

# Trends in palatine tonsillar cancer incidence and mortality rates in the United States

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Abstract – Objective: The purpose of this paper is to describe the extent of the public health problem presented by palatine tonsillar cancer in the United States by analyzing recent incidence and mortality rate trends. *Methods:* Using the National Cancer Institutes' Surveillance, Epidemiology and End Results (SEER) Program database, age-adjusted incidence rates (1973-2001) for five histological types of palatine tonsillar cancer by race and sex were calculated. For total palatine tonsillar cancer age-specific incidence (1973–2001) and mortality (1969– 2001) rates by race and sex were calculated. Mortality and population data were obtained from the National Center for Health Statistics (NCHS) and the U.S. Census Bureau. The Joinpoint Regression Model was employed to establish the statistical significance of incidence and mortality rate trends. Results: The majority of palatine tonsillar cases diagnosed in SEER-9 registries from 1973 to 2001 occurred among white males, age 40-64 years, with squamous cell carcinoma (SCC). The highest incidence of palatine tonsillar cancer occurred in black males, followed by white males with SCC. For age 40-64 years, palatine tonsillar incidence rates significantly declined for white females and black females, rose and then declined for black males, but increased from 1988 for white males. For age 65+ years, incidence significantly declined among white males. Palatine tonsillar cancer mortality rates for age 40-64 years significantly declined for white females. Rates also declined for black females (1981-2001) and black males (1985-2001) in this age group while rates for white males declined significantly from 1969 to 1987, but stabilized at nearly 0.4 through 2001. Mortality for the age group, 65+, significantly rose and fell for white females and declined for white males. Conclusions: Beginning in the late 1980s, and continuing through 2001, the risk for white males, age 40-64 years, of developing palatine tonsillar cancer increased. In contrast, the risk for white males, age 65 years and older, of developing palatine tonsillar cancer and of dying from this disease decreased during the study period.

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A broad range of tumors occurs in the tonsil (1). Treatment for tonsillar cancer may include surgery, radiotherapy or chemotherapy (2, 3). Patients have a high risk of primary-treatment failure and death. If cured, they are often disfigured or lose their ability to speak or to swallow (4). Survival for the most common type of tonsillar cancer, squamous cell carcinoma (SCC), has improved little in the last 20 years despite advances in surgical reconstruction and combined modality treatment (2, 5). Costs

charged by hospitals for diagnostic codes related to palatine tonsillar malignancy (ICD-9-CM 146–146.2) totaled \$76 929 928 for the year, 2003 (6).

Major risk factors for tonsillar cancers include the use of tobacco and/or alcohol. Studies suggest that Human papillomavirus (HPV) may also play an etiological role and represents a unique risk factor in a subset of tonsillar cancer cases (7–12). Recently, it has been reported that a significant proportion of new cases of tonsillar cancer cases have developed in young people without traditional risk factors (3). This increase is of concern considering that smoking-related cancers in the general population decreased dramatically from 1991–1995 (13). It is also a concern because tonsillar cancer has long been considered to be highly preventable (14).

Two of the Healthy People 2010 National Health Promotion and Disease Prevention objectives are to increase the proportion of oral and pharyngeal cancers detected at the earliest stage and to reduce oropharyngeal cancer deaths to no more than 2.7 deaths per 100 000 people (15). Considering these objectives, and that cancers of the palatine tonsil and oropharynx are the most prevalent types of pharyngeal cancer (4, 14), periodic detailed statistical information on tonsillar cancer trends is needed to assess the burden of this disease in the population and to evaluate progress against it. Routine Surveillance, Epidemiology and End Results Cancer Statistics Review (SEER CSR) monographs provide detailed age, sex and race specific data for oral and pharyngeal cancers as a combined group. Therefore, trends in some site-specific cancers such as tongue cancer in young adults (16) cannot be observed from these monographs. The most recent separate statistics review monograph focusing on oral and pharyngeal cancers was published in 1991 using SEER data from 1973 to 1987 (14). As the publication of that monograph, a detailed study of tonsillar SCC incidence trends in the United States, was performed by Frisch et al. (17), who noted an increase in rates of white males younger than 60 years from 1973 to 1995. In 2001 Canto and Devesa also reported increasing total tonsillar cancer incidence rates in white males in the U.S. using data from 1975 to 1998, but did not study subgroups by age (18). More recently Shiboski et al. (19), using data from 1973 to 2001, noted an increase in tonsillar SCC incidence among white adults aged 20-44 and a higher 5-year relative survival rate in young adults, age 20-44 years, when compared with adults aged 45 years or older. Information in this study regarding tonsillar SCC incidence and survival was limited to the groups mentioned. Tonsillar cancer mortality rate trends have not been examined since 1987. Thus, presently, significant gaps exist in the knowledge base regarding recent tonsillar cancer rate trends.

