Five-Year Survival Rates and Time Trends of Laryngeal Cancer in the US Population

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Objectives: To provide comprehensive temporal trend analysis of 5-year relative survival rates of laryngeal cancer using the Surveillance, Epidemiology, and End Results database; and to expand on prior reports by including inclusion of laryngeal tumor location, stage, age at diagnosis, treatment strategy, and histologic grade.

Design: Retrospective cohort analysis using the Surveillance, Epidemiology, and End Results database of the National Cancer Institute. The Surveillance, Epidemiology, and End Results data were used to design 5 cohorts of patients with laryngeal cancer: 1977-1978, 1983-1984, 1989-1990, 1995-1996, and 2001-2002. Five-year survival rates were analyzed according to tumor site, stage, and grade; age at diagnosis; and treatment strategy. The joinpoint regression model was used to assess survival trends and their statistical significance.

Results: Among patients with supraglottic cancer, 5-year relative survival rates for distant disease worsened over time while rates for local and regional disease did not change (P = .01 and P > .05, respectively). For localized glottic cancer, survival remained stable from 1977-1978 to 2001-2002. However, patients with regional and distant glottic cancer demonstrated a significant decrease in survival in the past 3 decades (P < .001). This trend was independent of treatment strategy. Finally, the proportion of well-differentiated tumors in patients with regional laryngeal cancer decreased over time (P < .001 for supraglottic and P = .007 for glottic).

Conclusions: A decreasing 5-year survival trend was found among patients with glottic cancer who had regional disease and in all patients with distant disease. Histopathologic trends not previously reported in those with laryngeal cancer seem to parallel those seen in other tobacco-related cancers. These trends may reflect the effect of birth cohorts and implicate the relationship between carcinogenic exposure and host factors, rather than the influence of treatment.


Several recent studies have suggested that the incidence of laryngeal cancer and other smoking-related cancers is declining in North America and Western Europe. One factor in this decline may be decreased exposure to carcinogens, specifically tobacco. It has been hypothesized that this declining incidence may reflect achievement in antismoking efforts.

Diagnostic technology and treatment for laryngeal cancer have undergone significant changes during the past several decades. However, the impact of these changes on survival rates of laryngeal cancer remains unclear. A recent study by Hoffman et al reports declining survival among patients with laryngeal cancer in the past 2 decades. Stratification by tumor location is an important aspect of laryngeal cancer survival data because glottic cancer is known to impart a better prognosis than cancers originating in the supraglottis. Notably, prior studies have not included other factors known to influence survival, such as histopathologic tumor grade, in their analyses. In this study, we analyzed changes in 5-year survival rate according to laryngeal subsites and tumor stage. We further considered the relationship between these survival trends and age at diagnosis, treatment strategy, and histologic tumor grade.

METHODS

We obtained data from the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute and applied information on cancer diagnosis only to the residents of 9 population-based registries (ie, 5 states [Connecticut, Hawaii, Iowa, New Mexico, and Utah] and 4 standard metropolitan areas [Atlanta, Georgia; Detroit, Michigan; San Francisco–Oakland, California; and Seattle–Puget Sound, Washington]).

We used SEER computer software (Stat 5.2.2) to conduct survival rate analysis. We selected cases of laryngeal cancer that contained follow-up information. The

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**RESULTS**

### INCIDENCE

Age-adjusted incidence rates for glottic and supraglottic cancer are shown in Figure 1. Overall, incidence trends at both sites varied with age and stage. A significant decrease in the incidence of local supraglottic cancer over time was found among all age groups (Figure 1D-F). In the oldest age group (those ≥65 years), the incidence of regional supraglottic disease increased (Figure 1F).

For glottic cancer, the incidence of local and regional disease decreased significantly in the youngest age group (those aged 20-49 years) (Figure 1A). In the 50- to 64-year-old subjects and in those 65 years and older, this decreased incidence was seen only in localized glottic disease (Figure 1B and C). Overall, incidence trends for regional glottic cancer were nonsignificant in both older age groups (Figure 1B and C).

