Optimizing Cancer Prevention in Adolescents by Improving HPV Vaccine Delivery

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Routine HPV vaccination can prevent six cancers. Best practices for achieving high adolescent HPV vaccination coverage include automatically scheduled appointments, presumptive provider recommendations, standing orders, feedback on vaccination rates, and incentives. Promising practices include school entry requirements and starting HPV vaccine recommendations and vaccine registry forecasting at age 9.

Introduction

An estimated 13 million new human papillomavirus (HPV) infections occur annually in the United States [1], most commonly among young adults [2, 3]. Persistent HPV infection causes cervical, vulvar, and vaginal cancer in women, penile cancer in men, and anal and oropharyngeal cancers in both sexes [4]. The United States has over 36,000 new HPV cancers each year [5]. Cervical cancer incidence in the United States varies across states, from 3.9 to 10.3 cases per 100,000 women annually [5], with only New Hampshire meeting the World Health Organization's Cervical Cancer Elimination Initiative goal of less than 4.0 [6]. As of 2021, oropharyngeal cancer incidence in men exceeded cervical cancer incidence in women, highlighting men as a critically important group for HPV cancer prevention [5].

Prevention of HPV infection through vaccination is the most widely accessible HPV cancer prevention method available given that routine screening is only available for cervical cancer. The immune response to HPV vaccination is strongest in the preteen years [7], and it persists for at least a decade. Thus, administration of two doses of the HPV vaccine to boys and girls before age 13 (i.e., up-to-date vaccination) is recommended by the US Centers for Disease Control and Prevention (CDC) to prevent HPV acquisition and HPV cancer development in adulthood [8].

Despite the clear need for early cancer prevention through HPV vaccination, complete and timely vaccination among US adolescents has been slow to reach the Healthy People 2030 goal of 80% coverage for up-to-date vaccination [9]. One problem is absent or low-quality HPV vaccine recommendations during, which a provider does not stress the importance of vaccination, describe the vaccine's role in cancer prevention, or recommend same-day vaccination [10]. In addition, caregiver hesitancy toward the vaccine, complexity of the multi-dose vaccination schedule, and lack of a school-entry requirement in most states have contributed to suboptimal vaccination rates.

North Carolina has a pressing need for HPV cancer prevention. The state's HPV cancer incidence is higher than the national incidence (13.2 versus 11.8 per 100,000) [5], with oropharyngeal cancers among men accounting for much of this difference. HPV vaccine initiation among 13-year-old North Carolinians was only 69% as of 2022, well below rates for other recommended adolescent vaccines: tetanus-diphtheria-acellular pertussis (85%) and meningococcal conjugate vaccines (85%) [11]. The up-to-date HPV vaccination rate was even lower, at 50%. In addition, up-to-date vaccination rates among adolescents from rural areas of the state and from underserved racial and ethnic groups tend to be even lower [12]. To ensure equitable and accessible HPV cancer prevention for all youth, primary care professionals, public health practitioners, and policymakers must strive to scale up effective HPV vaccination approaches and develop novel ones.

Best Practices

A best practice for increasing HPV vaccine uptake is a primary care professional's recommendation of HPV vaccine [13]. Clear and strong recommendations can counteract hesitancy or indifference toward vaccination, particularly in states where HPV vaccination is not required for middle school and caregivers can choose to opt out. An evidence-based intervention that fosters strong recommendation is the Announcement Approach Training [14]. In the training, providers and other clinical staff learn to start discussions by assuming that families will accept HPV vaccination along with other adolescent vaccines, removing any suggestion that the HPV vaccine is somehow different or less important than the school-required vaccines. CDC recommends co-administration with tetanus-diphtheria-acellular pertussis and meningococcal conjugate vaccines, which can reduce

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missed opportunities for HPV vaccination [15]. Parents with questions then get those answered using evidence-based scripts.

Systemic approaches that some call "nudges" can help caregivers make and keep vaccination appointments for their children. First, centralized reminder and recall systems inform caregivers of upcoming vaccinations and provide appointment reminders by relying on information in state and regional immunization information systems (IIS) or electronic medical records [16]. These centralized reminder and recall systems have had mixed success in boosting HPV vaccine uptake but have shown effectiveness for other recommended childhood and adolescent vaccines and require few resources to implement [17, 18]. Second, automatically scheduling appointments for the second HPV vaccine dose during the first dose visit, especially using IIS forecasting functions that automatically calculate the due date, can avoid missing the second dose and improve vaccine completion rates. Anchoring vaccinations to annual well-child visits also reduces scheduling confusion and forgetfulness, particularly if annual visits occur on or near the child's birthday [19]. Third, standing orders are effective in many settings and may be promising for HPV vaccination [20]. Finally, monitoring HPV vaccination coverage for health care systems, clinics, and providers, and even providing incentives for increasing their rates, increases motivation to recommend HPV vaccination consistently and strongly to eligible patients [21]. The North Carolina Department of Health and Human Services began reimbursing Medicaid providers for recommending COVID-19 vaccination to patients in 2021 [22], and ongoing studies are currently evaluating the effectiveness of provider incentives for HPV vaccination.

