

FROM THE AMERICAN HEAD AND NECK SOCIETY

Expanding Indications for the Human Papillomavirus Vaccine One Small Step for the Prevention of Head and Neck Cancer, but One Giant Leap Remains

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In the US, the incidence of human papillomavirus (HPV)-related oropharyngeal cancer (OPC) has been growing at an alarming rate for the past 4 decades.¹⁻³ In 2011, HPV-related OPC was predicted to surpass cervical cancer in annual incidence in the US by 2020.² However, because of the continued decreasing incidence of cervical cancer and the accelerating incidence of OPC, HPV-related OPC actually surpassed cervical cancer to become the most common HPV-related malignancy in the US in 2015.⁴ Currently, nearly 19 000 new cases of HPV-related OPC are diagnosed in the US annually.⁵ The decrease in cervical cancer incidence is partially attributable to effective screening programs and the early detection of precancerous lesions.⁶ Unfortunately, effective screening tests for precancerous HPV-related lesions of the oropharynx are lacking. Therefore, the best opportunity to curb the epidemic of HPV-related OPC is through vaccination against the oncogenic strains of HPV responsible for OPC.⁴

Against this background, the announcement by the US Food and Drug Administration on June 12, 2020, to expand the indications for the 9-valent HPV (9vHPV) vaccine (Gardasil 9; Merck)⁷ to include the prevention of oropharyngeal and other head and neck cancers caused by HPV represents an important step forward in preventing HPV-related head and neck cancer (HNC). The expanded indication for the 9vHPV vaccine, which applies to males and females age 9 through 45 years, was issued based on biologic plausibility as well as epidemiologic and pharmacologic data.⁷ As a condition of the accelerated approval, further study is required to demonstrate the efficacy of the vaccine in preventing oral persistent infection (>6 months) with oncogenic HPV types in men age 20 through 45 years.^{7,8} The surrogate end point of persistent oral infection was chosen based on evidence that it is a clinically relevant intermediate end point for the prevention of HPV-related OPC.^{7,8}

The rate of HPV vaccine initiation and completion in the US, although improving over time, remains poor. It is estimated that only 53% of adolescent girls and 44% of adolescent boys were up to date on HPV vaccination in 2017.⁹ With such a poor HPV vaccination uptake, the potential gains of the expanded indication for the prevention of HPV-related OPC will never be fully realized. To date, our role as otolaryngologists and head and neck oncologists has been the treatment of HPV-related OPC, an interaction that occurs years after the causative infection and (potentially) years after missed opportunities for vaccination. Therefore, it is not surprising that we

have focused our efforts primarily on diagnosis and treatment of HPV-related OPC while neglecting our concomitant public health duties. In so doing, we are missing a critical opportunity to save lives, decrease morbidity, and practice cost-effective population health.¹⁰ This need not be the case any longer. To help transform this small step for preventing HNC into a giant leap, we offer the following 4 suggestions:

1. Launch a public health campaign to provide education and raise awareness that (1) HPV is a major cause of OPC, and (2) that there is now a vaccine that should be given to prevent HPV-related OPC.

Over the past 3 decades, we have made substantial strides raising awareness of the new patient with HNC within the otolaryngology and head and neck oncology communities.¹¹ However, marked knowledge gaps associated with HPV as a cause of OPC still exist among the lay public and broader medical community.¹² A recent survey of adults in the US found that 85% of men and 78% of women did not report knowing that HPV was a cause of oral cancer.¹³ Men are consistently less knowledgeable than women about HPV, the association between HPV and cancer, and HPV vaccination.^{13,14} This knowledge gap is particularly concerning because 75% of OPC cases occur in men. In addition, many primary care clinicians and pediatricians report being unaware of the etiologic link between HPV and OPC.¹² As a precondition to raising awareness that the HPV vaccine can prevent OPC, a substantial amount of education will be necessary to span the knowledge chasm in the lay population and general medical community.¹⁰

The recent expanded indication for the HPV vaccine provides a convenient and powerful opportunity for a public health campaign to improve knowledge and raise awareness across 2 key domains: (1) HPV is the major cause of OPC, and (2) there is now a vaccine that should be given to prevent HPV-related OPC. In addition, we should leverage existing community-based partnerships with OPC survivors, head and neck advocacy groups, and national organizations to disseminate information that HPV causes HNC and that there is now a vaccine that should be given to prevent HPV-related OPC. In today's environment, allaying public concerns about the vaccine's safety through multimodal educational efforts will be critical to achieving widespread uptake and will likely require the use of traditional and social media channels (eg, #cancervaccine, #stopthroatcancer, #hpvvaxforboys). Finally, the head and neck society, as well as national thought leaders, should continue to engage insurance companies and policy makers to align

incentives for education about the HPV-related OPC epidemic and the newly approved tool in our arsenal.