Joinpoint regression analysis allows for an innovative approach to the description of cancer rate trends. To date, this approach has not been employed to describe and to analyze tonsillar cancer incidence and mortality data by sex, age and race. Such analyses would provide important information on long-term tonsillar cancer trends including both number and timing of statistically significant changes in trends.

The goal of this study is to update and expand upon previous findings by exploring palatine tonsillar incidence and mortality rate trends among adults grouped by age, race and sex in the United States using joinpoint regression analysis to characterize trends. A comparison of adult tonsillar cancer incidence and mortality trends among population subgroups will add to the tonsillar cancer knowledge base and better describe where disparities related to the burden of tonsillar cancer exist in the U.S. population. It is hoped that these analyses may also act as a springboard for further research related to identification of causes for significant trends such as changes in risk factor exposure for segments of the population, and help to direct future public health efforts to prevent and to control this disease.

# Methods

Data for the analyses were obtained from the Surveillance, Epidemiology and End Results Program (SEER) (20). Nine registries (San Francisco-Oakland, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah and Atlanta) for cases diagnosed from 1973 to 2001 were included in the analysis of incidence. These registries account for approximately 10% of the U.S. population. Population estimates were derived by SEER using data provided by the U.S. Census Bureau.

Early in the study period, tumors were coded according to the Manual of Tumor Nomenclature and Coding (MOTNAC) (21). Later, they were coded according to the International Classification of Diseases for Oncology, first, second and third editions (ICDO, ICDO-2, ICDO-3; 22–24). While no changes in the topographical codes occurred for palatine tonsillar cancer, morphological coding changes did occur for subtypes of the category of lymphoma. Because rates were calculated for the overall category of lymphoma rather than for individual subtypes, it is thought that the effects of changes in coding upon rate trends would be minimal. ICDO-3 codes used in the analyses are listed in Table 1.

Using SEERstat statistical software (25), and SEER-9 cases with primary site palatine tonsillar

#### Golas

Table 1. ICDO-3 codes for	topography and morphology
used in the analyses	

	ICDO-3 code
Topography	
Tonsil	090–099
Morphology	
Squamous cell carcinoma	8052-8082
Adenocarcinoma	8140-8573
Kaposi's sarcoma	9140
Lymphoma	9590–9989
Other and NOS	8000-8049, 8083-8139,
	8574–9139, 9141–9589
Total	8000–9989

cancer, age-adjusted (2000 U.S. standard) and agespecific incidence rates for malignant cancers of the palatine tonsil (ICDO-3 codes C09.0-C09.9) were calculated and expressed per 100 000 person-years. Specifically, age-adjusted (2000 U.S. standard) incidence rates for five histological types (Table 1) of palatine tonsillar cancer by race and sex were calculated and age-specific incidence rates for the age groups, 20-39, 40-64 and 65+ years were calculated for total palatine tonsillar cancer by race and sex. Analyses using the joinpoint regression model were performed to establish statistical significance of age-specific total palatine tonsillar cancer trends. The percentage change in incidence rates was calculated for the period from 1974-1980 to 1995–2001 by histological type, race and sex. The percentage change for Kaposi's sarcoma for all groups studied and for Other and Not Otherwise Specified Tonsil (NOS) among black females was not determined because of the presence of zero case frequency in these cohorts.

