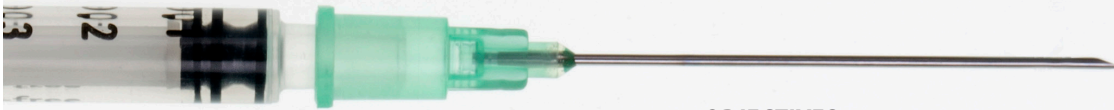


# Knowledge of HPV-Related Oropharyngeal Cancer and Use of Human Papillomavirus Vaccines by Pediatricians in Louisiana

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## OBJECTIVES

To determine the level of knowledge of HPV related oropharyngeal cancer and practice patterns of HPV vaccine use by pediatricians.

## STUDY DESIGN, SUBJECTS, METHODS

IRB approved 18-question survey was administered to members of the Louisiana Chapter of the American Academy of Pediatrics.

## RESULTS

We received 116 responses (response rate: 15.9%). 104 respondents (89.66%) routinely recommend/offer HPV vaccine, 6 (5.17%) occasionally or only at caregiver request, and 6 (5.17%) do not offer the vaccine. 17 (15.5%) reported having no awareness of the link between oropharyngeal cancer and HPV, and only 50 (45.9%) had knowledge that HPV-related oropharyngeal cancer incidence was increasing. Strength of recommendation for males and knowledge of HPV-related oropharyngeal cancer were not associated with years in practice, practice type or patient population served.

## CONCLUSIONS

Increased awareness regarding HPV-related oropharyngeal cancers among primary care providers may increase HPV immunization rates, especially in males.



## INTRODUCTION

The incidence of human papillomavirus (HPV) related oropharyngeal cancer (OPC) has increased by 225% over the past 30 years with HPV detection in OPC tumor specimens increasing 16% to 70%.<sup>1</sup> Males are diagnosed with the HPV-related OPC 5 times more often than women.<sup>1,2</sup> If current incidence trends continue, the annual incidence in the U.S. of HPV positive oropharyngeal cancer will surpass HPV related cervical cancer by 2020.<sup>1</sup> Several thousand U.S. adults are diagnosed with HPV positive OPC annually with an annual direct cost of over \$300 million to the national healthcare system.<sup>3,4</sup> While the overall survival for HPV positive OPC is excellent, the lifelong morbidity of treatment remains significant for those patients afflicted with this disease. Currently, there are no markers that would allow early identification of at-risk persons, which makes primary prevention of HPV infection through vaccination essential to preventing HPV (+) OPC.

In September 2010, the U.S. Food and Drug Administration's (FDA) Vaccines and Related Biological Products Advisory Committee and The Centers for Disease Control and Prevention (CDC)'s Advisory Committee on Immunization Practices (ACIP) expanded the recommendations for the HPV vaccine to include boys.<sup>5,6</sup> Despite this recommendation and the potential benefits to women and men, current vaccination rates for U.S. adolescents remain abysmal.<sup>7</sup> This is especially true for males who had vaccination rates of 1.4% in 2010 and who are disproportionately more often diagnosed with HPV positive OPC.<sup>1,2,7,8</sup>

HPV vaccination campaigns and research into HPV-related cancers have largely been limited to the impact on cervical cancer and the prevalence of infection in young women. Physicians are the most vital component in patient education, as they often hold the most trusted role on the health care team from a patient's perspective. The focus of this investigation was to ascertain practice patterns among pediatricians in Louisiana with regards to HPV vaccine administration and their understanding of the role of HPV in the development of OPC, as well as to determine whether knowledge gaps exist which would identify need for further education.

## METHODS

An eighteen-question survey was constructed. After obtaining Institutional Review Board approval from LSU Health Shreveport, the survey was sent electronically (Survey Monkey®), and a duplicate by mail, to all 730 members of the Louisiana Chapter of the American Academy of Pediatrics. Respondents provided informed consent and were not compensated for participating in the survey.

