

# Esophageal Adenocarcinoma Incidence: Are We Reaching the Peak?

Heiko Pohl<sup>1,2,4</sup>, Brenda Sirovich<sup>1,3,4</sup>, and H. Gilbert Welch<sup>1,3,4</sup>

## Abstract

**Background:** A steep increase in the incidence of esophageal adenocarcinoma has been observed between 1973 and 2001, but recent trends have not been reported. Our aim was to examine recent trends in esophageal adenocarcinoma incidence.

**Methods:** We used the Surveillance Epidemiology and End Results database of the National Cancer Institute to identify all patients who were diagnosed with esophageal adenocarcinoma between 1973 and 2006. Incidence trends were analyzed for esophageal adenocarcinoma overall and by stage using joinpoint regression.

**Results:** Overall esophageal adenocarcinoma incidence increased from 3.6 per million in 1973 to 25.6 per million in 2006. Incidence trend analysis, however, suggests that the increase has slowed, from an 8.2% annual increase prior to 1996 to 1.3% increase in subsequent years ( $P = 0.03$ ). Stage-specific trend analyses suggest that the change in overall esophageal adenocarcinoma incidence largely reflects a plateau in the incidence of early stage disease. Its slope has changed direction, from a 10% annual increase prior to 1999 to a 1.6% decline in subsequent years ( $P = 0.01$ ).

**Conclusions:** The incidence of early stage esophageal adenocarcinoma seems to have plateaued.

**Impact:** Although definitive conclusions will require additional years of data, the plateau in early stage disease might portend stabilization in the overall incidence of esophageal adenocarcinoma. *Cancer Epidemiol Biomarkers Prev*; 19(6); 1468–70. ©2010 AACR.

## Introduction

Previously, we reported on the increase in esophageal adenocarcinoma incidence in the United States between 1973 and 2001 (1). During this period, the incidence of this malignancy increased 6-fold, an increase greater than that seen for melanoma, breast cancer, or prostate cancer. The increase in incidence was seen in all stages, was limited to the distal esophagus, and was accompanied by a similar increase in mortality. We concluded that the increased incidence reflected a true increase in disease burden, as it could not be explained by reclassification of adenocarcinoma of the cardia or esophageal squamous cell carcinoma, or overdiagnosis due to increased screening efforts.

We have followed esophageal adenocarcinoma incidence trends since our previous publication. The purpose

of this brief report is to update and analyze these time trends—in terms of both overall and stage-specific incidence.

## Materials and Methods

We used data from the Surveillance Epidemiology and End Results (SEER) database of the National Cancer Institute. SEER 9 has collected information on all newly diagnosed malignancies since 1973 among residents of the nine original SEER geographic areas, representing approximately 10% of the population from the United States.

We first examined the change in the age-adjusted overall esophageal adenocarcinoma incidence. Esophageal adenocarcinoma was defined anatomically as being located in the esophagus [International Classification of Diseases for Oncology, third edition (ICD-O-3) codes 150-159] and histologically as adenocarcinoma (ICD-O-3 codes 8140-8573).

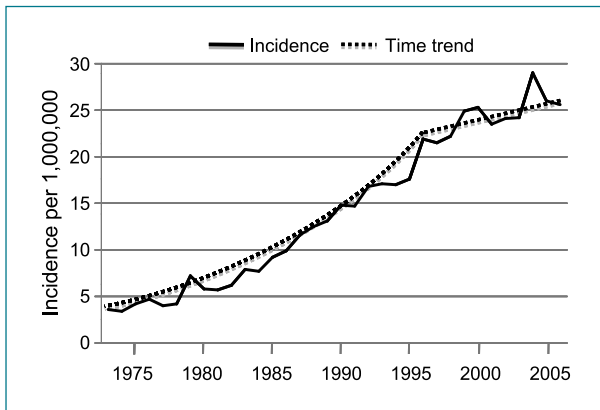
We also examined the stage-specific distribution using the SEER historic stage A variable, which defines localized stage (subsequently referred to as early stage) as a cancer limited to the primary organ, regional stage as cancer extending beyond the primary organ into adjacent tissue or regional nodes, and distant stage as metastatic cancer detected. We used this older staging metric, as SEER does not provide tumor-node-metastasis staging