For analyses of mortality trends, malignant palatine cancer cases were coded using ICDO-3 topography codes (C09.0–C09.9). Deaths were identified with the use of the International Classification of Disease Codes (146-146.2; 26), for underlying death because of malignant neoplasm of the tonsil, tonsillar fossa and tonsillar pillars. Total palatine cancer mortality statistics from 1969 to 2001 based on death certificates were obtained from public-use files from the National Center for Health Statistics (NCHS) via the SEER Program website (27). Age-adjusted rates (2000 U.S. standard) for total palatine tonsillar cancer for the total population by race, and sex and age-specific mortality rates for total palatine tonsillar cancer for the age groups, 20–39, 40–64 and 65+ years, by race and sex were derived by combining case data with estimated midyear population values obtained from the U.S. Bureau of the Census via the SEER website (28). All mortality rates were expressed per 100 000 person-years.

The joinpoint regression model (29) was applied to characterize trends in palatine tonsillar incidence and mortality rates. The program did not analyze cohorts with zero values; these included all cohorts, age 20-39 years, for total palatine tonsillar cancer incidence and mortality rate trends, and black females and males, age 65+ years, for total palatine tonsillar cancer incidence rate trends. In the joinpoint model, the response variables for analyses are the natural logarithms of age-adjusted rates and the independent variable is the calendar years of diagnosis. The statistics derived from these models are the estimated annual percent change (APC), 95% confidence intervals (CIs) for the APCs, and any possible joinpoints (calendar years) at which there is a change in the trends.

## Results

## Descriptive statistics by histological type

During the 1973-2001 period, a total of 8588 malignant cancers of the palatine tonsil were diagnosed. The majority of palatine tonsillar cancers, 84%, were SCC. Lymphoma was the second most common type of cancer comprising 12% of total tonsillar cancer cases. Other and NOS histological types made up 4% of total tonsillar cancers. Adenocarcinoma made up <1%, and Kaposi's sarcoma made up 0.5% of total tonsillar cancers. Table 2 lists absolute numbers of incident cases and percentages of tonsillar cancer types by race and age group (0-19, 20-39, 40-64 and 65+) with male-to-female count ratios for the period 1973-2001. The greatest absolute number of cases of tonsillar cancer occurred among whites in the age group 40-64 years that were diagnosed with SCC. For each of the five histological tonsillar cancer types studied in whites and blacks, the highest number of cases occurred in the age group, 40-64 years with the exception of lymphoma and Other and NOS types which had higher numbers in whites, age 65+ and for Kaposi's sarcoma with the highest number in whites in the age group, 20-39 years (32 cases). Higher absolute numbers of cases occurred in men compared with women for all histological types for both races except for lymphomas in the age group, 65+ years, in whites and blacks.

	Age (years)											
	0–19			20–39			40–64			65+		
	п	$\%^{a}$	M:F <sup>b</sup>	п	% <sup>a</sup>	M:F <sup>b</sup>	п	$\%^{a}$	M:F <sup>b</sup>	п	$\%^{a}$	M:F <sup>b</sup>
White												
SCC	0	0	N/A	140	2	3.4	3502	59	2.6	2282	39	1.9
Adenocarcinoma	0	0	N/A	5	11	0.3	24	55	1.4	15	34	1.5
Kaposi sarcoma	0	0	N/A	32	84	N/A	5	13	N/A	1	3	N/A
Lymphoma	30	4	1.7	90	11	3.1	272	34	1.7	413	51	0.9
Other and NOS	2	1	1.0	11	4	2.7	118	47	3.5	120	48	2.2
Total (all values)	32	0	1.7	278	4	3.6	3921	56	2.5	2831	40	1.7
Black												
SCC	0	0	N/A	35	3	2.5	795	77	3.1	205	20	2.9
Adenocarcinoma	0	0	N/A	0	0	N/A	9	75	1.3	3	25	N/A
Kaposi sarcoma	0	0	N/A	2	50	N/A	2	50	N/A	0	0	N/A
Lymphoma	1	1	N/A	15	21	1.1	35	49	1.7	21	29	0.5
Other and NOS	1	3	N/A	0	0	N/A	27	69	1.7	11	28	4.5
Total (all values)	2	0	N/A	52	4	2.1	868	75	2.9	240	21	2.5

Table 2. Palatine tonsillar cancer incident cases by age, race, sex and histological type from SEER-9 registries for the period, 1973–2001

<sup>a</sup>Row percentages may not add to 100 because of rounding.

<sup>b</sup>Male-to-female ratio by race.

