

Increasing Trend of HPV-Associated Oropharyngeal Cancers among Males in Rhode Island, 1987–2011

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Evidence linking human papillomavirus (HPV) with the development of oropharyngeal cancers has accumulated since the 1980s, culminating in the conclusion that HPV plays a *causal* role in the development of some oropharyngeal neoplasms.¹ These particular cancer types are on the rise in the United States,²⁻⁴ and as this report will show, in Rhode Island as well. Authors will discuss strategies for prevention and control efforts, based on Rhode Island-specific epidemiology and growing body of research of HPV-associated oropharyngeal cancers.

METHODS

The Rhode Island Cancer Registry (RICR) has collected cancer case reports since October 1986. Since 1995, this effort has been supported in part by the National Program of Cancer Registries of the Centers for Disease Control and Prevention (CDC). Using RICR data for the period 1987–2011, newly diagnosed malignant squamous cell carcinomas of the head and neck were identified. In parallel with a previous analysis of similar data,⁵ these cancers were categorized either as “HPV-associated oropharyngeal cancers” or as “comparison cancers.”

HPV-associated malignancies include those of the tonsil (including the pharyngeal lymphoid ring), posterior one third (base) of the tongue and lingual tonsil, and certain oropharyngeal sites (including overlapping lesions of the tongue, the lateral wall of the oropharynx, overlapping lesions of the oropharynx, non-specified oropharynx and pharynx, and overlapping lesions of the lip, the oral cavity, and the pharynx). Comparison cancers were those diagnosed in selected sites in the head and neck that are anatomically near the oropharyngeal cancer sites but are sites not associated with HPV infection based on epidemiologic and pathologic studies.⁵ **Table 1** contains a complete description of HPV-associated oropharyngeal cancers and

comparison cancers with specific cancer classification codes.

Please note that tumors categorized as “HPV-associated” were *not verified* as testing positive for HPV DNA. The RICR does not routinely collect this information. Nonetheless, recent studies reveal HPV positivity as high as 70% in “HPV-associated oropharyngeal cancers.”^{4,6}

Incidence rates for HPV-associated oropharyngeal cancers and comparison cancers in a subset of head and neck cancers were examined by sex and year of diagnosis. SEER* Stat software was used to calculate the number of cancers and age-adjusted rates per 100,000 population, standardized to the U.S. 2000 standard population (see <http://www.seer.cancer.gov/seerstat/index.html>). Annual percentage change (APC) was computed for cancer trends, using the CDC’s JoinPoint regression software (see <http://surveillance.cancer.gov/joinpoint/>), evaluating statistical significance of at the $p \leq 0.05$ significance level.