The questions were constructed based on a framework developed from national guidelines and existing literature. The initial questions were to determine if the provider routinely offered HPV vaccine, to what age group vaccine was offered, specifically gauging if the vaccine was offered to 11-12 year olds as recommended in national guidelines.<sup>9</sup> The next questions

were mainly focused on the factors associated with strength of recommendation including the patient's gender. The following questions were asked to gauge parents' response to the providers' recommendation and reasons for refusing the vaccine. The next series of questions focused on HPV associated oropharyngeal cancer and whether increased knowledge of the disease and its increasing incidence would influence providers' recommendation of the vaccine. Lastly, we gathered demographic data about the pediatricians including the number of years in practice, work setting, percentage of Medicaid funded patients, and gender. Pediatricians were chosen due to the majority of the HPV vaccines being delivered by providers in this specialty.<sup>10</sup>

Responses were received electronically or by return of the paper survey. All results were entered into Survey Monkey® to facilitate analysis. Eleven of the 18 questions were chosen for further examination via chi-square or Fisher exact test to determine statistical significance of correlations among specific question answers (i.e. length of practice, practice setting etc) with the knowledge about the vaccine, knowledge about HPV associated oropharyngeal cancer, and recommendation of the HPV vaccine for males. Statistical analysis was done using Stata 12.0.

## RESULTS

We received 116 responses, which was a response rate of 15.9%. About half the respondents (44.6%) have practiced for more than 16 years and 35.4% practiced for less than 5 years. Many of the practitioners (40.9%) belong to a single specialty group and 34.5% practiced in an academic hospital or in a public clinic. The majority of the respondents (55.4%) indicated that Medicaid funds more than 40% of their patients. The majority (60.9%) of the respondents were females (Table 1).

One hundred four (89.66%) reported that they routinely recommend/offer the HPV vaccine, 6 (5.17%) occasionally or only at caregiver request, and 6 (5.17%) do not offer the vaccine. Of those who do not offer the vaccine, four are pediatric surgeons and two work in pediatric ERs. These six respondents were removed from further analysis, as their practice does not include vaccinations of any kind. Almost all (96.4%) recommend HPV vaccine for both boys and girls. One person does not recommend it for boys. A significant percentage of respondents indicated that the strength of their recommendation for the vaccine depends on the age (36.4%) or gender of the patient (14.6%). The majority (81.8%) gave an equally strong recommendation for boys and girls.

Almost one-third of the providers did indicate that the strength of the recommendation depends on the caregivers' response when discussing HPV vaccine and transmission. The willingness of the parent to provide consent for vaccination was only "somewhat willing" the majority of the time (61%), with only 34% of the responders reporting caregivers being very willing to consent to HPV vaccination. The most common reason cited by the pediatricians that caregivers give when refusing vaccine was fear of the side effects/safety. The second most common reason was that the caregiver was uncertain about the potential

benefit. These reasons were then followed by “fear that it would condone sexual activity” and the “desire to avoid vaccines altogether” as the third and fourth, respectively.

Only 32.7% of respondents were very familiar with the link between HPV and oropharyngeal cancer. The majority (51.8%) of respondents indicated that they have only some awareness of this link and 15.4% were not aware of HPV positive oropharyngeal cancer. Among the respondents, 45.9% believed rates of HPV associated with oropharyngeal carcinoma are rising, and 44% reported not having knowledge about the increasing rate. A number of respondents (17.2%) did indicate that more knowledge of HPV-associated oropharyngeal cancers would increase their recommendation of the vaccine for males. Practice setting and length of practice did not correlate with knowledge of the link between HPV and oropharyngeal cancer (Table 2, Table 3,  $p = 0.35$  and  $p = 0.88$ , respectively).