NOS, not otherwise specified tonsil; SCC, squamous cell carcinoma; N/A, not applicable.

#### Palatine tonsillar cancer incidence trends

Overall, age-adjusted total palatine tonsillar cancer incidence rates (1973-2001) for the total population significantly increased by 0.35 % per year to 1.5 (Fig. 1). Rates for the same period, fell among white and black women, rose for white males from 1988 to 2001, and remained stable among black males after 1975 at a level of 4.0. Age-adjusted incidence rates (1973-2001) for each of the five types of tonsillar cancers studied (Table 3) were higher among males than females. By histological type, the male/female rate ratios (1973-2001) ranged from 1.57 among whites for adenocarcinoma to 3.65 for Other and NOS. Among blacks the male/female ratio ranged from 1.34 for lymphoma to 3.72 for SCC. The black to white incidence rate ratio (1973-2001) was highest among males for adenocarcinoma at 3.36. Among males, incidence rates for SCC were nearly two times higher among blacks than among whites. For Other and NOS, rates among black males were 56% higher than among white males. Rates for Kaposi's sarcoma among white and black males were about equal. Rates of lymphoma among white males were 20% higher than among black males. SCC rates were 46% higher in black women than in white women. Rates of Other and NOS types were 87% higher in black than white women. Rates for adenocarcinoma and lymphoma were equal in these groups. Percent change (Table 4) calculations revealed that total tonsillar cancer incidence rates declined from 1974-1980 to

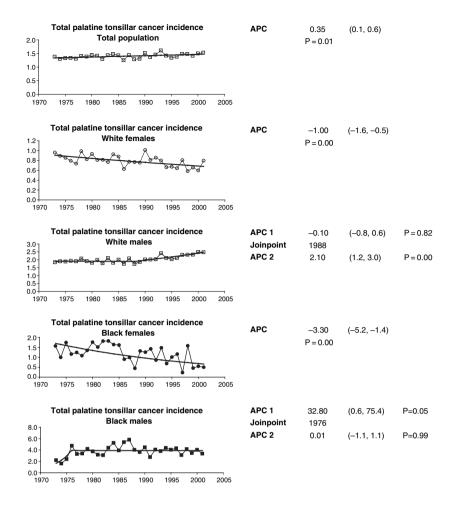
1995–2001 among white and black women, but increased among white and black men.

During the period, 1973–2001, significant findings for age-specific total palatine tonsillar cancer incidence rate trends for the age group, 40–64 years, included a decline in incidence among white and black females. Among black males incidence rose from 1973, and then fell from 1986 through 2001 to a level of 6.0. In contrast rates among white males in this age group increased by 3.7% per year from 1988 to 2001 to end at a high of nearly 5.0. For the age group, 65+ years, incidence declined significantly among white males by 0.7% per year. Please see Fig. 2 for a graphical representation of findings.

## Palatine tonsillar cancer mortality trends

Age-adjusted total palatine tonsillar cancer mortality rates (1969–2001) for the total population declined significantly beginning in 1977. A slowing of the rate of decline occurred in 1987, which continued through 2001 (Fig. 3). A significant overall decrease in mortality rates occurred among black and white women. Declines in rates also occurred for white and black males, but a slowing in the rate of decrease beginning in 1987 was noted for white males. Age-specific mortality rates (1969– 2001) for those, age 40–64 years, significantly declined among white females. Among black females, rates declined from 1981 through 2001. Rates in black males, also, declined significantly

#### Golas



*Fig. 1.* Total palatine tonsillar cancer incidence rate trends by sex and race (1973–2001).

Table 3. Incidence rates<sup>a</sup> for tonsillar cancer by sex, race and histologic type, SEER-9, 1973–2001

	All races male and female		All races male		White males		Black males		All races female		White females		Black females	
	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate
Total	8588	1.42	5929	2.15	4835	2.07	854	3.82	2659	0.81	2227	0.79	308	1.11
Histological type														
SCC	7189	1.19	5078	1.83	4133	1.76	777	3.47	2111	0.64	1791	0.64	258	0.93
Adenocarcinoma	58	0.01	33	0.01	24	0.01	8	0.04	25	0.01	20	0.01	4	0.01
Kaposi's sarcoma	43	0.01	43	0.01	38	0.01	4	0.01	0	0.00	0	0.00	0	0.00
Lymphomas	990	0.17	553	0.21	456	0.20	38	0.16	437	0.13	349	0.12	34	0.12
Other and NOS	308	0.05	222	0.09	184	0.08	27	0.13	86	0.09	67	0.02	12	0.04

<sup>a</sup>Per 100 000 person-years, age-adjusted using the 2000 U.S. standard.