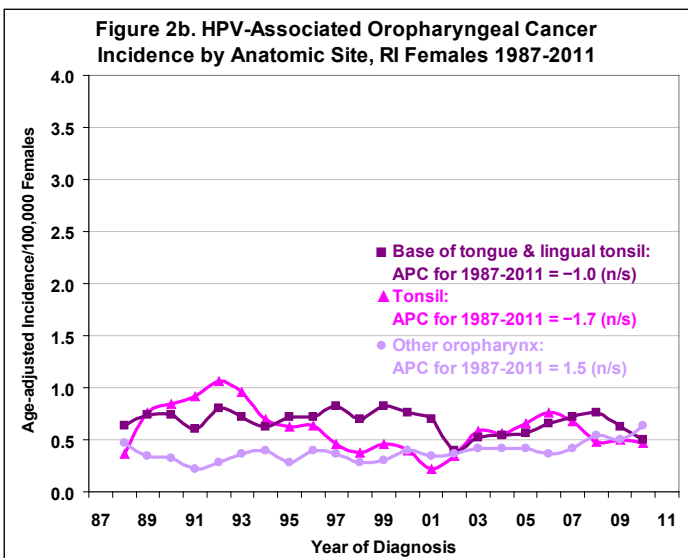
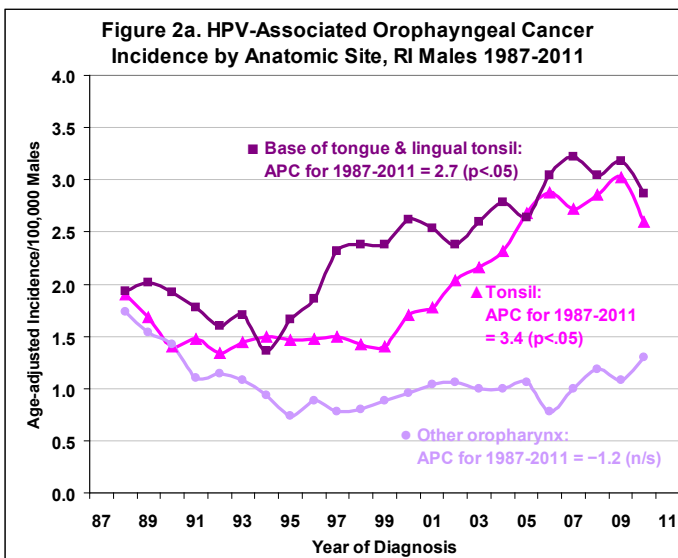
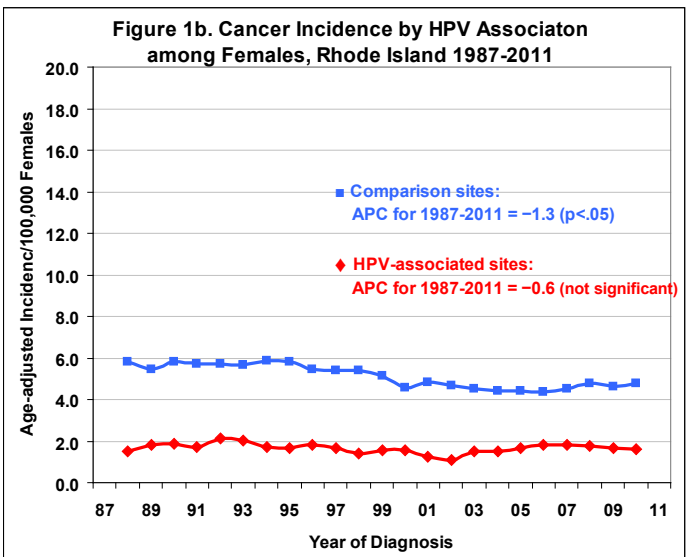
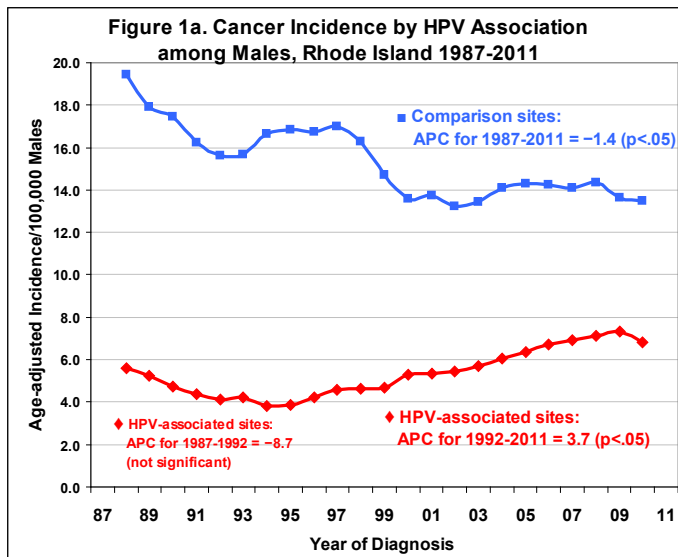
RESULTS

A total of 940 HPV-associated oropharyngeal cancers were reported to RICR during 1987–2011, as compared with a

Table 1. ICD-O-3 topography code* and anatomic site description used to define HPV-associated and comparison cancers in selected sites in the head and neck.

HPV-associated sites	
Tonsil, including pharyngeal lymphoid ring	C090, C091, C098, C099 (Tonsil) C142 (Pharyngeal lymphoid ring or Waldeyer’s ring)
Base of tongue and lingual tonsil	C019 (Base of tongue) C024 (Lingual tonsil)
Other oropharynx	C028 (Overlapping lesion of tongue) C102, C108, C109 (Oropharynx) C140 (Pharynx) C148 (Overlapping lesion of lip, oral cavity and pharynx)
Comparison sites	
Tongue	C020, C021, C022, C023, C029 (Tongue)
Other oral cavity	C030, C031, 039 (Gum) C040, C041, C048, C049 (Floor of mouth) C050 (Hard palate) C060, C061, C062, C068, C069 (Other/unspecified parts of mouth)
Larynx	C320, C321, C322, C323, C328, C329 (Larynx)
Other oropharynx	C051, C052, C058, C059 (Palate) C100, C101, C103 (Other Oropharynx)

* International Classification of Disease for Oncology, 3rd edition, [ICD-O-3].



total of 2,675 comparison cancers in a subset of head and neck cancers.