## DISCUSSION

The possible role of HPV in the development of OPC was first suggested in 1983 and then became established in the late 80s and 90s.<sup>11-15</sup> However, it took almost a decade to gather the epidemiological evidence for the association and to understand the biological mechanisms behind the viral-mediated tumorigenesis.<sup>16-18</sup> Similar to the HPV related cervical cancer, OPC (approximately 90%) is driven primarily by HPV 16 with the rest attributed to HPV 18.<sup>18</sup> In a study of a representative sample of the U.S. population in 2009-2010, the prevalence of HPV type 16 was 1% in 14-69 year old men and women.<sup>19</sup> HPV(+) Head and Neck Squamous Cell Carcinoma (HNSCC) predominantly arises in the oropharynx, the middle portion of the throat that, compromises the soft palate, palatine tonsils, base of tongue, and lateral and posterior pharyngeal walls. Traditional risk factors for HNSCC include tobacco and alcohol abuse. However, HPV (+) HNSCC possesses a unique molecular pathology compared to the other HNSCCs,<sup>20,21</sup> and therefore represents a distinct clinical entity. HPV (+) patients tend to be younger compared to HPV (-) patients, male, Caucasian, college educated, have an annual income greater than \$50,000 and are more often non-smokers or drinkers.<sup>22</sup>

No direct studies of the effect of HPV vaccine on persistent infection with HPV 16 have been reported. However, in a single evaluation of the prevalence of oral infection in a vaccinated population, decreased carriage of HPV 16 was demonstrated after immunization with bivalent HPV 16/18 vaccine. During the fourth year evaluation of subjects in a double blind randomized trial of bivalent HPV 16/18 vaccine in 7,466 women in Costa Rica, an oral wash was obtained from 5,840 women (91.9% of the eligible population). Fifteen control subjects and one vaccinated subject were positive for HPV 16/18, giving a vaccine effectiveness of 93.3%.<sup>23-24</sup> These findings support the concept that HPV vaccines will afford protection against the development of HPV (+) OPC.

Despite the observed safety, early demonstrated effectiveness, and predicted long-term benefits of HPV vaccination in the

prevention of HPV associated malignancies, rates of vaccination in the U.S. remain unacceptably low.<sup>7</sup> The 2014 National Immunization Survey- Teen (NIS-Teen) showed that 60.0% of females and 41.7% of males ages 13-17 years received one or more doses of HPV vaccine.<sup>25</sup> These rates are well below those for Tdap and meningococcal vaccines, both of which are recommended for the same age group.<sup>26</sup> The disparity between male and female vaccination rates are particularly concerning given males have a 4.7 fold higher risk of developing HPV(+) OPC.<sup>27</sup> While federal mandates in other countries have achieved high rates of vaccination, only three states in the U.S. have passed legislation for school mandated vaccination. As the subject of mandatory vaccination for a sexually transmitted virus has been controversial in this country, more widespread use of mandates is unlikely at this time.<sup>28</sup> Therefore, education of providers and parents is likely to be the most productive effort to improve current vaccination rates.

This study examined practice patterns amongst pediatricians in Louisiana. Although the majority of pediatricians routinely recommend vaccination, we found that for some, the strength of the recommendation depends on the age or sex of the patient. This study also demonstrates that even amongst medical professionals who consistently offer HPV vaccine there is limited knowledge of its role in the prevention of HPV (+) OPC. Despite the high rate of recommendation, less than one third of participants were highly familiar with the link between HPV and OPC and only half were aware of any association. In addition, the majority of participants were unaware of the rising rate of HPV (+) OPC. There was no correlation between practice setting or length of practice in regards to knowledge of HPV (+) OPC.