2. Improve our understanding of the barriers to HPV vaccine uptake among our target population.

There is a wealth of literature on the topic of barriers to HPV vaccination, with commonly reported barriers including safety, cost, attitudes, knowledge, perceived risk, social influences, and access to care.^{15,16} Recommendation by a health care professional is one of the most important factors in the decision to initiate and complete the HPV vaccine.¹⁶ Conversely, and of particular relevance to the current expanded indication, is that lack of perceived benefit of the HPV vaccine is one of the most frequently reported barriers for parents of sons.¹⁵ However, it is not understood how the lack of perceived benefit is associated specifically with the prevention of HPV-related OPC, limiting the potential for tailoring educational messages. Therefore, the expanded indication of the HPV vaccine to prevent HPV-related OPC provides an important opportunity for otolaryngology and head and neck oncology clinicians to contribute to improving our understanding of the determinants of HPV vaccine uptake in the US to optimize tailored messaging and evidence-based interventions in this clinical context.

3. Enhance ongoing efforts to develop and implement evidence-based interventions to improve HPV vaccination uptake.

Although otolaryngologists and head and neck oncology clinicians may feel removed from the day-to-day business of delivering vaccinations, we can enhance ongoing efforts to develop and implement evidence-based interventions to improve HPV vaccination uptake in numerous concrete ways. First, because recommendation by a health care professional is one of the strongest predictors of HPV vaccine uptake,¹⁶ it is incumbent on head and neck oncology clinicians to be at the vanguard. By virtue of our clinical care to patients with HPV-related OPC, we are uniquely positioned to deliver a timely, effective, and strong recommendation to patients, families, and the hopefully the public writ large about the importance of vaccination for preventing HPV-related OPC. Second, as a head and neck community, we should lead the discussion about how to craft an informed, thoughtful, and potentially tailored message about the benefit of HPV vaccination in preventing HPV-related OPC. Third, recognizing that it takes 17 years for evidence-based interventions to diffuse into clinical care, the head and neck oncology community should actively

contribute to the dissemination and implementation of multilevel, evidence-based interventions to increase uptake of HPV into widespread clinical practice.¹⁷ Fourth, recognizing the growing literature supporting alternative venues for vaccine delivery,¹⁸ the head and neck oncology community could explore the opportunity to participate directly in vaccine delivery when appropriate.

4. Develop strategic and sustained clinical, scientific, policy, and funding collaborations with relevant stakeholders across numerous fronts.

Although we have outlined several specific steps for the otolaryngology and head and neck communities, by virtue of our limited interaction with the population at large, we cannot affect the program that would be required to radically improve HPV vaccination uptake alone. Therefore, strategic and sustained clinical collaborations with pediatric, primary care, and family medicine communities, as well as scientific partnerships with population health and health care delivery researchers, will be necessary. These collaborative interactions may include presentations at their national meetings, sponsoring webinars, and hosting conference calls to help empower and enable these other clinicians who are more strategically positioned to help deliver the educational message to its intended audience. In addition, collaborating with policy makers and grant-funding agencies will be critically important to create an environment conducive to sustaining and accelerating research into HPV-related OPC and implementation efforts to improve HPV vaccine uptake.

The recent US Food and Drug Administration announcement that the 9vHPV vaccine is now indicated for preventing HPV-related OPC is an important moment in the fight against HNC. At that same time, it also reminds us how much work remains to be done. It is incumbent on us as a community to seize this critical opportunity and renew our dedication to cancer prevention. By (1) launching a public health campaign, (2) improving our understanding of the barriers to HPV vaccination uptake, (3) enhancing the development and implementation of evidence-based interventions to improve HPV vaccination uptake, and (4) developing varied, sustained, and strategic partnerships and engagements, we can hope to capitalize on this opportunity and prevent another generation of Americans from experiencing the debilitating and lethal effects of HPV-related OPC.

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