Among Rhode Island males, the annual age-adjusted incidence rate of HPV-associated cases increased between 1992 and 2011 (APC = 3.7, $p < 0.05$), whereas the incidence of comparison cases steadily decreased between 1987 and 2011 (APC = -1.4, $p < 0.05$) (Figure 1a). Among women, the annual percent change in age-adjusted incidence of HPV-associated cases was not statistically significant over the period of observation, whereas the incidence of comparison cases steadily decreased between 1987 and 2011 (APC = -1.3, $p < 0.05$) (Figure 1b).

Assessment of HPV-associated oropharyngeal cancers by anatomic site revealed that tumors of the tonsil and base of the tongue (including the lingual tonsil) increased between 1987 and 2011, particularly among males (APC = 3.4 and 2.7, respectively, Figure 2a). A similar trend was not observed among women (Figure 2b).

DISCUSSION

The findings in this report are subject to at least two limitations. First, the potential exists for misattribution of oral and pharyngeal cancers to HPV infection. HPV association is based solely on anatomic site, not on case-specific HPV data. Second, only incomplete information on comorbidities, smoking history, and alcohol use history is available in cancer case reports made to the RICR, that prevents use of such variables for further assessment. In the future, focused surveillance of oropharyngeal cancers, including the careful collection of information on HPV positivity and other risk factors, will assist in unraveling the importance of HPV as an emerging risk factor in the development of tumors at specific anatomic sites, and also in establishing the effectiveness of HPV vaccination in preventing those tumors.

Meanwhile, using the information available to us for the past two-and-a-half decades, RICR data reveal a *robust* increase in HPV-associated oropharyngeal cancer incidence

among men, in contrast to a steady decrease in the incidence of non-HPV-associated head and neck cancers among men and women.

Historically, tobacco use and heavy alcohol consumption were considered the major risk factors for head and neck cancers.⁷ Recent research, however, reveals an increasing occurrence of oropharyngeal cancers in young(er) men who have never smoked, but whose sexual behaviors are consistent with increased risk of HPV infection, e.g., reporting numerous sexual partners or an early sexual debut.^{6,8}

As in the case of other HPV-associated cancers, HPV infection in the mouth and throat, typically HPV-16 infection, is a precursor of oropharyngeal cancer development.⁹ Recent analysis of data from the 2009-2010 National Health and Nutrition Examination Survey (NHANES) estimated an overall prevalence of oral HPV infection among United States residents aged 14–69 years of 10.1% among males and 3.6% among females.¹⁰

Recognizing the significant contribution of HPV infection to recent oropharyngeal cancer trends – especially among men – suggests important implications for oropharyngeal cancer prevention and control. Available HPV vaccines may be effective in reducing the burden of HPV-associated oropharyngeal cancers, either *directly*, by preventing HPV infection of the mouth and throat, or *indirectly*, by preventing HPV infection of the genitals or anus, potential sources of oral HPV infection.

CDC's Advisory Committee on Immunization Practices (ACIP) has recommended routine vaccination against HPV for young females since 2007 and young males since 2011.^{11,12} As recommended, Rhode Island includes HPV vaccine as part of the universal state supplied vaccine program, for all adolescents regardless of insurance status, through primary care providers and school- and community-based vaccination clinics. Although clinical trials have as yet to determine the efficacy of HPV vaccines for the prevention of oropharyngeal cancers, currently available HPV vaccines offer good protection against HPV-16, the dominant strain associated with oropharyngeal cancers.^{11,13}

On the basis of current, state-specific epidemiologic trends of HPV-associated cancer rates, healthcare professionals are encouraged to promote vaccines and other preventive measures in their practices. However, many healthcare professionals may be reticent to discuss sexual behavior with their patients, and, understandably, may be undecided about the role of HPV vaccines in the prevention of oropharyngeal cancers. The Rhode Island Department of Health, partnering with a statewide cancer coalition, and immunization and oral health advocates, conducts educational sessions on this subject for licensed medical and dental care professionals and also develops educational modules to be used in the curricula of health professionals-in-training.

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Disclosures

The authors and/or spouses/significant others have no financial interests to disclose.

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