### SURVIVAL

Figure 2 depicts 5-year relative survival rates for supraglottic cancer. In 1995-1996, the 5-year survival was 63.0% for localized disease, 46.1% for regional disease, and 6.4% for distant disease. While survival rates for local and regional stage supraglottic cancer have not significantly changed over time, a significant decrease was found in 5-year survival of distant stage supraglottic cancer (Figure 2C).

Survival trends of glottic cancer also differ by stage (Figure 3). The most current 5-year survival statistics by stage are as follows: from 1995-1996, 5-year survival was 90.6% for localized disease, 60.6% for regional disease, and 27.4% for distant disease. For localized disease (Figure 3A), 5-year relative survival rates were nearly identical for 1977-1978 and 1995-1996 (89.6% and 90.6%, respectively). Thus, no significant survival trend was found. On the other hand, a nearly 20% decrease in survival over time was observed for regional and distant glottic disease (RRs, 0.80 and 0.74, respectively; P < .001 for both). Specifically, the 5-year relative survival rate of regional glottic cancer decreased from 78.6% in 1977-1978 to 60.6% in 1995-1996 (Figure 3B); and for distant stage disease, it decreased from 52.7% to 27.4% (Figure 3C). There was no significant change in survival for unstaged disease (Figure 3D).

Additional analysis of the decreased survival trend of regional glottic cancer is demonstrated in Table 1. Patients with regional glottic cancer are grouped by age at diagnosis, and survival rates are categorized by cause, thereby distinguishing cancer- and non–cancer-related deaths in each age group. In the 50- to 64-year-old subjects, the 5-year glottic cancer– and all cancer–specific survival rates significantly decreased between 1977-1978 and 1995-1996. While not significant, the exact opposite trend was seen in the other 2 age groups: glottic and all cancer–related survival rates increased over time in the 20- to 49-year-old and the 65 years and older age groups. In non–cancer-specific survival rates, all groups showed a slight, but insignificant, decrease over time.

The RRs (95% CIs) by age are as follows (ratios were calculated by dividing the survival rate of 1995-1996 by the survival rate of 1977-1978). For laryngeal cancer, in the 20- to 49-year-old group, the RR was 1.1 (95% CI, 0.8-1.4); in the 50- to 64-year-old group, the RR was 0.8 (95% CI, 0.7-0.9) (P = .002); and in the 65 years and older group, the RR was 1.1 (95% CI, 0.9-1.2). For all cancer, in the 20- to 49-year-old group, the RR was 1.1 (95% CI, 0.8-1.6); in the 50- to 64-year-old group, the RR was 0.8
The RR was 0.9 (95% CI, 0.8-1.0); and in the 65 years and older group, the RR was 1.0 (0.8-1.2).

Exercising trends in survival of regional stage glottic cancer by age and birth cohort revealed an overall de-

(95% CI, 0.7-0.9) (P < .001); and in the 65 years and older group, the RR was 0.9 (95% CI, 0.8-1.1). For non–cancer-specific data, in the 20- to 49-year-old group, the RR was 0.9 (95% CI, 0.8-1.1); in the 50- to 64-year-old group,
crease in survival in patients of late cohorts (Figure 4). The effect of birth cohort was particularly evident in the survival curve of the group aged 50 to 59 years, with a significant decrease beginning in the 1924 to 1929 cohort (Figure 4B). Restated, patients with regional glottic cancer in this age group had a lower 5-year survival if they were born after 1923.

Analysis according to treatment strategy is shown in Figure 5. In the 50- to 64-year-old age group, a decreasing survival trend was observed across all treatments, including surgery only, radiation only, and combined surgery and radiation. Cancer-specific 5-year survival of those with regional glottic cancer did not vary with treatment modality. A significant trend in survival was found in non–cancer-specific mortality in patients treated with surgery only (Figure 5D). Further analysis on the proportion of patients treated with each modality is depicted in Table 2. Over time, there is a significant trend toward increased use of radiation therapy and decreased treatment with surgery alone. Last, regional stage tumors in this age group were classified according to histologic tumor grade (Table 3 and Table 4). The proportion of well-differentiated tumors in patients with regional glottic disease decreased significantly over time. In 1977-1978, 28.2% of regional disease was histologically well differentiated, significantly higher than the 15.8% of well-differentiated disease seen in 2001-2002. No significant time-dependent changes in tumor grade were found in localized disease. A similar trend was found in regional supraglottic disease.

