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Cancers of the oral cavity and pharynx account for 2.7% (9,462 cases) of all cancers diagnosed in Illinois between 2016 and 2020. Cancers at these sites can differ anatomically and histologically and can also have different causal factors including tobacco use, alcohol use, and infection with human papillomavirus (HPV).[1] In the United States the incidence of oral cavity and pharyngeal cancers steadily declined during the 1980s but began to increase around 1999.[2,3] With the national decline in tobacco use and a concomitant decline in tobacco-related cancers, researchers have suggested that the increase could be associated with cancer sites and cell types in which HPV DNA are often found.[4,5] The current examination focuses on the rates and trends in cancer of the oral cavity and pharynx in Illinois residents with an examination of HPV-related sites.

Cancer incidence data was analyzed for all Illinois residents on cancers diagnosed between 2000 and 2020. The Illinois State Cancer Registry (ISCR) has attained the North American Association of Central Cancer Registries Gold certification for all years in this examination (2000-2020). Incidence rates were examined by sex, cancer site, stage at diagnosis (early stage - localized, and late state – regional or distant), age, and race-ethnicity (three mutually exclusive groups, including, non-Hispanic White, non-Hispanic Black, non-Hispanic Asian/Pacific Islander) and expressed per 100,000 people and were age-standardized to the 2000 U.S. standard population.

All cancer cases were analyzed using SEER*Stat software.[6] Rates were also examined by site and histological combinations associated with HPV (HPV-associated) as defined by the Centers for Disease Control and Prevention (https://www.cdc.gov/cancer/uscs/public-use/predefined-seer-stat-variables.htm).[7] The case definition of HPV-associated cancers in this examination includes microscopically confirmed squamous cell carcinoma cell types (histology codes: 8050-8086 and 8120-8131) within the following anatomic sites (as defined by ICD-O-3 codes) – base of tongue (C01.9, C02.4, C02.8), soft palate and uvula (C05.1, C05.2), tonsil (C09.0-C09.9), oropharynx (C10.0-C10.9), and other oral cavity and pharynx (C14.0-C14.8). Non-HPV-associated cancers were constituted as all other oral cavity and pharynx cancers that were not defined by HPV-associated cancers. More specifically, the subsites for non-HPV-associated oral cavity and pharynx cancers were non-HPV-associated squamous cell carcinoma cell types (excluding histology codes 9050-9055, 9140, 9590-9993) within the lips (C00.0-C00.9), dorsal, ventral, anterior, and border of the tongue (C01.9-C02.9); gum (C03.0-C03.9); floor of mouth (C04.0-C04.9); hard palate (C05.0, C05.8, C05.9); other/unspecified parts of the mouth (C06.0-C06.9); salivary glands (C07.9-C08.9); tonsils (C09.0-C09.9); oropharynx (C10.0-C10.9), nasopharynx (C11.0-C11.9); hypopharynx (C12.9, C13.0-C13.9); and other oral cavity and pharynx (C14.0, C14.2, C14.8).

Temporal trends in incidence rates were examined by the site from 2000 through 2019. Annual percent change (APC) estimates were generated using Joinpoint software.[8] In 2020, public health interventions and hospital resource reallocation during the COVID-19 pandemic influenced the availability and willingness of the public to access health and screening services resulting in a subsequent drop in the observed case counts for most cancers in Illinois and the United States as a whole. The Joinpoint model was not designed to accommodate a one-time anomaly in the rates for the most recent year. Including 2020 in the Joinpoint trends would

bias the interpretation of the impact of longer-term trends in oral cancers. For this reason, Joinpoint analysis was limited to the years 2000-2019.

Oropharyngeal Cancer by Demographics

In Illinois, during the years 2016 through 2020, oral and pharyngeal cancers ranked as the eighth most commonly diagnosed cancer in men and the 14th in women. The incidence rate of oropharyngeal cancers in Illinois (12.2 per 100,000) was not significantly different from that of the United States (11.9 per 100,000). Table 1 displays Illinois' oral and pharyngeal cancer rates by sex, race-ethnicity, and age. Within sex, significantly higher rates were observed in males and were roughly three times that of females. Non-Hispanic White Illinois residents displayed significantly higher rates of oral and pharyngeal cancer when compared to other racial-ethnic groups. Examination of age groups revealed that the highest rates of oral and pharyngeal cancers were observed to be in the 55-64 and 65 and above age groups with these two groups comprising roughly 80% of the cases.

