



Rhode Island Oral Health Issue Brief

HPV and Oropharyngeal Cancers in Rhode Island

There is an alarming rise in Human Papilloma Virus (HPV)-associated oropharyngeal cancers among Rhode Island males since the 1990s. Oropharyngeal cancers are the most common type of HPV-associated cancer among Rhode Island males. The implications for cancer prevention and control efforts are discussed in this brief based on the Rhode Island-specific epidemiological review.

Oral and Pharyngeal Cancer in Rhode Island

Cancer of the oral cavity or pharynx is one of the top ten most occurring cancers in Rhode Island. During 2005-2009 there were 16 new oral and pharyngeal cancer cases reported annually per 100,000 Rhode Island male adults [age-adjusted to 2000 US population].¹ The incidence rate of oral and pharyngeal cancer is comparable to leukemia (17 per 100,000 males) and higher than pancreatic cancer (13 per 100,000 males). Newly reported and diagnosed oral and pharyngeal cancers among men are twice as high as women.

The consequences of oral and pharyngeal cancer can be devastating when detected in a later stage of cancer growth, e.g., Impairment of speech, eating, and swallowing functions, and facial disfigurement.

The Connection between Oropharyngeal Cancer and Human Papilloma Virus (HPV)

The majority of oral and pharyngeal cancers develop on the lips, floor of the mouth, gingiva, and anterior two-thirds of the tongue. Although genetic and environment-related factors also have been identified as risk factors for oral and pharyngeal cancer, tobacco use and heavy alcohol consumption are considered major causes of approximately 75% of all oral and pharyngeal cancers.^{2,3} The incidence of oral and pharyngeal cancer has declined since the number of smokers in the United States has substantially decreased since the 1970s.⁴

Recent national cancer statistics suggest that a subset of oral and pharyngeal cancers, primarily those of the oropharynx (the rear of the oral cavity, including the base of the tongue and the tonsils, Figure 1), has increased steadily since the 1970s.^{5,6} Epidemiologic and pathologic study results indicate that development of these base-of-the-tongue and the tonsillar cancers is causally associated with sexually transmitted Human Papilloma Virus (HPV) infections, in particular Type 16 (HPV-16), that are also responsible for cancers in the cervix, anus, and penis.^{7,8} Substantial evidence has recently mounted in favor of the distinction between HPV-associated and non-HPV-associated oral and pharyngeal cancers. HPV-associated and non-HPV-associated oral and pharyngeal cancers are distinct in clinical and patho-biological features, patient risk factor profiles, detection, and management of disease.⁹ Compared with cancers associated with traditional risk factors (i.e. tobacco and alcohol use), HPV-associated oropharyngeal cancers are more likely to occur among younger white males (<60 years), and those who practice certain sexual behaviors but who never smoked or heavily consumed alcohol.

About the Data Source: The Rhode Island Cancer Registry

The Rhode Island Cancer Registry has collected, managed, and analyzed data about cancer cases and cancer deaths since 1986.

The registry has been supported in part by the Centers for Disease Control and Prevention (CDC) National Program of Cancer Registries (NPCR) since 1995.

The state of Rhode Island collects cancer reports from medical facilities such as hospitals, physicians' offices, therapeutic radiation facilities, freestanding surgical centers, and pathology laboratories.

Vital information about cancer cases and cancer deaths is necessary for public health agencies to report on cancer trends, address the state's cancer burden, assess the impact of cancer prevention and control efforts, participate in research, and respond to reports of suspected increases in cancer occurrence.

For more information visit:
Rhode Island Cancer Registry
www.health.state.ri.us/programs/cancerregistry/index.php and
National Program of Cancer Registries (NPCR)
www.cdc.gov/cancer/npcr/about.htm

HPV-associated Oropharyngeal Cancer Trends in Rhode Island

Newly diagnosed oral and pharyngeal cancers included in this report were retrieved from the Rhode Island Cancer Registry from 1987-2009. Based on the literature review on anatomic site preference of HPV, the malignant oral and pharyngeal cancers were classified into two groups: (1) "HPV-associated oropharyngeal cancers" detected in the base of the tongue, lingual and palatine tonsils, and certain sites within the oropharynx (n=835), and (2) comparison cancers mostly in the oral cavity and in the larynx, in parallel with previous epidemiologic report (n=2,461).⁶ Table 1 summarizes specific cancer classification codes and descriptions used to categorize subsets of oral and pharyngeal cancers by HPV association.