These results further imply that there is a greater need for improved awareness among all medical professionals irrespective of practice setting and experience. Additionally, although offering vaccination against HPV is an important step in increasing vaccination rates in the U.S., many parents may not feel compelled to vaccinate their children if they are not made aware of its major benefit: the prevention of HPV-related cancers. In a survey of 102 participants consisting of health care providers, community leaders, parents with adolescent sons, and young adult men ages 18-26, few had even heard of the availability of the vaccine for men and its role in throat cancer.<sup>29</sup> Health care professionals (HCP) play an integral role in education of the public. In a recent systematic review concerning barriers to HPV vaccination in US adolescents, parents consistently mentioned HCP's recommendations as one of the most influential considerations in their choice to vaccinate their children.<sup>30</sup> In a study examining young women ages 19-26, patients were found have a 4-fold greater rate of vaccination if their physician gave a strong recommendation versus one that was not strong.<sup>31</sup> Another study based on a 2009 U.S. national panel of 18- 59-year-old men reported factors associated with HPV vaccine acceptability and demonstrated that more respondents were willing to be vaccinated when the vaccine was presented as preventing genital warts and anal, oral, or penile cancer than when framed as preventing genital warts alone.<sup>32</sup> Additionally, parents in another investigation identified

TABLE 1: Results of 18 question survey

Demographics:	Answer Given	n (%)
I am:	Male	43 (39.1)
	Female	67 (60.9)
For what age group do you routinely recommend the vaccine	11-12 years	94 (81.0)
	13-15	13 (11.2)
	16-18	3 (2.6)
	I do not recommend	6 (5.2)
Does the strength of your recommendation depend on the age of the patient?	Yes	40 (36.4)
	No	69 (62.7)
	I do not recommend it	1 (0.9)
Does the strength of your recommendation depend on whether the child is a girl or boy?	Yes	16 (14.6)
	No	93 (84.6)
	I do not recommend it	1 (0.9)
Do you give as strong a recommendation for HPV vaccine for a boy as a girl?	Yes	90 (81.8)
	No	19 (17.3)
	I do not recommend it	1 (0.9)
Practice:	Answer Given	n (%)
Do you routinely recommend/offer HPV Vaccine for you Patients?	Routinely	104 (94.6)
	Occasionally	4 (3.6)
	Only at caregiver request	1 (0.9)
	I do not recommend it	0 (0)
	I do not offer it	1 (0.9)
For whom do you recommend HPV vaccine?	Females	2 (1.8)
	Males	1 (0.9)
	Both	106 (96.4)
	Do not recommend it	1 (0.9)
I have been in practice for:	< 5 years	39 (35.4)
	5-10 years	11 (10.0)
	11-15 years	11 (10.0)
	16+ years	49 (44.6)
I currently work in the following setting (select all that apply):	Academic hospital	29 (26.4)
	Public clinic	6 (5.4)
	Academic hospital or Public clinic	2 (2.7)
	Private multispecialty Group	45 (40.9)
	Single specialty group	10 (9.1)
	Solo practice	
What percentage of your patient population is funded with Medicaid?	<10%	20 (18.2)
	10-40%	29 (26.4)
	>40%	61 (55.4)
Knowledge:	Answer Given	n (%)
How familiar are you with the link between HPV and oropharyngeal carcinoma?	Very familiar	36 (32.7)
	Some awareness	57 (51.8)
	No awareness	17 (15.5)
I believe that rates of HPV associated oropharyngeal carcinoma are:	Rising	50 (45.9)
	Falling	3 (2.8)
	Remaining stable	8 (7.3)
	Don't know	48 (44.0)
	Missing	1
If you are not recommending HPV vaccine for males, would you be more likely to do so with increased knowledge of HPV associated oropharyngeal lesions?	Yes	20 (17.2)
	No	6 (5.2)
	I am currently already recommending for males	90 (77.6)