Table 1: Oral and pharyngeal cancer incidence rates by sex, race-ethnicity and age, Illinois, 2016-2020

	Rates	Lower CI	Upper CI	Cases	% Cases
Illinois	12.2	11.9	12.4	9,462	
Sex					
Males	18.3	17.9	18.8	6,677	70.6%
Females	6.8	6.5	7.0	2,785	29.4%
Race-Ethnicity					
Non-Hispanic White	13.5	13.1	13.8	7,524	79.5%
Non-Hispanic Black	9.5	8.9	10.1	954	10.1%
Non-Hispanic API	8.5	7.6	9.5	329	3.5%
Non-Hispanic AIAN	11.7	6.5	19.4	16	0.2%
Hispanic	7.4	6.8	8.1	545	5.8%
Age					
0-14	0.1	0.1	0.2	17	0.2%
15-34	0.9	0.8	1.1	161	1.7%
35-44	4.7	4.3	5.2	381	4.0%
45-54	16.0	15.2	16.9	1,339	14.2%
55-64	36.4	35.1	37.7	3,037	32.1%
65+	45.6	44.3	47.0	4,527	47.8%

Source: Illinois State Cancer Registry data as of 11/22

Rates are age-adjusted to the 2000 U.S. standard population

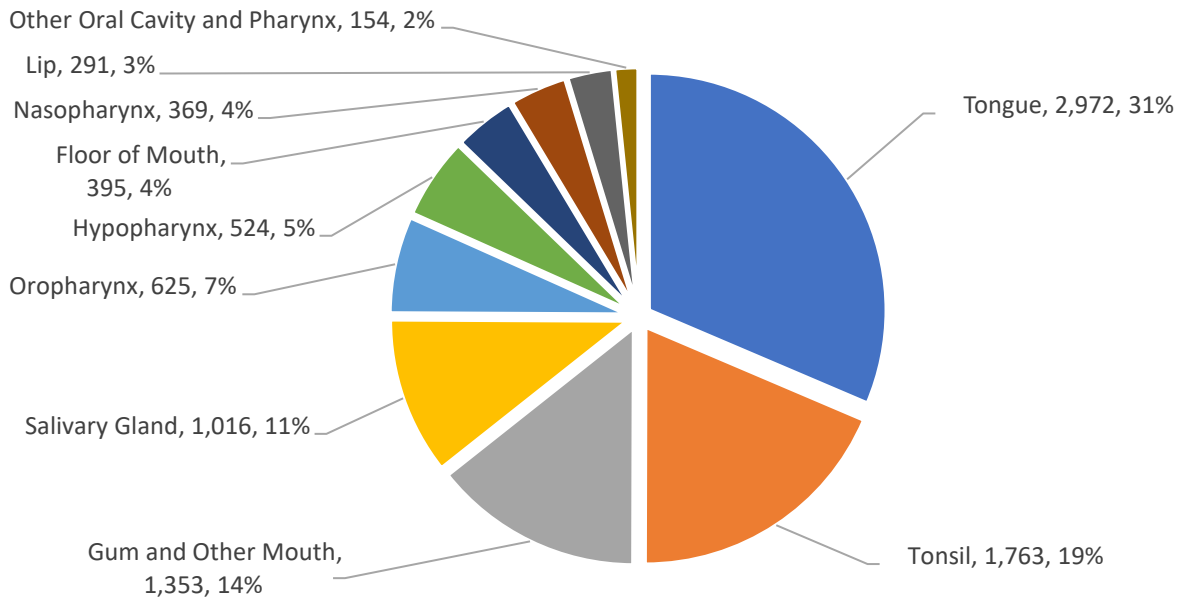
API – Asian and Pacific Islanders

AIAN – American Indian and Alaskan Native

Oropharyngeal Cancer by Subsites

The distribution of oral and pharyngeal cancers is displayed in Figure 1. The majority of oropharyngeal cancers occur in the tonsils and tongue. These subsites represent approximately 50% of oropharyngeal cancers occurring between 2016 and 2020.

