4 of every 5 parents would, if given the opportunity, pay a modest amount (\$3-\$6) more per month in family health plan premiums to guarantee that their private health plans would cover all new vaccines recommended by ACIP.³⁶ From an actuarial per-

spective, \$6 more per month greatly exceeds the increase in premiums that would result if a health plan decided to cover HPV vaccine for its eligible population. Healthcare providers can advise parents who want HPV coverage for their adolescents to lobby their employers and plan benefits boards for such coverage. Such appeals from plan enrollees may be more effective than appeals from healthcare providers themselves.

In the public sector, the federal Vaccines for Children (VFC) pays for all ACIP-recommended vaccines for children and adolescents who are enrolled in Medicaid, who are uninsured, who are of American Indian or Alaska Native heritage, or who are underinsured and seek vaccination in federally qualified health centers or rural health centers.³³ As an entitlement program, VFC assures qualified children and adolescents free recommended vaccines, and the federal government pays prices for these vaccines that are discounted slightly from retail prices paid in the private market. The quadrivalent HPV vaccine manufactured by Merck & Co was added to the VFC program in late 2006.

For adolescents to receive VFC-purchased vaccine, physicians must participate in the VFC program. Formal participation is required because vaccine doses are distributed by the government free of charge to VFC-enrolled healthcare providers, who then must store, administer, and track the distributed doses separately from doses of the same vaccines that these providers purchase from manufacturers and distributors for administration to their private patients. The proportion of children younger than 36 months who receive recommended vaccine series from VFC-participating healthcare providers differs substantively across states (from 80% to 99%),³⁷ for reasons that are not altogether clear; similar data are not yet available for adolescent vaccinations.

Although adolescents and their parents can anticipate that the vast majority of pediatricians and family physicians participate in the VFC program, it is unlikely that many obstetrics/gynecology practices will participate in, or even be familiar, with it. To the extent that HPV vaccine is administered to adolescents in obstetrics/gynecology practices, participation of these practices in VFC

will be critical to the success of HPV vaccination efforts in 2 key respects. First, provider participation in VFC assures that adolescents who are VFC-eligible will be able to receive the vaccine free of charge. Without obstetricians/gynecologists participating in VFC, VFC-eligible adolescents will potentially face a 2-tiered system in which privately insured teens can receive the vaccine in these clinics but adolescents who are on Medicaid or uninsured (who together comprise more than 90% of VFC-eligible children³⁷) cannot. Second, in selected states, the state government allocates additional funds to purchase ACIP-recommended vaccines so that privately insured children whose plans do not cover all recommended vaccines (a situation called “underinsurance”) can receive such vaccines in participating private practices. In other words, these states extend the VFC provisions for underinsured children (which are limited under VFC to federally qualified health centers and rural health centers) to private practice settings. In states where funds are available to support vaccination for the underinsured in this way, participation by providers in underinsured programs often goes hand in hand with VFC participation. Thus, facilitating VFC enrollment of obstetricians/gynecologists could have a substantial impact on HPV vaccination rates, especially in settings where a high percentage of adolescents receive the majority of their care through obstetricians/gynecologists.

Because of the anticipated cost of the HPV series, state-level provisions for underinsurance will be particularly important for HPV vaccine—not just in obstetrician/gynecology practice settings, but in pediatrics and family practice settings as well. As vaccines have become more numerous and more expensive, states have begun to taper back on the vaccines for which they allocate public funds for purchase.³⁸ The vaccines they have generally been more reluctant to fund have been those that are more expensive (eg, pneumococcal conjugate vaccine series). Whether HPV vaccine will be broadly funded by such states for underinsured adolescents will likely depend on the anticipated effectiveness of the vac-

cine and the public demand for the vaccine as perceived by state immunization program officials and state legislators, who advise and ultimately appropriate state monies, respectively, for initiatives to vaccinate underinsured children.