**Authors' Affiliations:** <sup>1</sup>The VA Outcomes Group, Departments of <sup>2</sup>Gastroenterology and <sup>3</sup>Medicine, Veterans Affairs Medical Center, White River Junction, Vermont; and <sup>4</sup>Dartmouth Medical School, Hanover, New Hampshire

**Corresponding Author:** Heiko Pohl, Department of Gastroenterology, Veterans Affairs Medical Center, White River Junction, VT 05009. Phone: 802-295-9363 ext. 5595; Fax: 802-296-6325. E-mail: heiko.pohl@dartmouth.edu

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**Figure 1.** Overall incidence trend in esophageal adenocarcinoma (1973-2006).

for esophageal adenocarcinoma. To evaluate time trends, we used Joinpoint regression analysis (2, 3). Developed by the National Cancer Institute for the analysis of SEER data, joinpoint analysis determines the simplest composite linear model that best fits the data and enables a test of whether an apparent change in trend at a particular inflection point (a so-called joinpoint) is significant.

## Results

### Overall incidence trends

Figure 1 shows the dramatic overall increase in incidence of esophageal adenocarcinoma between 1973 (3.6 cases per million) and 2006 (25.6 per million), a 7-fold increase. Figure 1 also suggests a change in the slope of the rising incidence curve in the late 1990s or early 2000s. Using joinpoint regression analysis, the inflection point is estimated as occurring in 1996. From 1973 to 1996, the incidence of esophageal adenocarcinoma increased from 3.6 to 21.9 per million, an annual increase of 8.2% (95% confidence interval, 7.7-8.8%). From 1996 to 2006, incidence increased only to 25.6 per million, reflecting an annual increase of 1.3% (95% confidence interval, 1.9-4.7%), a significant decline in the slope of the incidence curve ( $P = 0.03$ ).

### Stage-specific incidence trends

Figure 2 shows that among all stage-specific incidence trends, it is the early stage trend that has changed the most over the last decade. Although there is no significant change in trend for regional or distant stage disease during this time period. Figure 3 shows a significant trend change for early stage disease. After a steep annual increase of 10.0% (95% confidence interval, 8.8-11.3%) prior to 1999, incidence subsequently declined by 1.6% (95% confidence interval, 9.5-7.0%) per year. The incidence of unstaged disease has declined over the same time period.

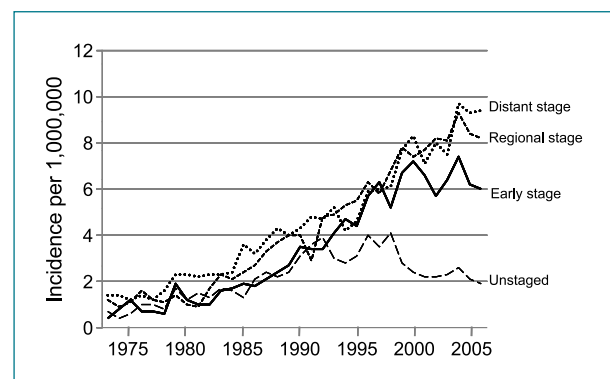
## Discussion

Our group and others have previously reported on a steep increase in esophageal adenocarcinoma incidence (1, 4, 5). Here, we provide an update on recent incidence changes through 2006 using the population-based SEER 9 registry. Our results suggest that the previously observed steady increase in esophageal adenocarcinoma incidence has slowed, which represents a significant change in trend. Perhaps most surprising is the more obvious incidence change for early stage cancer. Although the incidence of more advanced stages at diagnosis (regional and distant cancer) has continued to increase, early stage disease seems to have plateaued in 1999. We found these results to be robust regardless of our assumptions about the true stage of disease categorized as unstaged. As for all cancers in SEER, the incidence of unstaged disease has been declining as staging techniques have improved. We imagine several possible explanations for the plateau in early stage disease without a concomitant slowing in regional/distant stage disease.