NOS, not otherwise specified tonsil; SCC, squamous cell carcinoma.

beginning in 1985–2001. In contrast, mortality rates among white males, age 40–64 years, declined from over 0.80 with an APC of 3.8% to 0.40 in 1987. After 1987, rates stabilized at just over 0.4 through 2001. In the age group, 65 years of age and older, rates significantly rose, and then, fell among white women and decreased among white men. See Fig. 4 for a graphical representation of findings.

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## Discussion

These data concur with previous reports and reveal that in terms of absolute number the vast majority of palatine tonsillar cancer cases reported in nine SEER registries from 1973–2001 were SCC and occurred in white males between 40 and 64 years of age. Results for the analysis of incidence trends showed, that of the five histological types studied,

Table 4. Percent change (1974–1980 to 1995–2001) in incidence rates for palatine tonsillar cancer by race, sex and histologic type from SEER-9

	White males	White females	Black males	Black females
Histologic type				
Total	20.3	-20.9	10.1	-42.0
SCC	20.4	-22.9	5.9	-45.0
Adenocarcinoma	-30.8	-30	147.4	-100
Kaposi's sarcoma	N/A	N/A	N/A	N/A
Lymphoma	69.1	7.6	84.8	-4.6
Other, NOS	-37.8	-65.9	12.6	N/A

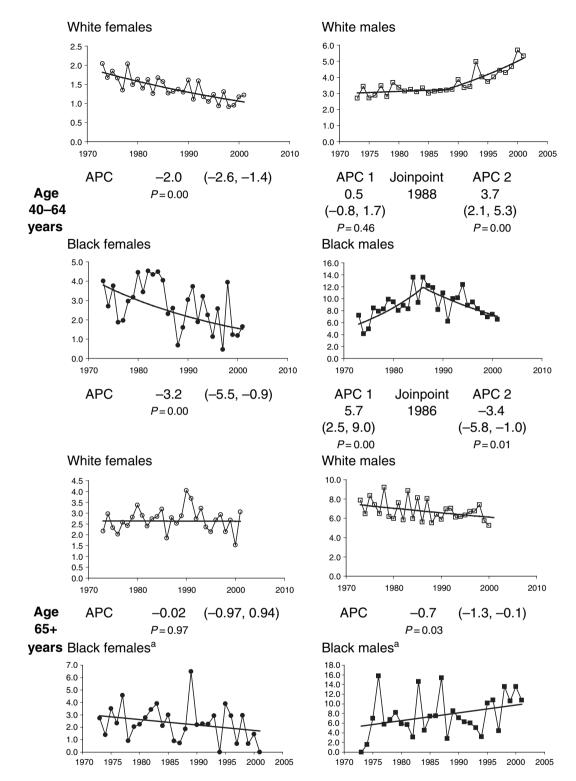
SCC, squamous cell carcinoma; NOS, not otherwise specified palatine tonsil; N/A, not applicable.

the highest incidence was for SCC among black males at 3.47. Palatine tonsillar cancer incidence rates were higher in males than in females for all five histological types studied. The black to white incidence rate ratio was highest among males for adenocarcinoma at 3.36 and among females 1.87 for Other and NOS types. Lymphoma among males was the only histological type in which incidence was higher among whites.