It should be noted that not all "HPV-associated" cases directly reflect HPV infection because Cancer Registry data does not indicate whether or not HPV is present in a tumor. The term "HPV-associated" in this brief refers to cancers that have been shown in the literature to be strongly associated with HPV infection. In 2000-2005, more than 70% of the cancer were confirmed HPV-positive in studies that tested HPV prevalence in oropharyngeal cancer tissue samples from population-based cancer registries and hospital-based cases.^{7,8}

Table 1. ICD-O-3 topography code* and anatomic site description used to define HPV-associated oropharyngeal and comparison cancers.⁶

ANATOMIC SITES OF HPV-ASSOCIATED OROPHARYNGEAL CANCER
C019 (Base of tongue)
C024 (Lingual tonsil)
C028 (Overlapping lesion of tongue)
C090-099 (Palatine tonsil)
C102, 108, 109 (Oropharynx)
C140 (Pharynx)
C142 (Waldeyer's ring)
C148 (Overlapping lesion of lip, oral cavity and pharynx)
COMPARISON ANATOMIC SITES
C020-023, C029 (Tongue)
C030-039 (Gum)
C040-049 (Floor of mouth)
C050-059 (Soft and hard palate)
C060-069 (Other/unspecified parts of mouth)
C100, 101, 103 (Oropharynx)
C320-329 (Larynx)

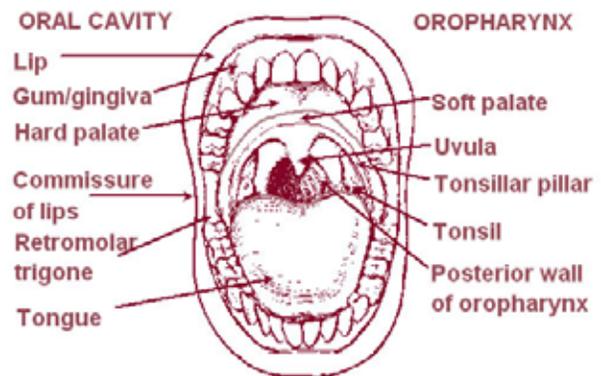
* International Classification of Disease for Oncology, 3rd Edition, [ICD-O-3]

Terminology:

Oral and pharyngeal cancer is a comprehensive term to include cancer of the lip, tongue, floor of the mouth, palate, gingiva and alveolar mucosa, buccal mucosa, salivary gland, tonsil, oropharynx, nasopharynx, and hypopharynx.

Oropharyngeal cancer includes cancer of oropharynx that refers the palatine and lingual tonsils, the posterior one-third (base) of the tongue, the soft palate, and the posterior pharyngeal wall.

Figure 1. Schematic View of oral cavity and oropharynx



National Cancer Institute, Surveillance, Epidemiology and End Results (SEER) Program Training Module
<http://training.seer.cancer.gov/head-neck/anatomy/mouth.html>

- In accordance with national trends,^{5,6} annual age-adjusted incidence rates of potentially HPV-associated oropharyngeal cancers among Rhode Island men increased from 1987 through 2009, (45% increase from 5.3 per 100,000 [1987-1991] to 7.7 per 10,000 [2007-2009]), whereas the incidence rates of comparison sites steadily decreased over the same period (24% decline from 17.9 per 100,000 to 13.6 per 10,000). There is a trend in HPV-associated oropharyngeal cancer that is escalating for males at an alarming rate. (Figure 2).
- The incidence rates of both HPV and non-HPV-associated cancers among women have remained stable during the period of 1987 through 2009 (Figure 3).

Figure 2. Oral and pharyngeal cancer incidence per 100,000 males by year – Rhode Island, 1987-2009*

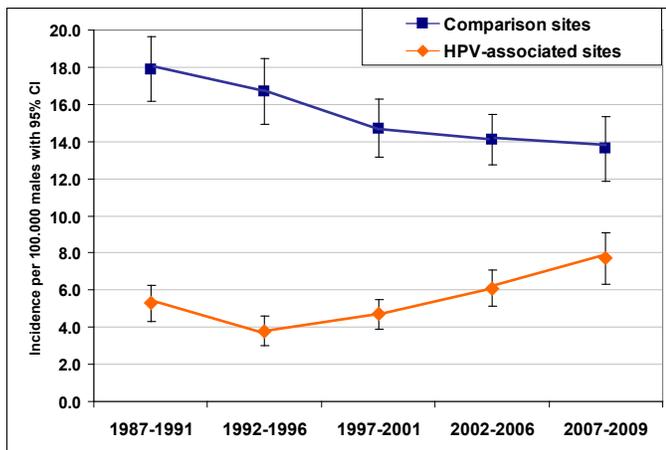
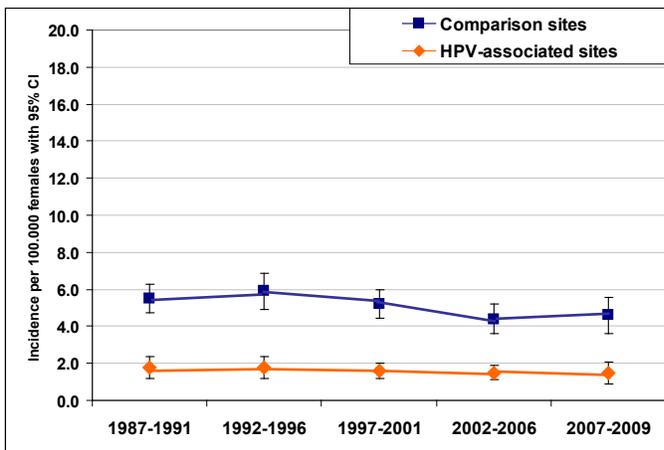


