Supplemental Online Content

Divakar P, Davies L. Trends in incidence and mortality of larynx cancer in the US. *JAMA Otolaryngol Head Neck Surg.* Published online November 17, 2022. doi:10.1001/jamaoto.2022.3636

This supplemental material has been provided by the authors to give readers additional information about their work.

eMethods

When combining staging variables for longitudinal analyses, it is important to pay close attention to changes made in each staging system regarding details of how cancer extent and spread are categorized. Changes observed across the systems can sometimes simply be harmonized, if the categories within the variables allow it. We used harmonization in the following way: we modified the variable "SEER Combined Summary Stage 2000 (2004+)" to match the "SEER Historic Stage A" system by creating one grouping ('regional') for the following categories: 'Regional by direct extension only', 'Regional lymph nodes involved only', 'Regional by both direct extension and lymph node involvement', and 'Regional, NOS'. This regrouping allowed the overall stage groupings to be more directly comparable.

If changes in the staging systems cannot be harmonized, they must be noted and interpreted in context in longitudinal analyses. Larynx cancer staging has changed significantly over time, also requiring the use of this approach. Specifically, cases of larynx cancer with abnormal vocal cord mobility or vocal cord fixation were staged as *regional* in the 'SEER Historic Stage A' staging system variable, but cancers with these qualities were *downstaged to localized* in the 'SEER Combined Summary Stage 2000 (2004+)' system variable. Cancers that involved submandibular, submental, and retropharyngeal lymph nodes were staged as *distant* in the 'SEER Historic Stage A' staging system variable, but cancers with these qualities were *downstaged to regional* in the 'SEER Combined Summary Stage 2000 (2004+)' system variable. Last, cases of larynx cancer with thyroid cartilage extension were staged as *regional* under SEER Historic A staging system were subsequently *upstaged to distant* under SEER Combined Summary Stage 2000 (2004+). These differences are visible in the results as shifts in the trend line as the staging system moved from the historic to the updated staging and are explained in context in that section.