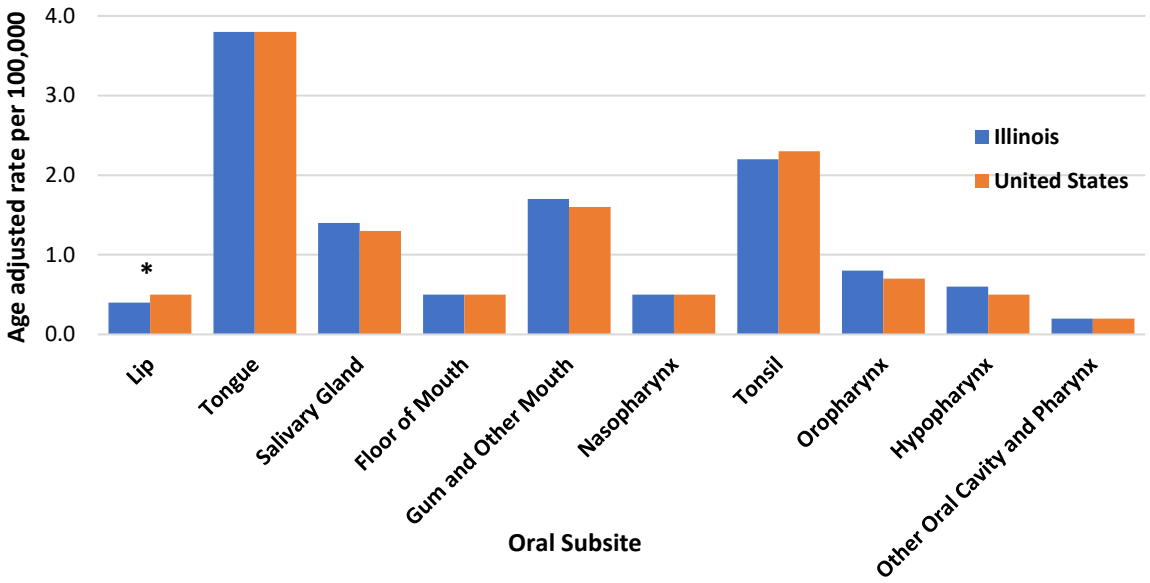
Figure 1: Distribution of oral and pharyngeal cancers by subsite, Illinois, 2016-2020



Labels: Oral Subsite, Case Count, Percent of Total
Source: Illinois State Cancer Registry data as of November 2022

Incidence rates for oropharyngeal subsites for Illinois and the United States are presented in Figure 2. Illinois incidence rates were found to be similar to that of the United States except for cancer occurring in the lip, which was statistically significantly lower in Illinois (0.4 per 100,000) than in the United States as a whole (0.5 per 100,000). When looking at oropharyngeal subsites by race and ethnicity, non-Hispanic whites had the highest incidence rates across subsites with three exceptions: cancer of the gums and other mouth, hypopharynx, and nasopharynx. Cancer of the gum and other mouth and nasopharynx were highest in non-Hispanic Asian Pacific Islanders, while cancers of the hypopharynx were highest among non-Hispanic Blacks (Table 2). Men displayed statistically significantly higher incidence rates across all oropharyngeal subsites compared to women (Table 3).

Figure 2: Oral and pharynx age-adjusted cancer incidence between Illinois and U.S.