Figure 3. Oral and pharyngeal cancer incidence per 100,000 females by year – Rhode Island, 1987-2009*



*Data source: Rhode Island Cancer Registry. Rates are age-adjusted to the 2000 U.S. Standard population.

- The difference in age at diagnosis between the two types of oral and pharyngeal cancers was assessed. Compared with cancers in the comparison sites, HPV-associated oropharyngeal cancers are more likely to be diagnosed at a younger age, particularly among male. The average age of oropharyngeal cancer diagnosis at the HPV preferred anatomic sites, among men, is 61 years, compared to cancers at the comparison sites of 64 years old. Women's ages, when oral and pharyngeal cancers were diagnosed, are not significantly different by HPV association (Figure 4 and 5).

Figure 4. Distribution of age at oral and pharyngeal cancer diagnosis among males – Rhode Island, 1987-2009*

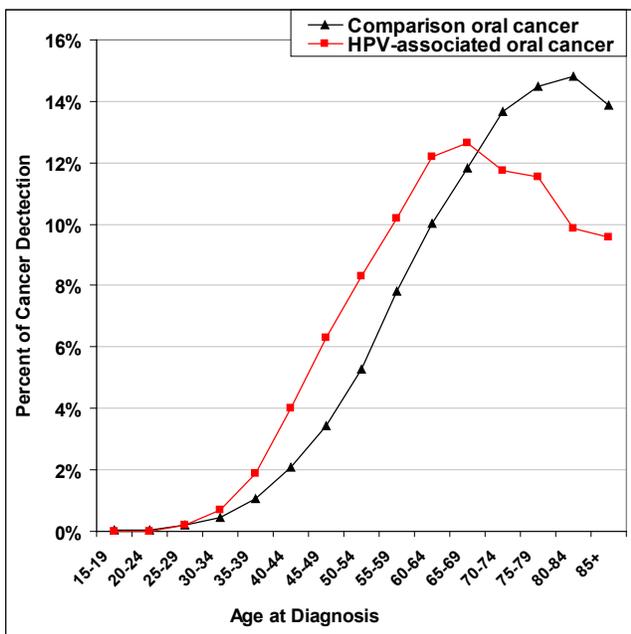
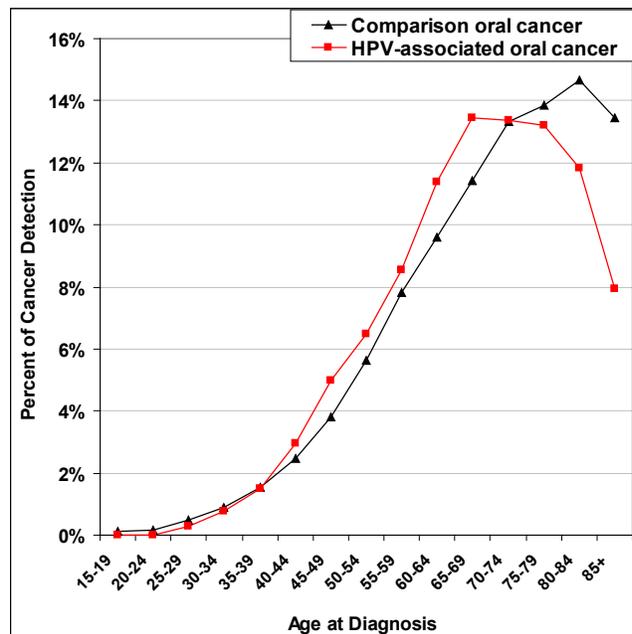


Figure 5. Distribution of age at oral and pharyngeal cancer diagnosis among males – Rhode Island, 1987-2009*



*Data source: Rhode Island Cancer Registry. Rates are age-adjusted to the 2000 US Standard population.

Conclusion: Implications for Oral and Pharyngeal Cancer Prevention and Control

The Cancer Registry confirms an alarming rise in HPV-associated oropharyngeal cancers among Rhode Islanders in the last twenty years. Among males, oropharyngeal cancers are the most common type of HPV-associated cancers. According to the 2007–2009 Cancer Registry, the oropharyngeal cancer incidence rate is 7.7 per 100,000 males; while anal and penile cancer incidences are 1.6 and lower than 1 per 100,000 males for the same period.