Promising Practices

An exciting opportunity to improve adolescent HPV vaccine coverage is the move toward recommending it at the earliest possible opportunity [23]. CDC recommends routine HPV vaccination at age 11 or 12 and says it can start as early as age 9, in line with FDA licensure [24]. The American Cancer Society and the American Academy of Pediatrics also recommend routine vaccination starting at age 9 [25, 26]. Recommending HPV vaccination at age 9 can encourage vaccination initiation and completion in several ways. First, compared to adolescents, younger patients are more likely to attend annual well-child checks [27], providing multiple convenient opportunities for vaccination by age 13. As the second HPV vaccine dose must be given within 12 months of the first, the earlier age allows more time to meet this goal. Second, the age 11–12 vaccine platform is already crowded with other vaccines, and over a quarter of providers will not administer more than two vaccines at one visit [28]. Initiating HPV vaccination earlier can space out the adolescent vaccination package and reduce the number of vaccines given in a single visit. Third, for caregivers who are concerned that HPV vaccination will encourage sexual activity, offering vaccination long before pubertal onset can alleviate this concern and increase uptake. Finally, if caregivers initially decline HPV vaccination at age 9, they still have ample time to consider it, plus additional opportunities for a provider to recommend it and provide education, while still achieving up-to-date vaccination by age 13. Several studies have shown that providers are willing and able to recommend HPV vaccination to their 9- and 10-year-old patients and that earlier recommendation is associated with higher rates of vaccination [19, 28–33].

All US jurisdictions have CDC funding to maintain IIS for monitoring childhood vaccination coverage [34]. These systems can now automatically estimate vaccine due dates and overdue dates based on a patient's age. Consulting a patient's IIS record before or during a clinic visit can easily guide the provider's vaccination recommendations. As these systems cover the vast majority of residents in each jurisdiction, they are invaluable for recommending HPV vaccination to as many age-eligible patients as possible [35–37]. While most IIS follow CDC recommendations for timing of HPV vaccination, several states have recently set age 9 as the recommended age for initiating vaccination. Washington State made this change in January 2023, and has already doubled the vaccination rates among these younger patients [38]. As of November 2023, nine states (Alabama, Illinois, Minnesota, North Carolina, North Dakota, Oregon, Texas, Utah, and Washington) set age 9 as the recommended age to initiate HPV vaccination and future research can determine the influence of these changes in rates of vaccination in those states. Improving interoperability of IIS with electronic health records and maintaining data and reporting standards can increase the utility of IIS support functions by ensuring that vaccination data are accurate, up to date, and consistent across health information systems [39, 40].

While middle school requirements for other adolescent vaccines are associated with higher uptake of these vaccines in North Carolina and most other states, only five US jurisdictions required HPV vaccination as of 2023: District of Columbia, Hawaii, Rhode Island, Virginia, and Puerto Rico [41, 42]. The effectiveness of school requirements is dependent on minimizing exemptions due to personal or religious beliefs, which are largely permitted in most states [43, 44]. In fact, in DC and Virginia personal belief exemptions are allowed exclusively for HPV vaccination [45], suggesting that school requirements alone may not be sufficient to overcome vaccine hesitancy. Stronger state legislation for HPV vaccine school entry requirements may help increase uptake as long as exemptions are only allowed for medical need.

Involving Key Stakeholders

Reducing the HPV cancer burden requires partnership with and support from diverse stakeholders that provide funding, data, and human power to carry out HPV vaccine research and program implementation, including:

The American Cancer Society, St. Jude Children's Research Hospital, and the National HPV Vaccination Roundtable (as well as the HPV Vaccination Roundtable of the Southeast, which provides training and collaboration opportunities among HPV vaccination stakeholders in states that historically have had the lowest vaccination coverage);

National and state chapters of the American Academy of Pediatrics, American Association of Family Physicians, and Pediatric Nurse Practitioner Association, which communicate recommendations and best practices to adolescent vaccine providers;

The Association of Immunization Managers, which shares information across jurisdictions on confronting immunization challenges and influencing immunization policy;

The North Carolina Department of Health and Human Services and its HPV Task Force, which brings together experts in HPV vaccination across the state to share resources and collaborate on research and programmatic efforts; and

HPV vaccine manufacturers, who have provided invaluable research funding and statewide advocacy to promote HPV vaccination in clinical settings.

North Carolina benefits from massive academic and clinical networks with unique capabilities for solving this pressing problem, and we anticipate that lessons learned from these partnerships can be disseminated and scaled up within the state and across the country. NCMJ

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