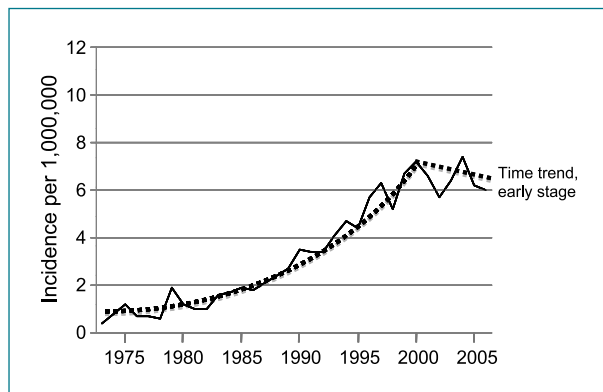
First, the observed incidence pattern may be due to chance and simply reflect annual fluctuations. We acknowledge that it may be too early to draw firm conclusions about changes in incidence. Joinpoint regression analysis, however, attempts to provide an objective tool to estimate when such changes occur, and has been applied in prior studies on cancer incidence (6, 7).

Second, improved staging techniques (such as endoscopic ultrasound and computer tomography) might have led to greater detection of affected regional lymph nodes or metastatic lesions. This may, in turn, have led to a stage migration (8), in which patients may have become more likely to be diagnosed as having regional or distant disease and less likely to be diagnosed with early stage disease. Given that we do not see a concomitant acceleration in later stage disease incidence, we think this is unlikely.

Third, it may be that the change in early stage disease incidence is real, but there has been insufficient time for a



**Figure 2.** Stage-specific incidence trends in esophageal adenocarcinoma (1973-2006).



**Figure 3.** Incidence trend of early stage of esophageal adenocarcinoma at diagnosis between 1973 and 2006 (SEER 9).

decreased incidence of later stage disease to appear. We can think of three possible explanations why early disease stage could truly be decreasing.

First, exposure to initiating factors may have plateaued. Risk factors such as reflux disease (9) or increased body mass index (10) might have exerted their maximal potential effect. Second, the transition from premalignant Barrett's esophagus to cancer might have slowed. This would imply either a change in the natural progression of Barrett's or an increased exposure to protective factors. Aspirin and proton pump inhibitors have been reported to decrease the risk of transition from Barrett's esophagus

to cancer (11, 12). Finally, Barrett screening and surveillance may be effective. Increased detection of dysplastic lesions with subsequent intervention might lead to a decrease in cancer incidence. For instance, the detection of high-grade dysplasia in a Barrett's segment is an indication for either endoscopic or surgical resection (13-16), because of the high risk of prevalent cancer and a 6% annual transition to cancer (17, 18). Hence, it is plausible that more patients will be detected with dysplastic but noncancerous lesions and would therefore not develop cancer after curative resection.

Although we have to await subsequent incidence data before making firm conclusions about esophageal adenocarcinoma incidence in general, it was our intention to alert readers about a possible change in esophageal adenocarcinoma incidence in general and in early stage disease in particular.

### Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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**Correction**

## Correction: Esophageal Adenocarcinoma Incidence: Are We Reaching the Peak?

In this article (1), which was published in the June 2010 issue of *Cancer Epidemiology, Biomarkers & Prevention*, it was reported that early stage disease has declined by 1.6% per year since 1999. The reported 95% confidence interval of 9.5% and 7.0% is incorrect. The correct 95% confidence interval around the 1.6% decline is -9.5% and 7.0%.

### Reference

1. Pohl H, Sirovich B, Welch HG. Esophageal adenocarcinoma incidence: are we reaching the peak? *Cancer Epidemiol Biomarkers Prev* 2010;19:1468–70.

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Heiko Pohl, Brenda Sirovich and H. Gilbert Welch

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