**COMMENT**

Release of newly expanded data from the SEER database program has prompted a reexamination of survival rates for a multitude of cancer types. Laryngeal cancer was unique among this group of 24 cancers as the only type to experience a decrease in 5-year survival rates.1 In a recent analysis of the SEER database, Carvalho et al13 report survival trends for various sites of head and neck cancer. In their analysis of laryngeal cancer, they report a decrease in 5-year survival for local disease, no change for patients with regional disease, and an improvement in 5-year survival in distant or late-stage laryngeal cancer. These results seem to conflict with the findings of
this study. One explanation for this discrepancy lies in the years of data included in each analysis. Carvalho et al use the SEER data from 1974 to 1997 in their calculation of overall survival trends; however, in their analysis of stage-specific survival, they include only the data from 1983 to 1997. In doing so, they exclude a period of relatively improved survival for regional and distant disease reported from 1974 to 1978. Exclusion of these data would contribute to the variance in results between studies. In addition, Carvalho et al grouped all subsites of laryngeal cancer, rather than a separate analysis of glottic cancer, thus adding to the differences between studies.

A recent report by Hoffman et al also examined trends in laryngeal cancer survival in the past 2 decades. Using the National Cancer Data Base and SEER data, their study reports a decrease in survival of patients with glottic and supraglottic laryngeal cancer that varied by TNM stage.1 In general, the results of the present study support those of Hoffman et al and report a more pronounced decline in survival in patients with advanced stage disease.

The present report uses the SEER database program to analyze 5-year survival in patients with laryngeal cancer by age, laryngeal subsite, tumor stage, histologic grade, and treatment strategy. Overall, the data depict a significant decline in survival in patients with regional stage glottic cancer; from 1977 through 2003, a nearly 20% decrease in 5-year survival rates of advanced glottic cancer was observed. In addition, a significant decrease was found in survival rates of distant disease of glottic and supraglottic cancer during these 2 decades. There are multiple factors that may explain these results, including (1) the phenomenon of stage drift; (2) changing trends in treatment; (3) spurious data from the early cohorts; (4) the nature of relative survival rates and the impact of comorbidities; (5) a change in causative factors or carcinogenic exposure, such as tobacco; and (6) a change in the disease itself.

To begin, the confounding influence of stage drift can be created by advances in diagnostic technology. Specifically, a lesion classified as early-stage disease in the pre–computed tomographic scan era would be diagnosed as advanced when more sophisticated imaging is used. Therefore, a trend toward increased incidence of advanced disease may reflect the introduction and application of improved diagnostic technology and not a change in the

![Figure 3. Time trends of 5-year relative survival rates by tumor stage for glottic cancer. A, Local stage; B, regional stage; C, distant stage; and D, unstaged. The Mantel-Haenszel method-calculated relative ratio of 5-year survival (other cohorts vs the 1977-1978 cohort) was 1.00 in A, 0.80 in B, 0.74 in C, and 1.02 in D. The numbers in parentheses after each year indicate the number of patients at the start of the study, and the percentages in brackets indicate the 5-year relative survival rates. In B, for 1983-1984, the rate ratio (RR) was 0.81 (95% confidence interval [CI], 0.7-0.9); for 1989-1990, the RR was 0.82 (95% CI, 0.7-0.9); and in 1995-1996, the RR was 0.77 (95% CI, 0.7-0.9) (P<.001 for all periods).]
aggressiveness or behavior of the disease itself. The over-
all trends in our data support a decreasing incidence in
local disease and an increase in regional disease over the
period studied. On the other hand, stage drift would likely
lead to a positive survival trend in categorical groupings.
For example, as radiologic sophistication restaged early
disease as more advanced, the advanced cancer group
would be “diluted” with patients who demonstrate an ear-
lier form of the disease. Thus, stage drift would likely mani-
fest in an overall increase in survival of advanced stage can-
cer. However, this was not demonstrated in our results.
In fact, our data support the opposite (ie, a decrease in sur-
vival of regional stage glottic cancer). Thus, the complex
phenomenon of stage drift cannot solely account for the
results of this study.