HPV plays a specific and unique role in oral and pharyngeal cancer development. The connection between HPV infections and oral and pharyngeal cancer suggests important implications for cancer prevention, research, and control initiatives. The risk factors, morbidity, and mortality of HPV-associated oropharyngeal cancers, most notably the cancers found in the base of the tongue and tonsils, differ from those of cancers in the oral cavity. As the tumors commonly develop close to the throat, HPV-associated oropharyngeal cancers are not as easily detected by traditional visual and tactile oral and pharyngeal cancer examinations and are more likely to be undetected until a later stage. Patients with HPV-associated cancers typically have a higher survival rate, a better response to radiation and chemotherapy, and a more favorable prognosis.¹⁰

Dental and medical care professionals should be more vigilant about the types of oral and pharyngeal cancers that can affect younger patients regardless of the presence of the traditional risk factors, particularly chronic tobacco and alcohol use. Healthcare professionals are encouraged to communicate with their patients about HPV as a cause of oropharyngeal cancer.

The Centers for Disease Prevention and Control's (CDC) Advisory Committee on Immunization Practices recommends the vaccination, HPV4; Gardasil, Merck & Co., Inc. (since 2006), or HPV2; Cervarix, GlaxoSmithKline (since 2009), against HPV for females, and HPV4; Gardasil, Merck & Co., Inc. for males (since October 2011).¹¹ Current HPV vaccination efforts effectively target cervical cancers in women as well as anal cancers and genital warts in both women and men. HPV vaccinations may offer opportunities to prevent infection and reduce the burden of HPV-associated oropharyngeal cancers. As a result of national and state HPV vaccination education and promotion, and the recent HPV vaccine recommendation to include male adolescents and young adults, a growing number of vaccinated Rhode Island teens and young adults will become protected against HPV. Clinical trials have yet to determine the efficacy of a HPV vaccine to prevent certain types of oral and pharyngeal cancer but recent studies have shown that more than 70% of oropharyngeal cancers are attributable to HPV infection.^{7,8} Potential effectiveness in preventing and reducing oropharyngeal cancer through HPV vaccination is promising.

Oral and pharyngeal cancer prevention efforts, including referrals to tobacco cessation programs and alcohol addiction and abuse treatment, should be continuously practiced in dental offices. Tobacco and alcohol use remain the primary risk factors for the majority of oral and pharyngeal cancers.

¹ *Rhode Island Cancer Registry, 2005-2009*. Rhode Island Department of Health.

² Blot WJ, McLaughlin JK, Winn DM, et al. "Smoking and Drinking in Relation to Oral and Pharyngeal Cancer" *Cancer Res* 1988;48 (11):3282- 3287.

³ The Oral Cancer Foundation <<http://oralcancerfoundation.org/facts/index.htm>>.

⁴ Sturgis EM, Cinciripini PM. "Trends in Head and Neck Cancer Incidence in Relation to Smoking Prevalence: An Emerging Epidemic of Human Papillomavirus-Associated Cancers?" *Cancer* 2007;110 (7):1429–1435.

⁵ Chaturvedi AK, Engels EA, Anderson WF, et al. "Incidence Trends for Human Papillomavirus-Related and -Unrelated Oral Squamous Cell Carcinomas in the United States" *J Clin Oncol* 2008;26(4):612-619.

⁶ Ryerson AB, Peters ES, Coughlin SS, et al. "Burden of Potentially Human Papillomavirus-Associated Cancers of the Oropharynx and Oral Cavity in the US, 1998-2003" *Cancer* 2008;113(10 Suppl):2901-2909.

⁷ Chaturvedi AK, Engels EA, Pfeiffer RM, et al. "Human Papillomavirus and Rising Oropharyngeal Cancer Incidence in the United States" *J Clin Oncol* 2011;29(32):4294-4301.

⁸ D'Souza G, Kreimer AR, Viscidi R, et al. "Case-Control Study of Human Papillomavirus and Oropharyngeal Cancer" *N Eng J Med* 2007;356:1944-1956.

⁹ Cleveland JL, Junger ML, Saraiya M, et al. "The Connection between Human Papillomavirus and Oropharyngeal Squamous Cell Carcinomas. Implications for Dentistry" *J Am Dent Ass* 2011;142(8):915-924.

¹⁰ Ang KK, Harris J, Wheeler R, et al. "Human Papillomavirus and Survival of Patients with Oropharyngeal Cancer" *N Engl J Med* 2010;363:24-35.

¹¹ Centers for Disease Prevention and Control (CDC) Advisory Committee on Immunization Practices (ACIP), Human papillomavirus (HPV) recommendations <<http://www.cdc.gov/vaccines/pubs/ACIP-list.htm#hpv>>.