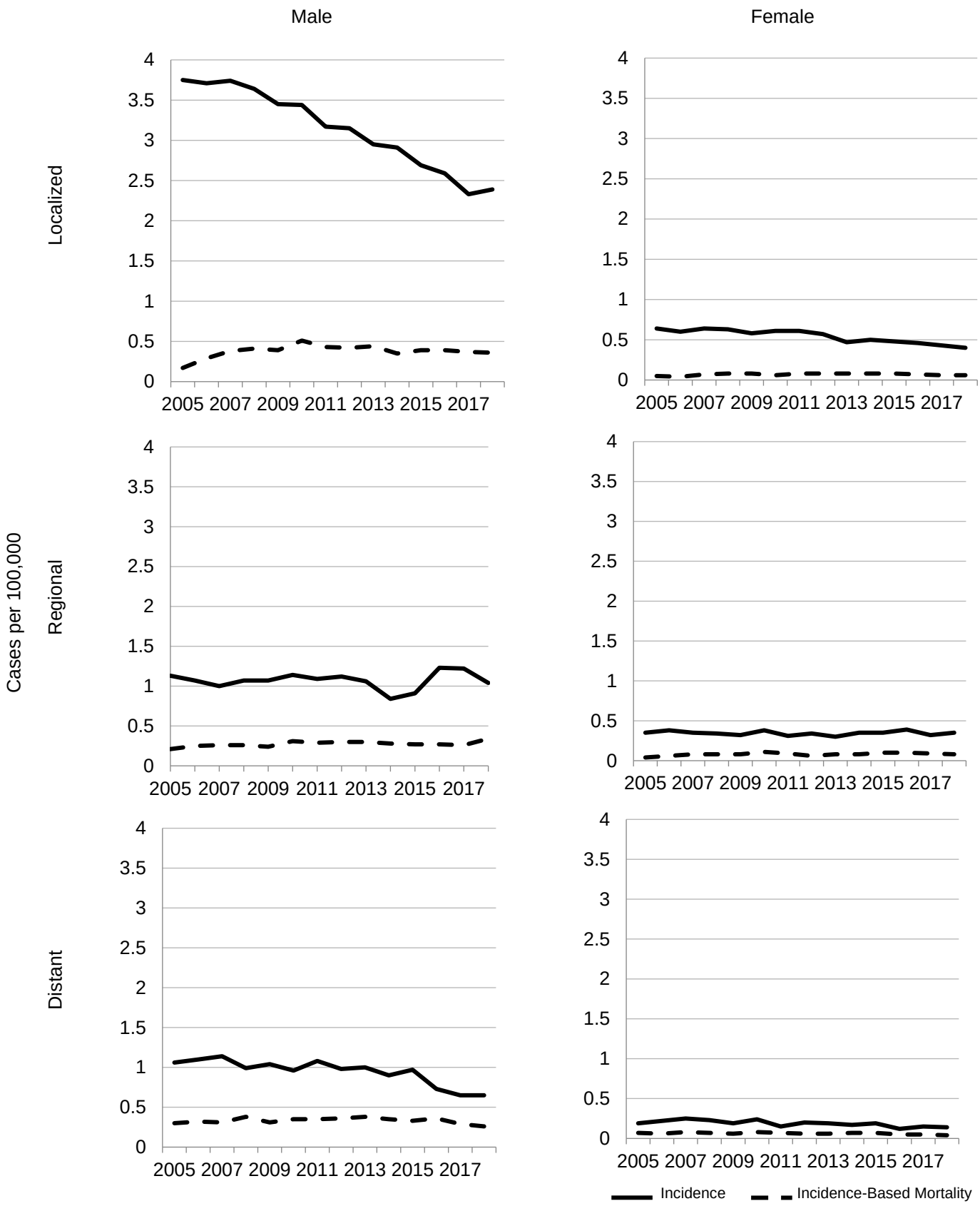
eResults

Incidence & Mortality Trends by Sex & Stage (eFigure 1)
The incidence rate of larynx cancer in male patients is higher in each stage than female patients and the main driver of the fall in incidence was in the fall of incidence of localized cancer in men. Incidence of larynx cancer decreased 36% for localized disease in men from 3.75 per 100,000 people (95% CI: 3.55 – 3.96) to 2.39 per 100,000 (95% CI: 2.25 – 2.53). The annual percent change was stable at -0.52% (95% CI: -4.2% – 3.3%) between 2005 – 2008 and then decreased -4.40% (95% CI: -5.0% – -3.8%). In women, new cases decreased 38% from 0.64 per 100,000 people (95% CI: 0.57 – 0.72) to 0.40 per 100,000 (95% CI: 0.35 – 0.46). The annual percent change decreased -3.44% (95% CI: -4.3% – -2.5%).

Incidence-based mortality of larynx cancer increased 112% over the period 2005-2018 for localized disease in men, increasing from 0.17 per 100,000 people (95% CI: 0.13 – 0.22) to 0.36 per 100,000 (95% CI: 0.31 – 0.42). The annual percent change was 56.68% (95% CI: 3.5% – 137.2%) between 2005 – 2007, note the very wide confidence intervals due to highly variable rates. The annual percent change in mortality then stabilized at -1.18% annually (95% CI: -5.0% – -3.8%) between 2007 – 2018. In localized disease in women, incidence-based mortality increased 17% over the same period, increasing from 0.05 per 100,000 people (95% CI: 0.03 – 0.07) to 0.06 per 100,000 (95% CI: 0.04 – 0.08). The annual percent change was 21.85% (95% CI: -5.6% – 57.3%) between 2005 – 2008, with very wide confidence intervals due to highly variable rates. The annual percent change in mortality in women stabilized at -1.72% (95% CI: -5.0% – 1.6%) between 2008 – 2018.