Not only the diagnostic modalities but also the treat-
ment of laryngeal cancer has changed in the past 20 years.
More important, nonsurgical treatment, specifically ra-
diation and chemotherapy, was introduced and widely
applied to laryngeal carcinoma.1 As depicted in Figure 5,
however, the decrease in survival of regional glottic can-
cer is likely not entirely attributable to a change in treat-
ment strategy. The magnitude of decrease in cancer-
specific survival rates was approximately 20% for all
treatment modalities, including surgery, radiation, and
combined therapy, from 1977 to 1996. Throughout the
period examined, there was a significant trend toward
more frequent use of radiation therapy alone and de-
creased use of surgery alone. While reflecting an evol-
ving treatment paradigm in laryngeal cancer, patients in
each treatment modality demonstrated decreased sur-
vival over time.

Evidence of the insignificance of treatment modality
is also found in the stable survival trends among pa-
tients with regional glottic cancer of the age groups 20
to 49 years and 65 years and older. If treatment plays a
role in promoting survival, it should impact all ages rather
than only patients aged 50 to 64 years, unless different
treatments are used at different ages. These data are not
an appropriate evaluation of therapeutic effectiveness of
a given treatment modality. However, they do demon-
strate a consistent decrease in relative survival indepen-
dent of changes or trends in treatment strategy.

Analysis of the data must mention the possibility of
spurious results. In Figure 4, patients in the earliest co-
horts demonstrate strikingly good survival. It is pos-
sible that these data are spurious and inappropriately in-
fluence the analysis toward significance.

Another potentially confounding factor is the influ-
ence of comorbid disease. Survival rates in this study re-
fer to relative survival rates. As the treatment of comor-
bidity improves with time, patients in later cohorts may
survive their comorbid disease and succumb to laryn-
geal carcinoma. This is somewhat unlikely, however, be-
cause this confounding variable should influence all pa-
tients within a given cohort equally.

Finally, the decrease in survival of patients with re-
ional glottic carcinoma may be explained by a change
in causative factors, including carcinogenic exposure. The
relationship between carcinogens, specifically tobacco and
alcohol, and laryngeal cancer has long been recog-
nized.14-16 Shifting trends in tobacco use may be implica-
ted in observed changes in survival statistics and dis-
ease characteristics. Although the absolute number of
tobacco users has decreased dramatically since 1965, re-
cent reports17,18 suggest that this may disproportio-
ately represent the occasional or limited tobacco user.
From 1993 to 2000, the percentage of smokers who re-
port everyday tobacco use has increased.17,18 Thus, while
overall tobacco use has clearly decreased, there seems to
be a trend toward increased intensity among remaining
smokers. Prior research19 examining carcinogenic expo-
sure on a cellular level has linked intensity of carcino-
genic exposure, amount of genetic damage, and carci-
nogenesis. This positive relationship supports the idea
that increasing intensity of tobacco exposure may be re-
lated to the increased incidence and decrease survival of
late-stage disease.

Table 1. Time Trend of Cause-Specific 5-Year Observed Survival Rates by Age for Patients
With Regional Stage Glottic Cancer\a

<table>
<thead>
<tr>
<th>Age Group, y</th>
<th>No. of Patients Alive at Start</th>
<th>Cause-Specific 5-y Observed Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Laryngeal Cancer Specific</td>
<td>All Cancer Specific</td>
</tr>
<tr>
<td>20-49</td>
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</tr>
<tr>
<td>1977-1978</td>
<td>28</td>
<td>80.8 (7.7)</td>
</tr>
<tr>
<td>1983-1984</td>
<td>24</td>
<td>82.6 (8.0)</td>
</tr>
<tr>
<td>1989-1990</td>
<td>28</td>
<td>88.8 (6.1)</td>
</tr>
<tr>
<td>1995-1996</td>
<td>23</td>
<td>88.4 (7.8)</td>
</tr>
<tr>
<td>50-64</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1977-1978</td>
<td>113</td>
<td>90.5 (2.9)</td>
</tr>
<tr>
<td>1983-1984</td>
<td>136</td>
<td>80.3 (3.7)</td>
</tr>
<tr>
<td>1989-1990</td>
<td>103</td>
<td>82.4 (4.0)</td>
</tr>
<tr>
<td>1995-1996</td>
<td>142</td>
<td>74.2 (3.9)</td>
</tr>
<tr>
<td>≥65</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1977-1978</td>
<td>98</td>
<td>72.2 (4.9)</td>
</tr>
<tr>
<td>1983-1984</td>
<td>119</td>
<td>71.3 (4.5)</td>
</tr>
<tr>
<td>1989-1990</td>
<td>116</td>
<td>74.6 (4.6)</td>
</tr>
<tr>
<td>1995-1996</td>
<td>160</td>
<td>76.4 (3.7)</td>
</tr>
</tbody>
</table>