Results for the age-specific total palatine cancer incidence trend analyses by joinpoint revealed statistically significant declines in rates for all groups analyzed by the end of the study period except for white males in the age group, 40-64 years and for white females, age 65+. For white males rates were at their lowest level in 1973. Rates remained stable from 1973 to 1988 where a significant joinpoint was found and a marked positive change in slope occurred. Rates continued to rise to reach their highest levels in 2001. This finding is in contrast with that for black males in this age group. Rates in this group rose to a high in 1986 where a joinpoint occurred. Then, rates markedly declined through 2001 to return to levels approaching the lowest rate in 1973. The findings among women, age 40-64 years, are encouraging as they indicate a continuous downward trend throughout the study period to their lowest levels in 2001 for both black and white women. Throughout the study period, the disparity between white and black women in incidence closed as rates in these groups, age 40–64, were nearly equal in 2001. Among males, age 40-64 years, the gap between whites and blacks also decreased by the end of the study period so that final rates in 2001 were nearly equal. Reasons for the rise in tonsillar cancer incidence seen during the study period among white males age 40-64 years are unknown. For the age group, 65+ years, rates declined significantly in white males, but remained stable among white females. By the end of the study period, however, rates in white males were more than twice as high as rates among white females.

For age-specific total palatine cancer mortality, significant declines in rates were seen in the latter half of the study period for all groups, age 40-64 years, except for white males. Among white males, age 40-64 years, mortality rates declined to their lowest levels in 1987 where a significant joinpoint was found, but a rising trend was not found to be significant. The apparent stabilizing trend from 1987 through 2001 for white males, age 40-64 years although not statistically significant is notable as this trend change offset a 17 year decline in mortality rates for this group. While rates among black females and males for the age group, 40-64 years, markedly decreased by the end of the study period to their lowest levels, rates in 2001 were still more than double those of white females and males in the same age group. Among those age, 65 years and older, significant decreases in rates were seen by 2001 for white males and females. In this age group, in 1973 the highest mortality rates occurred in white females and males. By the end of the study period the disparity between white and black mortality rates among women was eliminated. While rates in white women, age 65+, rose to a high and then fell to a new low during this period, a rising trend among black females was not found to be significant. Among males in the 65+ age group the disparity in mortality rates decreased by means of a continuous decline in rates in whites and a slower decrease in blacks. By 2001 rates in black males, age 65+, were twice as high as those in white males of the same age group. Reasons for the declines seen in the latter half of the study period for all groups analyzed except for white males, age 40-64 years, are unknown.

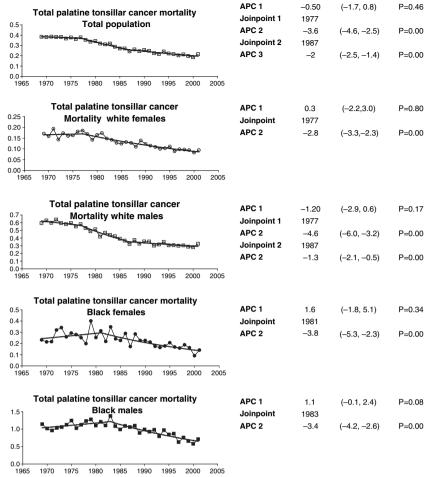
Given the decline in smoking (13) and drinking (30, 31) levels in men and women in both racial groups since the 1970s, and the recent decline seen in smoking-related head and neck cancers (13), it is unlikely that the increases in trend for white males, aged 40–64 years, in incidence noted in this study would be explained solely by gender and racial differences in smoking and drinking levels (32). To the author's knowledge, no major change in disease classification occurred and no new screening process or technological advancement was introduced for tonsillar cancer during the study period that might explain the rising trend noted.



*Fig.* 2. Total palatine tonsillar cancer incidence rate trends by sex, race and age (1973–2001). <sup>a</sup>Trend not analyzed by Joinpoint.

However, the timing of the start of the upward trend in incidence and the apparent stabilizing trend in mortality rates, for middle aged white males in the mid-1980s at the start of the HIV epidemic raises questions as to whether the elevated risk for this group may be because of the emergence of a new risk factor such as HIV, or to the additive or synergistic effects of exposure to other oncogenic viruses and traditional risk factors.

