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Incidence trends for upper aerodigestive tract cancers in rural United States counties

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Abstract

Background: Recent declines in cancer incidence and mortality have not been distributed equally across the United States. Factors such as tobacco cessation and human papillomavirus presence might differentially affect urban and rural portions of the country.

Methods: We used the Surveillance, Epidemiology, and End Results database to assess cancer incidence rates and trends from 1973 to 2015. We compared incidence rates for oral cavity, oropharynx, and larynx cancer in urban and rural counties and identified trends using Joinpoint software.

Results: Incidence of larynx and oral cavity cancer are decreasing faster in urban areas than in rural areas, while incidence of oropharynx cancer is increasing faster in rural areas than urban areas.

Conclusions: Relative trends in incidence of larynx, oral cavity, and oropharynx cancer over the past 40 years are unfavorable for rural United States counties compared with urban areas. Cancer control programs should take this into account.

Keywords

Head and neck cancer; Incidence trends; rurality; oropharynx cancer; disparities

Introduction

Several health-related and socioeconomic factors have been identified as mediating the “rural disadvantage,” an association between rurality and a variety of adverse health outcomes.¹ Residents of rural areas have higher death rates from leading causes of mortality

in the US than residents of urban areas.² With roughly 1 in 5 Americans living in a rural area, disparities affecting this population can have a significant impact nationwide.

Head and neck squamous cell carcinomas are strongly associated with tobacco use and human papillomavirus (HPV), and tobacco- and HPV-related cancers are more common in rural populations. Although overall there has been a decline in cancer incidence and mortality, this trend has not been seen across all demographic groups, with declines in incidence greater in urban areas than rural areas.³ Current epidemiologic trends related to head and neck cancer are not well described in rural populations. Recent analyses have shown decreasing incidence of tobacco-related cancers across the board, and head and neck sites have shown the same trend.⁴ In contrast, however, the recent trend with oropharyngeal cancer has been rising incidence related to HPV.

Zuniga and Lango recently reported a higher incidence rate of laryngeal cancer among rural US residents.⁵ Hashibe et al focused on residents of one state and identified a lower incidence of all types of cancer, but poorer survival in rural areas compared to urban areas.⁶ Other studies have demonstrated a higher incidence and mortality for tobacco- and HPV-related cancers in most rural areas.^{3,4} However, not all of these studies examined trends over time or focused on upper aerodigestive subsites. Moreover, rural populations may not be reached to the same extent as urban populations by preventative interventions such as smoking cessation campaigns and HPV education or vaccination measures.^{7,8} We sought to report the incidence trends of oral cavity, oropharynx, and larynx cancers over the past four decades with respect to rurality in the US.

Methods

We used data from the National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) database using SEER*Stat 8.3.5 software.⁹ Data derived from nine registries, each providing cancer incidence data from a defined geographic region (San Francisco/Oakland, Utah, Iowa, New Mexico, Seattle-Puget Sound, Atlanta, Detroit, Connecticut, and Hawaii), and together comprising about 10% of the US population. We included cases diagnosed between 1975 and 2015, and only invasive squamous cell carcinomas (ICD-O-3 histology codes 8050-8089 and behavior code 3). Oral cavity sites were defined by ICD-O-3 topography codes C00.3-6, C00.8, C00.9 (lip); C02.0-3, C02.8, C02.9 (tongue); C03.0, C03.1, C03.9 (gum), C04.0, C04.1, C04.8, C04.9 (floor of mouth); C05.0, C05.8, C05.9 (hard palate); C06.0-2, C06.8, C06.9 (cheek, vestibule, and mouth NOS). Oropharynx sites were defined by codes C01.9, C02.4 (base of tongue / lingual tonsil); C05.1, C05.2 (soft palate); C09.0, C09.1, C09.8, C09.9 (tonsil); C10.0, C10.2, C10.3, C10.8, C10.9 (other oropharynx). Larynx sites were defined by codes C10.1 (anterior surface of epiglottis); C32.0-C32.3, C32.8, C32.9 (larynx).

Rurality was defined by Rural Urban Continuum Codes (RUCC) defined and updated by United States Department of Agriculture. A county was defined as rural if it was not within a metropolitan statistical area and had an urban population less than 20,000. Cases with unknown rural/urban status were not included in additional analysis; this occurred in a small number of cases in 1999 and earlier. Counties were dichotomized into urban and rural for

each year based on their RUCC code for that year; codes are updated each decade. Age-adjusted incidence data were calculated in SEER*Stat and adjusted to the 2000 US standard population.