\(\text{aData are given as rate (SE), measured in percentages, for each age group at each year.}\)
In addition, histologic changes in disease characteristics seem to parallel trends in tobacco use and disease survival. To our knowledge, trends in histopathologic differentiation among laryngeal cancer tumors have not been previously reported. However, this phenomenon has been examined in other tobacco-related cancers, specifically lung cancer. The leading histologic type of lung cancer has undergone a well-documented shift from a squa-

Figure 4. Cancer-specific survival rates by age and birth cohort for patients with regional stage glottic cancer. A, Patients aged 50 to 54 years; B, patients aged 55 to 59 years; C, patients aged 60 to 64 years; D, patients aged 65 to 69 years; and E, patients aged 70 to 74 years. The overall Mantel-Haenszel method-calculated rate ratio (RR) of cancer-specific survival was 0.78 (95% confidence interval [CI], 0.7-0.9) (P=.003) in A, 0.73 (95% CI, 0.6-0.9) (P<.001) in B, 1.66 (95% CI, 0.8-1.0) (P=.20) in C, 0.81 (95% CI, 0.7-0.9) (P=.005) in D, and 1.35 (95% CI, 1.0-1.8) (P=.03) in E. The numbers in parentheses after each year indicate the number of patients at the start of the study, and the percentages in brackets indicate the 5-year relative survival rates. In A, for 1929 to 1934, the RR was 0.87 (95% CI, 0.7-1.1) (P=.39); for 1935 to 1940, the RR was 0.79 (95% CI, 0.6-1.1) (P=.18); and for 1941 to 1946, the RR was 0.69 (95% CI, 0.5-0.9) (P=.03). In B, for 1924 to 1929, the RR was 0.67 (95% CI, 0.5-0.9) (P=.009); for 1930 to 1935, the RR was 0.76 (95% CI, 0.6-1.0) (P=.08); and for 1936 to 1941, the RR was 0.75 (95% CI, 0.6-1.0) (P=.04). In D, for 1914 to 1919, the RR was 0.83 (95% CI, 0.7-1.1) (P=.24); for 1920 to 1925, the RR was 0.85 (95% CI, 0.7-1.1) (P=.03).
mous cell carcinoma to adenocarcinoma, and this evolution has paralleled the change in cigarette composition and tobacco use.3,20 The introduction and widespread use of filtered cigarettes in the 1950s is believed to have changed smoking behaviors and may account for the histologic trends observed in lung cancer.3,20,21 Thun et al20(p1580) suggest that “the increase in lung adenocarcinoma since the 1950s is more consistent with changes in smoking behavior and cigarette design than with diagnostic advances.” Our histologic analysis of regional