*Significantly different between Illinois and national ($p \leq 0.05$).
Data Sources: Illinois State Cancer Registry as of November 2022; North American Association of Central Cancer Registries, CiNA Public Use Data File, 2000-2020, as of December 2022

Table 2: Oropharyngeal subsite incidence rate by race-ethnicity, Illinois, 2016-2020

Subsite	**Non-Hispanic White**	**Non-Hispanic Black**	**Non-Hispanic Asian/Pacific Islander**	**Non-Hispanic Native American /Alaskan Native**
Lip	0.4 (0.4-0.5)	0.0 (0.0-0.1)	0.1 (0.0-0.2)	~
Tongue	4.5 (4.3-4.6)	2.0 (1.8-2.3)	2.0 (1.6-2.6)	1.9 (0.4-5.9)
Salivary Gland	1.4 (1.3-1.5)	1.6 (1.3-1.9)	1.0 (0.7-1.4)	0.8 (0.0-4.6)
Floor of Mouth	0.6 (0.5-0.6)	0.4 (0.3-0.6)	0.2 (0.1-0.5)	~
Gum and Other Mouth	1.8 (1.7-1.9)	1.4 (1.1-1.6)	2.7 (2.2-3.2)	1.6 (0.2-5.9)
Nasopharynx	0.4 (0.4-0.5)	0.6 (0.5-0.8)	1.5 (1.1-1.9)	0.9 (0.0-4.7)
Tonsil	2.7 (2.5-2.8)	1.6 (1.4-1.9)	0.3 (0.2-0.6)	4.4 (1.6-9.9)
Oropharynx	0.9 (0.8-1.0)	0.8 (0.6-1.0)	0.1 (0.1-0.3)	1.0 (0.1-4.4)
Hypopharynx	0.6 (0.6-0.7)	0.8 (0.6-1.0)	0.4 (0.2-0.6)	~
Other Oral Cavity and Pharynx	0.2 (0.2-0.2)	0.2 (0.1-0.3)	0.2 (0.1-0.4)	1.1 (0.0-5.3)

Data represented as 2000 U.S. standard population age-adjusted incidence rates per 100,000 cases (95% confidence interval)
~ No cases
Source: Illinois State Cancer Registry as of November 2022

Table 3: Oropharyngeal subsite incidence by sex, Illinois, 2016-2020

Subsite	Males	Females
Lip	0.6 (0.6-0.7)	0.2 (0.1-0.2)
Tongue	5.7 (5.5-6.0)	2.1 (2.0-2.3)
Salivary Gland	1.7 (1.6-1.9)	1.2 (1.0-1.3)
Floor of Mouth	0.7 (0.6-0.8)	0.3 (0.3-0.4)
Gum and Other Mouth	2.1 (2.0-2.3)	1.4 (1.3-1.5)
Nasopharynx	0.7 (0.6-0.8)	0.3 (0.2-0.3)
Tonsil	3.9 (3.7-4.2)	0.7 (0.6-0.8)
Oropharynx	1.3 (1.2-1.4)	0.3 (0.3-0.4)
Hypopharynx	1.1 (1.0-1.2)	0.3 (0.2-0.3)
Other Oral Cavity and Pharynx	0.3 (0.3-0.4)	0.1 (0.1-0.1)

Data represented as 2000 U.S. standard population age-adjusted incidence rates per 100,000 cases (95% confidence interval)
Source: Illinois State Cancer Registry as of November 2022

Oropharyngeal Cancer by Stage

During 2016-2020, women diagnosed with oral cancer had their tumors diagnosed more frequently in an early stage (41.8%) versus men (25.6%)(data not shown). Moreover, 64.6% of oral cancers were diagnosed at a late stage (regional or distant stages) and 30.4% were diagnosed at an early stage (local stage). Table 4 shows the distribution of early versus late oral cancer diagnosis by race and ethnicity. Cases of oral cancer in non-Hispanic Black and non-Hispanic Native Americans and Alaskan Natives were diagnosed at later stages compared to non-Hispanic Whites. Percentages for non-Hispanic Native Americans and Alaskan Natives were based on 14 cases and should interpreted cautiously. The sex difference in stage at diagnosis was seen in all racial-ethnic groups. In addition, the difference in early-stage diagnosis between non-Hispanic White and non-Hispanic Black cases was seen in both males and females.