Patient demographic variables included age at diagnosis, year of diagnosis, sex, and race. Tumor characteristic variables included cancer site, stage, and grade. The stage variables used were SEER Historic Stage A for cases diagnosed before 1995, SEER Summary Stage 1977 for cases diagnosed 1995-2000, SEER Summary Stage 2000 for cases diagnosed 2001-2003, and Derived SEER Summary Stage 2000 for cases diagnosed 2004+.

Data were imported into Joinpoint¹⁰ for trend analysis using methods described by Kim et al.¹¹ In short, the Jointpoint Regression Program fits the simplest joinpoint model that the trend data allow. It starts with straight regression line and uses Monte Carlo Permutation methods to test whether more joinpoints (i.e., apparent changes in the trend) are statistically significant and should be added to the model. Annual percent changes (APCs) in incidence were compared. This study was not considered human subject research and did not require institutional review board approval.

Results

During the study period, there were 107,683 cases meeting study criteria, including 36,183 oral cavity, 32,793 oropharynx, and 38,707 larynx cases. There were 7,592 cases arising in residents of rural counties, comprising 7.1% of the total. Demographic data are shown in Table 1.

For larynx cancers, in urban residents the adjusted incidence rate changed from 4.9 cases per 100,000 in 1975 to 2.5 in 2015, and in rural residents was 3.0 in 1975 and 2.5 in 2015, having risen to a high of 5.1 in 1996. Incidence and joinpoint regression trends are shown in Figure 1. Rural residents have experienced a decreasing incidence of 0.5% annually ($p=0.02$), while urban residents since 1987 have seen a much steeper decline in incidence of 2.6% annually ($p<0.01$). The difference in the incidence trends was statistically significant (test of parallelism $p<0.001$).

Adjusted oral cavity cancer incidence varied in urban patients from 4.4 cases per 100,000 in 1973 to 3.5 in 2015, and in rural residents from 3.1 in 1975 to 4.1 in 2015. A plot showing oral cavity cancer incidence rates and joinpoint regression results for urban and rural residents is shown in Figure 2. There was an annual percentage increase of 0.5% in rural residents over the entire study period. Among urban residents there was a sharp decrease of 1.7% per year between 1981 and 2005 before returning to a 0.8% annual increase from 2006 to 2015 ($p<0.05$). Over 41 years, oral cavity cancer has gone from a substantially lower incidence in rural patients to a higher incidence in rural patients. Incidence trends were statistically significantly different (test of parallelism $p<0.001$).

For oropharynx cancers, in urban residents the incidence rate changed from 2.9 cases per 100,000 in 1975 to 4.4 in 2015, and in rural residents from 1.3 in 1975 to 3.6 in 2015. Incidence and joinpoint regression results appear in Figure 3. Most importantly, incidence trends for oropharynx cancers have changed in the past 20 years: while urban residents have

experienced a 2.6% annual increase in incidence since 1999, rural residents have seen a 4.6% annual increase beginning in 1991 ($p<0.05$), so that in 2015 the urban incidence rate was 4.4 per 100,000 compared to 3.6 per 100,000 in rural counties. The incidence trends, as with larynx and oral cavity sites, were statistically significantly different between urban and rural groups (test of parallelism $p<0.001$).

A Forest plot demonstrating the APC for each segment of the joinpoint regression results for each cancer subtype based on urban-rural setting is shown in Figure 4.

Discussion

We evaluated differences in upper aerodigestive cancer incidence rates and trends based on rurality in the United States. We found that the incidence of oral cavity and larynx cancer is not declining as quickly in rural areas as in urban areas and that the incidence of oropharynx cancer is increasing more steeply in rural areas. Polednak described this phenomenon recently, comparing oropharynx cancer incidence in metropolitan counties with non-metropolitan areas and showing trends similar to those in the present work.¹² Similarly, Zahnd et al. described a more acute increase in incidence for all HPV-associated cancers in rural areas between 1995 and 2015 compared to urban settings, though this included non-upper aerodigestive cancers as well.³ Our methods differed based on our definition of rurality; Polednak and Zahnd et al. grouped all nonmetropolitan counties, including those with urban population of 20,000 or more, in the rural group. Since we aimed to focus on trends in more rural populations, we chose to assign counties as rural if they were outside metropolitan statistical areas and had urban populations less than 20,000 (RUCC 6-9). The rural population represented in our study comprises individuals living in low-density counties without strong economic ties to more urban areas.