**Figure 5.** Survival rates for patients with regional stage glottic cancer aged 50 to 64 years. A, Cancer-specific rates for those who underwent surgery only; B, cancer-specific rates for those who underwent radiation only; C, cancer-specific rates for those who underwent surgery and radiation; D, non–cancer-specific rates for those who underwent surgery only; E, non–cancer-specific rates for those who underwent radiation only; and F, non–cancer-specific rates for those who underwent surgery and radiation. The overall Mantel-Haenszel method-calculated rate ratio of survival was 0.76 (P < .001) in A, 0.85 (P = .04) in B, 0.84 (P = .03) in C, 0.76 (P < .001) in D, 1.02 (P = .83) in E, and 0.98 (P = .90) in F. In A, for 1983-1984, the rate ratio (RR) was 0.79 (95% confidence interval [CI], 0.6-1.0) (P = .11); for 1989 to 1990, the RR was 0.83 (95% CI, 0.6-1.1) (P = .34); for 1995 to 1996, the RR was 0.68 (95% CI, 0.5-1.0) (P = .03). In B, for 1983-1984, the RR was 0.89 (95% CI, 0.7-1.1) (P = .50); for 1989-1990, the RR was 0.85 (95% CI, 0.6-1.1) (P = .36); and for 1995-1996, the RR was 0.81 (95% CI, 0.6-1.0) (P = .17). In C, for 1983-1984, the RR was 0.83 (95% CI, 0.6-1.1) (P = .27); for 1989-1990, the RR was 0.86 (95% CI, 0.7-1.1) (P = .36); and for 1995-1996, the RR was 0.82 (95% CI, 0.6-1.1) (P = .22). In D, for 1983-1984, the RR was 0.77 (95% CI, 0.6-1.0) (P = .02); for 1983-1984, the RR was 0.71 (95% CI, 0.5-1.0) (P = .01); and for 1995-1996, the RR was 0.77 (95% CI, 0.6-1.0) (P = .83).
### Table 2. Treatment of Patients With Regional Stage Glottic Cancer, Aged 50 to 64 Years, Over Time<sup>a</sup>

<table>
<thead>
<tr>
<th>Type of Treatment</th>
<th>1977-1978 (n = 113)</th>
<th>1983-1984 (n = 136)</th>
<th>1989-1990 (n = 103)</th>
<th>1995-1996 (n = 142)</th>
<th>2001-2002 (n = 331)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery alone</td>
<td>41 (36.3)</td>
<td>38 (27.9)</td>
<td>19 (18.4)</td>
<td>26 (18.3)</td>
<td>64 (19.3)</td>
</tr>
<tr>
<td>Radiation alone</td>
<td>37 (32.7)</td>
<td>45 (33.1)</td>
<td>30 (29.1)</td>
<td>51 (35.9)</td>
<td>145 (43.8)</td>
</tr>
<tr>
<td>Surgery plus radiation</td>
<td>30 (26.5)</td>
<td>47 (34.6)</td>
<td>50 (48.5)</td>
<td>54 (38.0)</td>
<td>96 (29.0)</td>
</tr>
<tr>
<td>No surgery or no radiation</td>
<td>3 (2.7)</td>
<td>0</td>
<td>2 (1.9)</td>
<td>6 (4.2)</td>
<td>3 (0.9)</td>
</tr>
<tr>
<td>Surgery or radiation refused</td>
<td>2 (1.8)</td>
<td>0</td>
<td>1 (1.0)</td>
<td>2 (1.4)</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Unknown surgery or radiation</td>
<td>0</td>
<td>6 (4.4)</td>
<td>1 (1.0)</td>
<td>3 (2.1)</td>
<td>22 (6.6)</td>
</tr>
</tbody>
</table>

<sup>a</sup>Data are given as number (percentage) of patients. Column percentages may not total 100 because of rounding. \( \chi_1^2 = 36.96 \ (P < .001) \) for testing the trend of treatment modality.  

<sup>b</sup>The increase in number of patients with glottic cancer is because of an increase in the population included in the Surveillance, Epidemiology, and End Results (SEER) database. The SEER regional catchment areas increased from 9 in 1973 to 1991 to 13 in 1992 to 1999 and to 17 in 2000 to 2003.