Table 4: Oral cancer case distribution by stage and race-ethnicity, Illinois, 2016-2020

	All Races-Ethnicities	Non-Hispanic White	Non-Hispanic Black	Non-Hispanic Asian/Pacific Islander	Non-Hispanic American Indian/Alaskan Native	Hispanic
Early Stage	30.4%	31.0%	22.9%	32.2%	12.5%	30.5%
Late Stage	64.6%	64.1%	71.5%	63.8%	75.0%	64.0%
Unknown	5.0%	4.9%	5.7%	4.0%	12.5%	5.5%

Source: Illinois State Cancer Registry as of November 2022

Early Stage - Includes cases diagnosed in the local stage

Late Stage - Includes cases diagnosed in regional and distant stages

Examination of the stage at diagnosis for oral cancer subtypes reveals several subsites (nasopharyngeal, tonsillar, oropharyngeal, and hypopharyngeal) with less than 20% of all cases diagnosed in the early stages of the disease. This is likely due to the physical location of the site in the human body and the difficulty of a visual examination by a physician or dentist.

Table 5: Oral cancer case distribution by stage and oral cavity subsite, Illinois, 2016-2020

	Early	Late	Unknown
Oral Cavity and Pharynx	30.4%	64.6%	5.0%
Lip	79.0%	12.7%	8.2%
Tongue	33.6%	62.3%	4.1%
Salivary Gland	48.0%	46.5%	5.5%
Floor of Mouth	43.0%	54.7%	2.3%
Gum and Other Mouth	39.5%	54.5%	6.1%
Nasopharynx	10.0%	83.2%	6.8%
Tonsil	13.3%	83.9%	2.7%
Oropharynx	12.2%	81.4%	6.4%
Hypopharynx	17.2%	79.4%	3.4%
Other Oral Cavity and Pharynx	10.4%	54.5%	35.1%

Source: Illinois State Cancer Registry as of November 2022

Early stage - Includes cases diagnosed in the local stage

Late stage - Includes cases diagnosed in regional and distant stages

Oral cancer by geography

The Illinois State Cancer Registry routinely reviews county-level data and has constructed four county groups (urban, suburban, small urban, and rural) for use in analyses (see Appendix A for full listing). Table 6 displays the rates of oropharyngeal cancers by county group. The incidence rate of oropharyngeal cancers can be seen to increase along with increasing rurality which was also observed in males and females. Figure 3 displays statistically significant differences in county oropharyngeal incidence and late-stage oropharyngeal incidence. All the counties with rates significantly higher when compared to the whole state are rural or small-urban counties.

Table 6: Oral cancer incidence by geography and sex, Illinois, 2016-2020

	Both Sexes	Male	Female
Illinois	12.2 (11.9-12.4)	18.3 (17.9-18.8)	6.8 (6.5-7.0)
Urban	11.1 (10.7-11.5)	16.6 (15.9-17.3)	6.6 (6.2-7.0)
Suburban	11.4 (10.9-11.9)	17.1 (16.3-18.1)	6.2 (5.7-6.8)
Small urban	13.7 (13.0-14.3)	20.7 (19.6-21.9)	7.5 (6.9-8.2)
Rural	14.1 (13.5-14.8)	21.4 (20.3-22.6)	7.3 (6.6-8.0)

Data represented as 2000 U.S. standard population age-adjusted incidence rates per 100,000 cases (95% confidence interval)