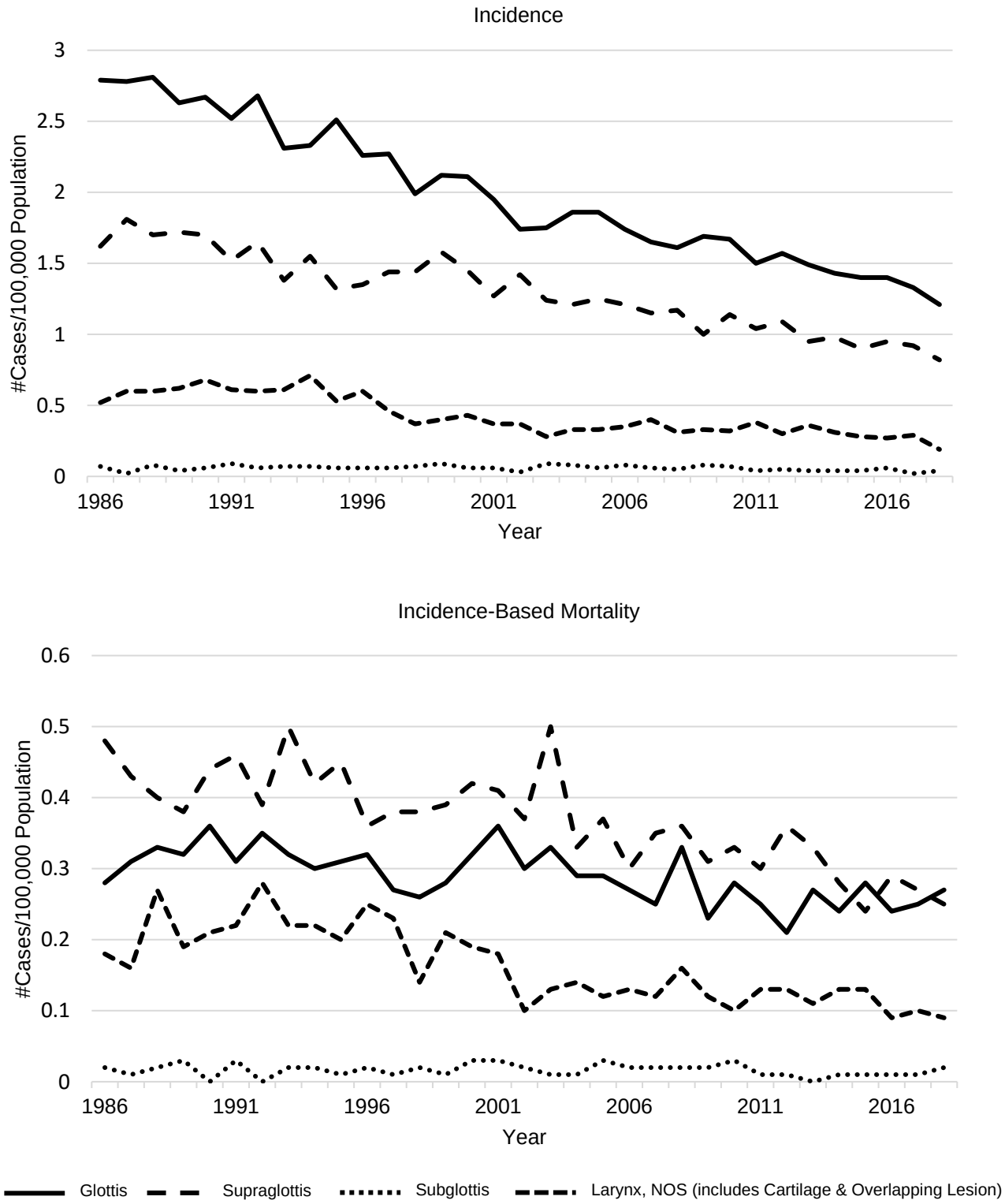
There were much smaller decreases in localized disease in women and distant disease in men. The incidence of regional disease stayed largely stable. We did not perform Joinpoint analyses for regional and distant disease because numbers were too small.

Incidence & Mortality Trends by Subsite (eFigure 2)
The larynx subsite with the highest incidence rate is glottis, followed by supraglottis, larynx, NOS (including cartilage and overlapping lesion), and subglottis. The larynx subsite with the highest incidence-based mortality is supraglottis, followed by glottis, larynx, NOS (including cartilage and overlapping lesion), and subglottis.



eFigure 1: Incidence & Incidence-Based Mortality of Larynx Cancer by Stage & Sex 2005 – 2018.

Data are from the Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database, released April 2021, based on the November 2020 submission from SEER 18 Research Data.



eFigure 2: Incidence & Incidence-Based Mortality of Larynx Cancer by Subsite 1986 – 2018.

Data are from the Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database, released April 2021, based on the November 2020 submission from SEER 9 Research Data.