A final point to consider regarding financing for HPV vaccine is that no public purchase program currently exists for non-elderly adults’ recommended vaccinations. Therefore, young adults without private insurance may be left with the decision of whether to pay out of pocket for HPV vaccination, unless individual states decide to make the vaccine available in public health departments and/or state Medicaid programs decide to cover the series as a benefit for beneficiaries.

Practice Infrastructure Barriers to Adolescent Vaccination

Challenges rooted in practice infrastructure may pose formidable barriers to successful implementation of an HPV vaccination program among adolescents. These challenges are chiefly related to patterns of adolescents’ healthcare-seeking behavior and to their insurance coverage.

National data indicate that adolescents seek routine healthcare less frequently than any other age group.³⁹ Moreover, until recently, adolescents have not typically sought healthcare that included vaccination as a common component; rather, they often require acute care and routine physical examinations for school or athletics.⁴⁰ With the recent recommendations of meningococcal conjugate vaccine and combined tetanus-diphtheria-acellular pertussis vaccine for adolescents, however,⁴¹ there is a growing awareness that adolescents’ visits may include vaccinations.

The expanding “adolescent platform” of newly recommended adolescent vaccinations may ultimately serve to draw adolescents in for routine healthcare on a more regular basis—as do the primary series of immunizations for young children. Such an effect will be magnified if states implement school entry mandates regarding newly recommended vaccines, similar to daycare and school entry mandates regarding the majority of vaccines that serve as the primary series for young

children. Daycare and school entry mandates have been associated with significantly higher vaccination coverage rates for children, above and beyond sociodemographic factors at the person and family levels,⁴² and recent analyses of school entry mandates for adolescents suggest that they may also work well to boost vaccination coverage for more recently recommended adolescent vaccines.⁴³

Another challenge is that adolescents are more likely to be uninsured than younger children.⁴⁴ Although the proportion of adolescents without insurance coverage has decreased from the mid-1990s (when the State Child Health Insurance Program came into effect), in 2002 more than 12% of adolescents were still uninsured.⁴⁴ The persistence of this problem has been attributed, in part, to recent declines in private insurance coverage for middle- and higher-income children. Even more important, lack of insurance remains disproportionately more common for adolescents living in households with an annual income less than the poverty line, with nearly 1 of every 5 poor adolescents uninsured.⁴⁴

Lack of insurance coverage may serve as a barrier to HPV vaccination in 3 ways. First, adolescents without health insurance coverage may be less likely to seek nonurgent or emergent healthcare in general, because of prohibitively high costs. Second, lack of coverage may lead adolescents who wish to get vaccinated against HPV to seek vaccination in settings such as teen clinics or school clinics, which are viewed as potential alternatives to traditional office practice settings for administration of HPV vaccine.⁴⁰ This could result in significant fragmentation of healthcare for adolescents, and would necessitate the potentially difficult task of coordinating the records of visits to school and other clinic sites with traditional office settings where adolescents may seek other care. Third, although uninsured adolescents will be eligible to receive HPV vaccine doses at no cost as part of the federal VFC program,³³ they may be unaware of this financial benefit and/or they may not attend a practice at which the providers participate in the program (as previously discussed).

Finally, based on studies that have explored physician attitudes of HPV vac-

cines,⁴⁵⁻⁴⁸ it appears that divergence between HPV vaccine recommendations and expected provider practices could also impact the utilization of HPV vaccines. The ACIP recommends HPV vaccines be "routinely given to girls when they are 11 or 12 years old,"⁴⁹ with catch-up immunization between the ages of 13 to 26 years, and vaccination allowable as young as age 9. Yet, studies of pediatricians, family practitioners, pediatric nurse practitioners, and gynecologists/obstetricians universally find that these practitioners are generally less inclined to recommend HPV vaccination for younger adolescents (11-13 years old) than for older ones (17 years old). It is postulated that this age effect may be due, at least in part, to provider reluctance to discuss sexuality with parents and minor children of younger ages. However, at least 1 study has found a similar age effect for a non-STI adolescent vaccine,⁴⁶ suggesting that other factors may also be influential. The extent to which individual provider attitudes, especially those that diverge from professional society recommendations, will affect overall HPV vaccine utilization remains to be determined.