Source: Illinois State Cancer Registry as of November 2022

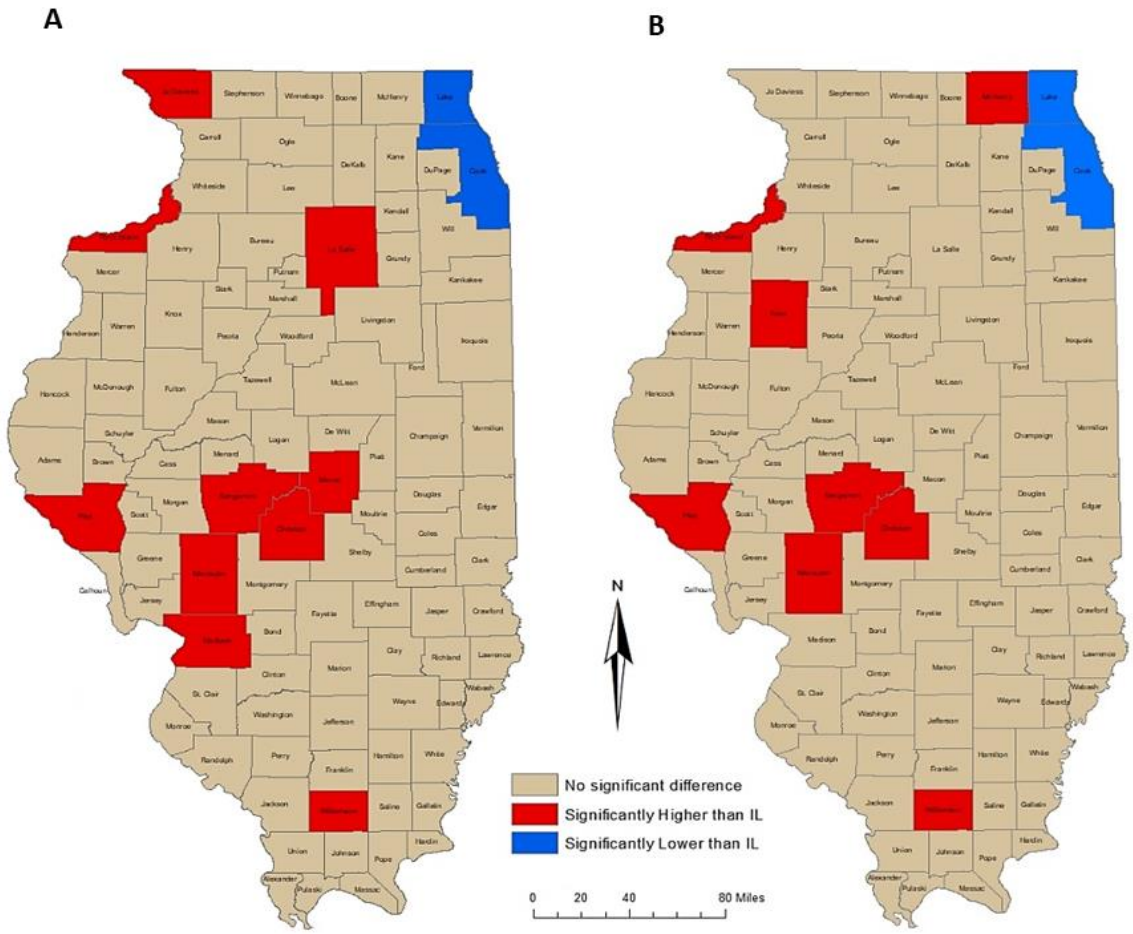


Figure 3 – Illinois county maps highlighting the various counties associated with a significantly higher (red) or lower (blue) age-adjusted incidence rate in comparison with statewide age-adjusted incidence rates for overall stage (12.2 per 100,000 cases) (A) and late-stage (7.8 per 100,000 cases) (B) oral and pharynx cancers.

Source: Illinois State Cancer Registry data as of November 2022

Trends in oral and pharyngeal cancer

Trends were examined by applying the average annual percent change to single year age-adjusted incidence rates for 2000 through 2019. Overall, oropharyngeal cancer in Illinois has shown a positive trend, increasing on average 0.88 percent per year. Table 7 highlights positive trends in demographic groups that appear to be contributing to the statewide upward trend in cancer incidence rates. People aged 55-64 years, males, non-Hispanic White, and small urban and rural demographics all displayed significantly positive trends over the 2000-2019 time period.

Table 7: Average annual percent change (AAPC) by demographics, Illinois, 2000-2019

	AAPC
Illinois	0.88*
Sex	
Male	0.85*
Female	0.68*
Age (years)	
00-14	~
15-34	0.66
35-44	-0.40
45-54	0.25
55-64	1.34*
65+	1.17*
Race-Ethnicity	
Non-Hispanic White	1.48*
Non-Hispanic Black	-1.81*
Non-Hispanic Asian Pacific Islander	0.02
Non-Hispanic American Indian Native Alaskan	~
Hispanic	1.16
Geography	
Urban	-0.04
Suburban	0.77*
Small Urban	1.21*
Rural	1.85*