### Table 3. Histologic Grade of Glottic Cancer by Year of Diagnosis for Patients Aged 50 to 64 Years<sup>a</sup>

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<tbody>
<tr>
<td>Regional</td>
<td></td>
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</tr>
<tr>
<td>Well differentiated</td>
<td>33 (28.2)</td>
<td>29 (20.6)</td>
<td>18 (17.3)</td>
<td>27 (18.6)</td>
<td>53 (15.8)</td>
</tr>
<tr>
<td>Moderately differentiated</td>
<td>46 (39.3)</td>
<td>55 (39.0)</td>
<td>51 (49.0)</td>
<td>76 (52.4)</td>
<td>192 (57.3)</td>
</tr>
<tr>
<td>Poorly differentiated</td>
<td>15 (12.8)</td>
<td>21 (14.9)</td>
<td>18 (17.3)</td>
<td>22 (15.2)</td>
<td>57 (17.0)</td>
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<tr>
<td>Undifferentiated</td>
<td>0</td>
<td>3 (2.1)</td>
<td>1 (1.0)</td>
<td>2 (1.4)</td>
<td>1 (0.3)</td>
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<tr>
<td>Unknown</td>
<td>23 (19.7)</td>
<td>33 (23.4)</td>
<td>16 (15.4)</td>
<td>18 (12.4)</td>
<td>32 (9.6)</td>
</tr>
<tr>
<td>Total&lt;sup&gt;b&lt;/sup&gt;</td>
<td>117 (100.0)</td>
<td>141 (100.0)</td>
<td>104 (100.0)</td>
<td>145 (100.0)</td>
<td>335 (100.0)</td>
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<tbody>
<tr>
<td>Localized</td>
<td></td>
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</tr>
<tr>
<td>Well differentiated</td>
<td>81 (27.6)</td>
<td>94 (29.8)</td>
<td>70 (26.7)</td>
<td>78 (25.9)</td>
<td>125 (26.2)</td>
</tr>
<tr>
<td>Moderately differentiated</td>
<td>91 (31.0)</td>
<td>109 (34.6)</td>
<td>93 (35.5)</td>
<td>135 (44.9)</td>
<td>213 (44.6)</td>
</tr>
<tr>
<td>Poorly differentiated</td>
<td>19 (6.5)</td>
<td>20 (6.3)</td>
<td>25 (9.0)</td>
<td>27 (9.0)</td>
<td>29 (6.1)</td>
</tr>
<tr>
<td>Undifferentiated</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2 (0.7)</td>
<td>2 (0.4)</td>
</tr>
<tr>
<td>Unknown</td>
<td>103 (35.0)</td>
<td>92 (29.2)</td>
<td>74 (28.2)</td>
<td>59 (19.6)</td>
<td>109 (22.8)</td>
</tr>
<tr>
<td>Total&lt;sup&gt;b&lt;/sup&gt;</td>
<td>294 (100.0)</td>
<td>315 (100.0)</td>
<td>262 (100.0)</td>
<td>301 (100.0)</td>
<td>478 (100.0)</td>
</tr>
</tbody>
</table>

<sup>a</sup>Data are given as number (percentage) of patients in each period for each stage of cancer. For regional data: \( \chi_1^2 = 7.25 \ (P = .007) \) for testing the trend of proportion of well-differentiated tumor. For localized data: \( \chi_1^2 = 0.81 \ (P = .37) \) for testing the trend of proportion of well-differentiated tumor.  

<sup>b</sup>The sum of column percentages may not total 100 because of rounding.