Does the strength of your recommendation depend on the parent's response to a discussion of HPV vaccine or transmission?	Yes	33 (28.5)
	No	77 (66.4)
In cases where you recommend the vaccine, how often are patients and parents willing to receive it?	I do not recommend it	6 (5.2)
	Somewhat willing	71 (61.2)
	Very willing	39 (33.2)
For patients/parents that refuse the vaccine, what are the most common reasons they refuse? Please rank in order of frequency from 1 to 5, with 1 being the most common	Not willing	0
	I do not recommend the vaccine	6 (5.17)
Do you keep a supply of HPV vaccine in your office?	Fear of side effects/anxiety	1.9*
	Yes	104 (89.7)
	Don't understand benefits	3.0*
	No routinely	5 (4.3)
If you do not currently offer the vaccine, please indicate the reasons:	Fear it will be detrimental	2.7*
	I do not offer the vaccine	7 (6.0)
	Desire to avoid vaccination	3.8*
	Limited knowledge of vaccine	0
	Other	3.9*
	Financial concerns	0
	Not routinely	5 (4.3)
	Vaccine safety concerns	0
Vaccine effectiveness	0	
Do you give as strong a recommendation for HPV vaccine for a boy as a girl?	Not sure about the health risks	2 (1.7)
	Uncomfortable with the discussion	111 (95.7)
	Other	

TABLE 2: Knowledge of the link between HPV and OPC in different clinical settings, (p = 0.35). The awareness of the link between HPV and OPC can vary depending on what clinical setting one is in on a daily basis. This table depicts differences in levels of knowledge compared between clinicians that work in various settings.

Practice setting	Aware of link (n=93)	Not aware of link (n=17)	Total (n=110)
Academic hospital and/or Public clinic	33 (86.8 %)	5 (13.2%)	38
Multispecialty or single specialty group	50 (80.6 %)	12 (19.4%)	62
Solo practice	10 (100 %)	0 (0)	10

TABLE 3: Knowledge of the link between HPV and OPC based on number of years in practice, (p = 0.88). The number of years a physician has been in clinical practice can also effect the level of knowledge on the link between HPV and OPC.

Length practice	Aware of link (n=93)	Not aware of link (n=17)	Total (n=110)
< 5 years	33 (84.6%)	6 (15.4%)	39
5 – 15 years	16 (72.3%)	6 (27.3%)	22
≥ 16 years	44 (89.8%)	5 (10.2%)	49

that knowledge about oropharyngeal cancer prevention greatly influenced their decisions positively about vaccinating their sons.<sup>33</sup> In the study of the 2010 National Health Interview Survey, those men who had increased interactions with their healthcare provider had much greater knowledge about HPV and the HPV vaccine.<sup>8</sup> Thus, a significant, potential source for improving male HPV vaccination rates lies with physicians and educating patients about its cancer-preventing properties. FDA approval of the vaccine in girls for prevention of cervical cancer clearly increases acceptance rates amongst parent of teenage girls. If the relationship of HPV with head and neck cancer in men was greatly emphasized by their physician, parents may be more likely to accept vaccination for their sons.

This current study is limited by the small sample size and somewhat low response rate. In addition, the views reflected by the respondents in the studies may not be applicable to other regions in the country. Louisiana's one or more HPV dose vaccination rate amongst 13-17 year olds in 2014 was 53.2% for girls and at 44.7% for boys, which was fairly similar to national rates of 60.0% and 41.7%, respectively.<sup>26</sup> Despite being a state with vaccination rates just above or below the U.S. overall rates, this study shows there is still a large educational gap, irrespective of years in practice, to be reconciled among primary health care providers. Although this survey demonstrates a lack of knowledge of HPV (+) OPC, it does not define why this educational gap exists. Further, research should focus on efficacy of education and awareness of HPV (+) OPC.

## CONCLUSION

Based on current projections, HPV (+) OPC may become the most common HPV associated malignancy in the early 21 century. Currently, vaccination rates in the U.S. are low compared to other countries, and state directed mandates are unlikely in the near future. Even though the health care providers who responded to this survey demonstrated a high rate of recommending vaccination to their patients, most were not aware of the role of HPV in OPC, and some demonstrated a difference in strength of recommendation based on age and gender. Parents may likely be more receptive to vaccination if they were made aware of HPV vaccine's role in prevention of cancer. Education and awareness of HPV (+) OPC is integral at not only the patient level, but to providers as well who are at the front line of vaccination. Otolaryngologists should actively educate pediatricians and primary care providers to increase vaccination rates.

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