*Significantly different from zero ($p<0.05$)

~ No cases

Source: Illinois State Cancer Registry data as of November, 2022

Trends in the cancer incidence rates for subsites within the oral cavity and pharynx were also examined and were not uniform across subsites. Average annual percent change (AAPC) across the 2000-2019 time period was significant and positive in the following subsites: tongue (AAPC = 2.47%), salivary gland (1.67%), tonsil (3.24%), and oropharynx (3.37%). The following subsites displayed a significant negative trend: the floor of the mouth (-3.44%) and hypopharynx (-1.74%). The subsites gum and other mouth (0.26%) and nasopharynx (-1.14%) displayed non-significant trends.

HPV associated cancers

HPV-associated oral cancers, as defined earlier in this report, are compared to non-HPV-associated cancers, and examined across sex, age, race-ethnicity, and geography (Table 8). In Illinois, during 2016-2020, HPV-associated oral cancers (N=4,126) represented roughly 44% of all oropharyngeal cancers. The rate of non-HPV-associated cancers was significantly higher than that of HPV-associated cancers. This generally held across demographic strata. The prior observations of increased oral cancer incidence rates in men, non-Hispanic Whites, adults over age 55, and less urban geographies held in both HPV and non-HPV-associated cancers, however, the rates and disparities within demographic groups were larger within the non-HPV associated group. Non-Hispanic American Indians and Alaskan Natives did display the highest rate of HPV-associated cancers, however, this rate was based on 10 cases and should be interpreted with caution. Non-Hispanic Asians and Pacific Islanders were the only racial-ethnic groups to display higher rates of non-HPV-associated cancers. Currently, a clear reason for that difference is unknown. However, this difference might be influenced by a high rate of nasopharyngeal and gum and other mouth cancers (non-HPV-associated) relative to other racial-ethnic groups. HPV-associated cancers were also seen to be diagnosed at more advanced stages of the disease.

Table 8: HPV associated oral and pharyngeal squamous cell cancer incidence rates by sex, race-ethnicity, age, geography, and stage, Illinois, 2016-2020

	HPV Associated				Non-HPV associated			
	Rates	Lower CI	Upper CI	Cases	Rates	Lower CI	Upper CI	Cases
Illinois	5.2	5.0	5.4	4,126	7.0	6.8	7.1	5,336
Sex								
Males	9.0	8.7	9.3	3,380	9.3	9.0	9.6	3,297
Females	1.8	1.6	1.9	746	5.0	4.8	5.2	2,039
Race-Ethnicity								
Non-Hispanic White	6.1	5.9	6.3	3,440	7.3	7.1	7.6	4,084
Non-Hispanic Black	4.0	3.6	4.4	411	5.5	5.0	6.0	543
Non-Hispanic API	1.0	0.7	1.4	41	7.5	6.6	8.4	288
Non-Hispanic AIAN	7.2	3.3	13.6	10	4.5	1.6	10.0	6
Hispanic	2.6	2.2	3.0	194	4.8	4.3	5.4	351
Age (years)								
0-14	~	~	~	0	0.1	0.1	0.2	17
15-34	0.1	0.1	0.2	18	0.8	0.7	1.0	143
35-44	1.7	1.4	2.0	134	3.1	2.7	3.5	247
45-54	8.3	7.7	9.0	699	7.7	7.1	8.3	640
55-64	18.8	17.8	19.7	1,563	17.7	16.8	18.6	1,474
65+	16.9	16.1	17.8	1,712	28.7	27.6	29.8	2,815
Geography								
Urban	4.4	4.2	4.7	1,357	6.6	6.4	7.0	1,984
Suburban	4.9	4.6	5.2	962	6.5	6.1	6.9	1,192
Small Urban	6.1	5.6	6.5	866	7.6	7.1	8.1	1,045
Rural	6.5	6.1	7.0	941	7.6	7.1	8.1	1,115
Stage								
Early	0.7	0.7	0.8	583	3.0	2.9	3.1	2,292
Late	4.3	4.1	4.4	3,390	3.5	3.4	3.7	2,720
Unknown	0.2	0.2	0.2	153	0.4	0.4	0.5	324