Barriers Related to the Dynamics of HPV Infection

Aspects of the biology of HPV infection and limitations in our current knowledge about HPV vaccine performance may serve as additional barriers to successfully implementing HPV vaccines. There are more than 100 types of HPV that have been identified, and approximately 20 of these are considered to be oncogenic.² Because HPV vaccines protect against only a handful of HPV types, these vaccines in their current iteration are not expected to prevent all cases of cervical cancer or other HPV-related diseases, even in the setting of widespread utilization. This means that ongoing adherence to cervical dysplasia and cancer screening guidelines will be needed, and that some level of HPV-associated illnesses will persist in the population. The concept that HPV vaccines do not provide protection against all HPV-related illness differs from the more comprehensive protection against a given disease or pathogen associated with most

other vaccines, such as hepatitis B, pertussis, polio, and diphtheria, but is similar to the level of disease protection offered by pneumococcal conjugate vaccine and meningococcal conjugate vaccine. Because protection from HPV vaccines will not be complete, it will be important to continue to educate patients about the need for ongoing routine cervical cancer screening, even after having received HPV vaccination.

Additional challenges to HPV vaccine implementation relate to several unanswered questions about the biological performance of HPV vaccines and the expected biological consequences in the population after widespread HPV immunization. For example, the duration of immunity afforded by HPV vaccines, and whether booster doses will be necessary in the future to provide ongoing protection, is a key question that could influence (either positively or negatively) public motivation to be immunized against HPV. Thus far, high antibody titers appear to be sustained for a number of years,^{5,8} but longer-term studies are needed before the issue of booster doses can be adequately addressed. Similarly, it is unknown whether widespread HPV vaccine utilization will lead to HPV “type replacement” (emergence of other HPV types as the predominant cause of disease after a reduction in the prevalence of HPV infection from the types included in the vaccine),⁵⁰ which could impact the overall clinical effectiveness of HPV vaccines at a population level. However, current data on the dynamics of HPV infection suggest that type replacement is probably unlikely to occur.

Finally, medical providers have anecdotally expressed concern that the relative infrequency of preventive care visits during adolescence will make adherence to the recommended HPV vaccination schedule (3 doses within a 6- to 12-month period⁵¹) exceedingly difficult for this target group. Spreading the doses to yearly intervals to better coincide with annual school physicals is 1 strategy that might improve overall vaccine uptake among this age group, in part because the “inconvenience factor” for parents is minimized, and because changes in the current preventive care infrastructure for adolescents would not be required.

However, the efficacy of this approach has not been studied, and the effects of this lengthened dosage schedule on the ability of these vaccines to adequately protect against HPV infection are unknown. Moreover, many feel that adherence to the currently recommended HPV vaccination schedule provides an opportunity to motivate infrastructural changes in adolescent well-child care that could enhance the scope of preventive care services to this vulnerable age group.⁵² Before such a “sea change” in adolescent healthcare expectations can be realized though, issues related to staffing and reimbursement for these more frequent visits would need to be addressed.

Summary

HPV vaccines hold remarkable promise for alleviating the clinical burden of illnesses related to HPV infection. Despite this, the complexity of issues surrounding HPV vaccination specifically, combined with the challenges of adolescent immunization more generally, means that thoughtful and carefully planned vaccine implementation strategies will need to be developed to ensure that these vaccines are widely utilized. The manner in which practitioners, payers, and parents address the barriers to HPV vaccination will not only impact HPV vaccine usage directly, but will also foreshadow how future vaccines against other sexually transmitted diseases, such as human immunodeficiency virus or herpes simplex, may be received.

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