### Table 4. Histologic Grade of Supraglottic Cancer by Year of Diagnosis for Patients Aged 50 to 64 Years<sup>a</sup>

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Localized</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Well differentiated</td>
<td>22 (18.3)</td>
<td>20 (16.9)</td>
<td>15 (15.0)</td>
<td>10 (11.1)</td>
<td>20 (12.5)</td>
</tr>
<tr>
<td>Moderately differentiated</td>
<td>43 (35.8)</td>
<td>54 (45.8)</td>
<td>40 (40.0)</td>
<td>49 (54.4)</td>
<td>83 (51.9)</td>
</tr>
<tr>
<td>Poorly differentiated</td>
<td>22 (18.3)</td>
<td>20 (16.9)</td>
<td>26 (26.0)</td>
<td>17 (18.9)</td>
<td>25 (15.6)</td>
</tr>
<tr>
<td>Undifferentiated</td>
<td>2 (1.7)</td>
<td>2 (1.7)</td>
<td>4 (4.0)</td>
<td>2 (2.2)</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>Unknown</td>
<td>31 (25.8)</td>
<td>22 (18.6)</td>
<td>15 (15.0)</td>
<td>12 (13.3)</td>
<td>31 (19.4)</td>
</tr>
<tr>
<td>Total&lt;sup&gt;b&lt;/sup&gt;</td>
<td>120 (100.0)</td>
<td>118 (100.0)</td>
<td>100 (100.0)</td>
<td>90 (100.0)</td>
<td>160 (100.0)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Regional</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Well differentiated</td>
<td>16 (11.3)</td>
<td>23 (13.6)</td>
<td>10 (5.6)</td>
<td>15 (8.6)</td>
<td>28 (5.6)</td>
</tr>
<tr>
<td>Moderately differentiated</td>
<td>65 (45.8)</td>
<td>58 (34.3)</td>
<td>89 (50.3)</td>
<td>81 (46.3)</td>
<td>263 (52.6)</td>
</tr>
<tr>
<td>Poorly differentiated</td>
<td>26 (18.3)</td>
<td>43 (25.4)</td>
<td>59 (33.3)</td>
<td>62 (35.4)</td>
<td>137 (27.4)</td>
</tr>
<tr>
<td>Undifferentiated</td>
<td>4 (2.8)</td>
<td>6 (3.6)</td>
<td>1 (0.6)</td>
<td>4 (2.3)</td>
<td>9 (1.8)</td>
</tr>
<tr>
<td>Unknown</td>
<td>31 (21.8)</td>
<td>39 (23.1)</td>
<td>18 (10.2)</td>
<td>13 (7.4)</td>
<td>63 (12.6)</td>
</tr>
<tr>
<td>Total&lt;sup&gt;b&lt;/sup&gt;</td>
<td>142 (100.0)</td>
<td>169 (100.0)</td>
<td>177 (100.0)</td>
<td>175 (100.0)</td>
<td>500 (100.0)</td>
</tr>
</tbody>
</table>

<sup>a</sup>Data are given as number (percentage) of patients. For localized stage: \( \chi_1^2 = 2.82 \ (P = .09) \) for testing the trend of proportion of well-differentiated tumor. For regional stage, \( \chi_1^2 = 9.42 \ (P < .001) \) for testing the trend of proportion of well-differentiated tumor.  

<sup>b</sup>The sum of column percentages may not total 100 because of rounding.
laryngeal cancer also documents a shift toward less differentiation, which seems to parallel decreasing survival trends and changing patterns in tobacco use. These data address the complex interaction between causative agents, including known carcinogens, such as tobacco and alcohol, and host factors that affect disease manifestation and patient survival.

The present study used fixed patient cohorts to describe temporal trends of survival in laryngeal cancer. Each of these cohorts had at least a 5-year observation period for survival, and these windows did not overlap each other in time. These methodological considerations are important in the use of cancer registry patients for whom follow-up periods are varied. In general, cancer survival is relatively high during the first several years. Because the last patient cohorts had observation periods of less than 5 years, their survival rate may be higher than those of earlier cohorts, with a greater window of observation.

Our analysis excluded patients with second or later cancer primary tumors. Such exclusion is necessary for analysis of cause-specific survival. Inherent in any database analysis, however, is the possibility of incorrect diagnosis or inappropriate attribution of mortality to non-cancer-related death when, in fact, a second primary or metastatic disease may be culpable.

In conclusion, decreasing 5-year relative survival trends were demonstrated among patients with glottic cancer and regional disease and in patients with both glottic and supraglottic cancer as well as distant disease. Histopathological trends not previously reported in laryngeal cancer seem to parallel those seen in other tobacco-related cancers. These trends may reflect the effect of birth cohorts with a unique exposure to carcinogens and changing trends in tobacco use over time, rather than an influence of treatment modality. Further research into the biological, genetic, and environmental interactions between carcinogenic exposure, specifically tobacco, and laryngeal cancer is warranted.

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Author Contributions: Drs Cosetti, Yu, and Schantz had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Cosetti, Yu, and Schantz. Acquisition of data: Yu. Analysis and interpretation of data: Cosetti, Yu, and Schantz. Drafting of the manuscript: Cosetti and Schantz. Critical revision of the manuscript for important intellectual content: Cosetti, Yu, and Schantz. Statistical analysis: Yu. Administrative, technical, and material support: Schantz. Study supervision: Schantz.

Financial Disclosure: None reported.

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REFERENCES