Source: Illinois State Cancer Registry data as of November 2022. Rates are age-adjusted to the 2000 U.S. standard population

~ Rate not calculated; API – Asian and Pacific Islanders; AIAN – American Indian and Alaskan Native

HPV-Associated – ICD-O-3 site codes C01.9, C02.4, C02.8, C05.1-C05.2, C09.0-C09.1, C09.8-C09.9, C10.0-C10.4, C10.8-C10.9, C14.0, C14.2, C14.8, with histology codes 8050-8086 and 8120-8131 and restricted to microscopically confirmed cases

Non-HPV associated – In accordance with site recode ICD-O-3/WHO 2008 definition, incorporates all site groups associated with oral cavity and pharynx [lip(C00.0-C00.9), tongue (C01.9-C02.9), salivary gland (C07.9-C08.9), the floor of the mouth (C04.0-C04.9), gum and other mouth (C03.0-C03.9, C05.5-C05.9, C06.0-C06.9), nasopharynx (C11.0-C11.9), tonsil (C09.0-C09.9), oropharynx (C10.0-C10.9), hypopharynx (C129, C13.0-C13.9), and other oral cavity and pharynx (C14.0, C14.2, C14.8), excluding 9050-9055, 9140, 9590-9993 and the histology codes of overlapping HPV-associated subsite ICD-O-3 codes.

The trend for HPV-associated oral and pharynx cancers has been significantly positive over 20 years (2000 through 2019). HPV-associated oral and pharynx cancers have seen a significant increase in new cases with an average 2.16% annual rise in Illinois. In contrast, non-HPV-associated oral and pharynx cancers have remained relatively steady with a non-significant change in the rate of new cases averaging a 0.05% annual increase.

Prevention/Intervention

Primary care and oral health providers have a role in prevention, early detection, and intervention when oral cancer is suspected. On the prevention front, providing actionable information and recommendations that result in reducing behavioral, environmental, and cultural risk factors (e.g., tobacco, alcohol, betel nut use) and increasing protective (e.g., immunocompetence, HPV immunization, sunscreen use) factors should be the first line of defense.

Routine oral cancer detection involves a thorough visual and tactile exam conducted by a medical or oral health professional. However, because many of the oral sites common to oral cancer are located deep inside the neck, they cannot be easily visualized or palpated. Thus, the oral cancer exam should be accompanied by a thorough medical history taking, documenting risk factors and symptoms or changes in oral tissues lasting more than two weeks. The intervention of a suspected pathology should include follow-up examination to observe tissues directly or indirectly with additional visualization aids and a biopsy of the tissue to obtain a definitive diagnosis.

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Appendix A

Illinois State Cancer Registry County Groupings

Rural			Small Urban	Suburban	Urban
Adams	Hardin	Piatt	Champaign	DuPage	Cook
Alexander	Henderson	Pike	DeKalb	Kane	
Bond	Henry	Pope	Kankakee	Lake	
Boone	Iroquois	Pulaski	Kendall	McHenry	
Brown	Jackson	Putnam	McLean	Will	
Bureau	Jasper	Randolph	Macon		
Calhoun	Jefferson	Richland	Madison		
Carroll	Jersey	Saline	Peoria		
Cass	Jo Daviess	Schuyler	Rock Island		
Christian	Johnson	Scott	St Clair		
Clark	Knox	Shelby	Sangamon		
Clay	LaSalle	Stark	Tazewell		
Clinton	Lawrence	Stephenson	Winnebago		
Coles	Lee	Union			
Crawford	Livingston	Vermilion			
Cumberland	Logan	Wabash			
DeWitt	McDonough	Warren			
Douglas	Macoupin	Washington			
Edgar	Marion	Wayne			
Edwards	Marshall	White			
Effingham	Mason	Whiteside			
Fayette	Massac	Williamson			
Ford	Menard	Woodford			
Franklin	Mercer				
Fulton	Monroe				
Gallatin	Montgomery				
Greene	Morgan				
Grundy	Moultrie				
Hamilton	Ogle				
Hancock	Perry				

Groups based on population density, rate of growth, and Beale codes.