These trends over time, across all populations, have reasonable explanations. The decreasing incidence trend for larynx cancer, as well as the initial decrease seen in oral cavity cancer in urban settings, seems most likely due to trends in tobacco use, which have declined over the past two decades.¹³ The slower decline in rural populations may reflect slower declines in smoking or use of chewing tobacco. In contrast to oral cavity and larynx sites, the incidence of oropharynx cancer is increasing in both urban and rural settings due to the increased prevalence of HPV, which has driven enormous changes in incidence of oropharyngeal cancer over the past decade. The current trend in oral cavity cancer incidence for both urban and rural areas is a slow increase. The cause for this increase is not entirely clear. A similar trend was reported by Karnov et al. in a study of the Danish population.¹⁴

Within those national phenomena, the trends in rural populations are not as well described. Residents of rural and urban areas are notably different in their demographic, environmental, and socioeconomic characteristics, which can impact the health-related issues each group faces. Rural areas tend to have higher rates of tobacco use and obesity, and rural residents are more likely to live in poverty compared with those in urban or suburban settings. Overall access to health care is generally lower in non-metropolitan areas, with metropolitan areas generally having a greater density and diversity of health-related resources.² These are

among the factors that are the basis for a “rural disadvantage” affecting health and healthcare delivery in the United States.¹

This study has several limitations. Large databases such as SEER are subject to errors in diagnosis and staging. The 9-registry SEER database covers 10% of the U.S. population. This study did not specifically examine the socioeconomic differences between inhabitants of urban and rural populations, which likely influence cancer trends in these populations, but many of the likely important factors, such as smoking status and comorbid illnesses, are not reported in public-use SEER data. We did compare adjusted incidence rates, which correct for differences in age, sex, and race/ethnicity distribution between geographic regions.

Despite limitations, our analysis brings to light the important finding that trends in rural populations may remain hidden in analyses that do not specifically look for them. This is especially critical since solutions to population health issues might be different for rural areas than for urban or suburban areas.

How can the unfavorable trends in rural upper aerodigestive tract cancer incidence be addressed? General knowledge of HPV and its link to cancers, other than cervical cancer, has been shown to be linked to sociodemographic factors, such as education level and income.¹⁵ Mohammed et al described differences in awareness of HPV, its link to certain cancers, and the existence of the HPV vaccine between US residents in urban and rural settings, with rural individuals much less likely to have heard of HPV.¹⁶ With regards to HPV vaccination, Henry et al showed that vaccination initiation and completion were both higher in urban populations compared to rural; the same study identified poverty as a factor associated with vaccine series completion, which may indicate success of programs providing free vaccines in those areas.¹⁷ Tobacco cessation efforts should continue in rural areas as well as urban areas, and efforts should be made to increase awareness of HPV as a cause of oropharynx cancer as well as vaccine uptake.

Conclusion

Individuals living in rural areas in the US are experiencing different trends in the rates of larynx, oral cavity, and oropharyngeal cancer over the past 40 years compared to those in urban or suburban areas, with notably a significantly greater increase in oropharyngeal cancer rates compared to those in urban or suburban areas. Our study indicates that these rural populations are vital targets for public health programs targeting increasing awareness about and prevention of HPV-related cancer, in particular oropharyngeal cancer.

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Figure 1:
Larynx age-adjusted incidence rates and Joinpoint trends by patient rurality, SEER-9, 1975-2015
p-value <0.05 on the parallelism test indicates that the trend between urban and rural incidence is significantly different.

Figure 2:
Oral cavity age-adjusted incidence rates and Joinpoint trends by patient rurality, SEER-9, 1975-2015
p-value <0.05 on the parallelism test indicates that the trend between urban and rural incidence is significantly different.

Figure 3:
Oropharynx age-adjusted incidence rates and Joinpoint trends by patient rurality, SEER-9, 1975-2015
p-value <0.05 on the parallelism test indicates that the trend between urban and rural incidence is significantly different.

Figure 4:
Forest plot of Joinpoint analysis of annual percent change of cancer incidence by subsite and rurality, SEER-9, 1975-2015. APC = annual percent change.

Table 1:

Patient and tumor characteristics of upper aerodigestive tract cancers by rurality, SEER-9, 1975-2015

		Rural			Urban	
		No. of patients	No. of patients	%	No. of patients	%
Age at diagnosis	<55 years	25133	1,457	19.2	23,676	23.7
	55-69 years	49818	3,417	45.0	46,401	46.4
	70+ years	32732	2,718	35.8	30,014	30.0
Sex	Male	78429	5,721	75.4	72,708	72.6
	Female	29254	1,871	24.6	27,383	27.4
Race	White	91410	7,520	99.1	83,890	83.8
	Other	16273	72	1.0	16,201	16.2
Cancer site	Larynx	38707	3,043	40.1	35,664	35.6
	Oral Cavity	36183	2,799	36.9	33,384	33.4
	Oropharynx	32793	1,750	23.1	31,043	31.0
Stage	Localized	44956	3,637	47.9	41,319	41.3
	Regional	43800	2,773	36.5	41,027	41.0
	Distant	13479	784	10.3	12,695	12.7
	Unstaged/Unknown	5448	398	5.2	5,050	5.1