Human papillomavirus, the causal agent of cervical cancer, appears to be etiologically involved in some cancers of the oropharynx (8, 33) and may



Trends in palatine tonsillar cancer rates

0.1 0.0 1965

*Fig. 3.* Total palatine tonsillar cancer mortality rate trends by sex and race (1969–2001).

play a role in the increasing trends of palatine tonsillar cancer. HPV has been detected in over 50% of tonsillar carcinomas (7). The most common HPV type in genital cancers (HPV 16) is also most common in head and neck tumors (8). The mechanism of transmission of HPV to the oral cavity and pharynx is unknown. A recent study showed the presence of HPV in the oral cavity was associated with increased risk of oropharyngeal or oral cavity cancer, independent of alcohol and tobacco exposure (9). It was also shown that husbands of patients with HPV associated cervical cancer had an increased risk of tonsillar cancer (34). HPVpositive head and neck cancer patients have risk factors similar to patients with HPV-positive genital cancers. These risk factors included young age at first intercourse, higher number of sexual partners, history of genital warts and history of performing oral sex (8, 12). In other studies, patients with HPV-16 positive tumors were found to have better overall and disease specific survival than HPV negative patients (5, 36). HPV-16 positive patients were also younger and the association with conventional risk factors – smoking and drinking-was less significant than in HPV negative patients (17). The findings of this study may identify a risk group that fits the profile for HPV associated cancers as the group consists of males of younger age and the trends began during the HIV epidemic. Other HPV-associated cancers have been found in excess among patients with HIV infection and among patients with transplantation-related immunosuppression (36, 37).

Alternative explanations for these findings include changes in tonsillectomy rates throughout the study period. Reliable long-term data for tonsillectomy and tonsillectomy and adenoidectomy procedure rates are not available. Therefore, temporal changes in tonsillectomy rates were not considered in the calculation of rates in this study. A previous study (17) reported that tonsillectomy rates decreased 70–80% from the 1970s to the 1990s in all groups. As per that discussion, it is unlikely that changes in tonsillectomy rates alone would explain the size of the trend increase found for white males, age 40–64 years, in this study.

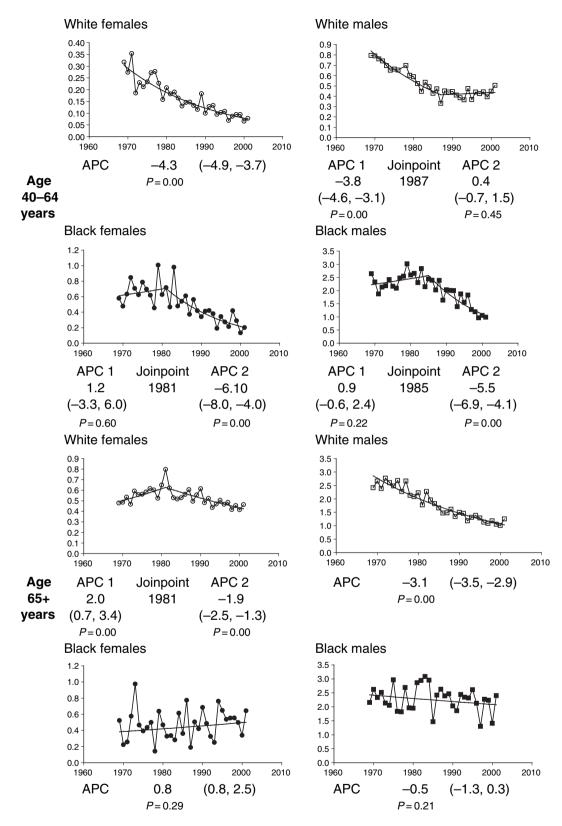


Fig. 4. Total palatine tonsillar cancer mortality rate trends by sex, race and age (1969–2001).

The performance of analyses using SEER data has limitations, which have been described previously (38, 39). Another limitation of this study was the consideration of only two racial/ethnic groups, white and black, in the analyses of rate trends. In the future when more long-term data for other racial/ethnic subgroups have been collected by SEER registries, analyses may be performed to further describe and to explore rate trends among other racial/ethnic groups in the U.S. population. In addition, various behavioral risk factors such as smoking and alcohol use, and oncogenic virus seropositivity have been associated with the occurrence of palatine tonsillar cancer. As information on these possible confounding factors is not collected by registries, they were not accounted for in these analyses.

Study results revealed upward trends in palatine tonsillar cancer incidence for white males, age 40–64, from the mid-1980s through 2001, and decreasing trends throughout the study period in palatine tonsillar cancer incidence and mortality for white males, age 65 years and older. Determination of reasons for racial, age and gender differences in palatine tonsillar cancer trends by future investigations may help to guide public health efforts to prevent and to control this disease.

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