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Trends in Esophageal Adenocarcinoma Incidence and Mortality

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Abstract

Background—Over the past several decades, the incidence of esophageal adenocarcinoma (EAC) has rapidly increased. The purpose of this analysis was to examine temporal trends in EAC incidence and mortality within the US population and, in addition, to explore these trends within subgroups of the population.

Methods—The National Cancer Institute (NCI) Surveillance, Epidemiology and End Results (SEER 9) data were used to examine incidence and incidence-based (IB) mortality in EAC from 1975 to 2009. Secular trends in incidence and IB mortality by cancer stage, sex, and race were further characterized using the NCI's Joinpoint Regression program.

Results—Based on SEER 9 data, EAC incidence and IB mortality continues to increase in the United States. However, since the mid-1990s, the overall rate of increase in both EAC incidence and IB mortality appears to be slowing. In addition, in early-stage cancers, there is a noticeable leveling off of IB mortality rates and divergence from incidence starting in the late 1990s. Over the study period, the average annual percentage increase in incidence was 6.1% in men and 5.9% in women.

Conclusions—EAC incidence and IB mortality rates continue to rise in the United States, although at a slower rate in more recent years. In early-stage cancers, IB mortality and incidence rates have diverged primarily because IB mortality rates have plateaued beginning in the late 1990s. Although EAC continues to be less common in women, the rate of increase in EAC incidence is similar in both sexes.

Keywords

esophageal neoplasms; adenocarcinoma; incidence; mortality; epidemiology; SEER program

Introduction

Over the past several decades, the incidence of esophageal adenocarcinoma (EAC) has increased rapidly in the United States and other Western countries.^{1,2} It is estimated that in the United States, 17,460 people will be diagnosed with esophageal cancer, and 15,070 people will die from the disease in 2012.³ The 2 main histologic subtypes of esophageal

cancer are squamous cell carcinoma and adenocarcinoma, with adenocarcinoma comprising the majority of cases in the United States.⁴ Published studies have suggested that the incidence of EAC may be decreasing⁵ and that incidence trends may be different by subgroups within the population such as sex, stage, and race/ethnicity.⁶⁻⁸

A study of EAC survival and mortality reveals that whereas long-term survival remains poor, there have been substantial improvements in survival over the past 3 decades.⁹ Factors such as earlier detection, advances in surgical care, and adjuvant therapy have been suggested as contributors to this improvement. If these survival benefits are large enough, they should be detectable in a temporal trend analysis of EAC incidence and mortality. However, to the best of our knowledge, a comparative analysis of these 2 rates has not been previously published.

We examined trends in EAC incidence and incidence-based mortality by sex, stage, and race/ethnicity in the United States using the National Cancer Institute (NCI) Surveillance, Epidemiology and End Results (SEER) program SEER 9 data from 1975 to 2009.

Materials and Methods

SEER 9 incidence, incidence-based (IB) mortality, and survival data were obtained using SEER*Stat software, version 7.0.5.¹⁰ SEER 9 data consist of information on all newly diagnosed malignancies among residents of the 9 original SEER geographic areas, representing approximately 9.5% of the population of the United States. All rates were age-adjusted to the 2000 US standard population.

Age-adjusted incidence rates per 100,000 individuals within the population were analyzed by sex and stage from 1975 to 2009. We examined the incidence over the study period of all stages of EAC, defined anatomically as being located in the esophagus and histologically as adenocarcinoma (International Classification of Diseases for Oncology, third edition [ICD-O-3] codes 8140-8141, 8143-8145, 8190-8231, 8260-8263, 8310, 8401, 8480-8490, 8550-8551, 8570-8574, and 8576).¹¹ To provide uniform staging classifications across all study years, we used SEER historic stage, which provides consistent definitions over time, as opposed to American Joint Committee on Cancer staging, which is more commonly used in clinical settings and is not available for many of the years analyzed. SEER historic stages were: localized (confined to primary site), regional (spread to regional lymph nodes), distant (cancer had metastasized), and unstaged (unknown).¹² Although we analyzed the proportion of unstaged cancers over time, we did not include unstaged EACs when analyzing by stage. We found that in 1975, approximately 15% of EAC cases were unstaged, whereas in 2008, only approximately 5% of cases were unstaged. Although the proportion of unstaged cases decreased during the study period, the stage distribution of localized, regional, and distant cases (when unstaged cases were excluded) remained relatively stable (Fig. 1). The limited number of nonwhite cases prevented analysis by race/ethnicity.

Age-adjusted EAC incidence-based mortality rates per 100,000 persons are reported by sex and stage for the period 1978 to 2009. Standard mortality statistics are not available for EAC because death certificates do not include the histology of the cancer. However, IB mortality data use cancer registry data to link characteristics of the incident cancer (eg, stage, histology) to the death certificate.¹³ For a given year, EAC IB mortality rate is the proportion of the total number of deaths in that year that are due to EAC: attribution to EAC is made when the cause of death on the death certificate is esophageal cancer and the deceased is listed in the registry, having been diagnosed with EAC at any prior time. We did not include the first 3 years (1975-1977) in our IB mortality analysis, because most of the deaths occurring during this initial time period would have been incident cases diagnosed

prior to 1975. Consequently, we chose to analyze IB mortality starting in 1978 to ensure that the vast majority of deaths corresponded to incident cases starting in 1975. This relatively short duration is justified because the 3-year relative survival for EAC patients from 1975 to 1979 was 9.6%.¹⁴

The NCI Joinpoint Regression Analysis program, version 3.5.2,¹⁵ was used to examine trends in overall EAC incidence and IB mortality as well as localized, regional, and distant EAC incidence and IB mortality by sex. The Joinpoint program selects the best-fitting piecewise continuous log-linear model, where the segments are connected at “joinpoints,” and statistical tests are performed to determine the minimum number of joinpoints necessary to fit the data. All Joinpoint program settings remained in the default mode; the incidence and IB mortality data were modeled in a segmented log-linear form where, in our case, y is the incidence or IB mortality and x is the year. For each linear segment, annual percentage changes (APC) in age-adjusted incidence and IB mortality were calculated, and 95% confidence intervals (CIs) were reported. Incidence and IB mortality trends for men and women over the entire study period were compared using average annual percentage changes (AAPC), which is an average of the APCs for each segment, weighted by the segment length. Joinpoint graphs for regional and distant EAC in women were not produced due to the sparseness of the data for these strata.

We also used SEER 9 data to examine trends in 5-year relative age-adjusted survival of EAC by stage for individuals diagnosed between 1975 and 2004. Survival by stage was examined to further explore the differences between stage-specific incidence and IB mortality plots. We were unable to examine 5-year survival data for cases diagnosed after 2004, because these data would have been based on deaths occurring after 2009, which are not yet available.

Results

Overall Trends

Based on SEER 9 data, overall EAC incidence continues to increase (Fig. 2). In 1975, EAC incidence was 0.40 cases per 100,000, whereas in 2009 EAC incidence was 2.58 cases per 100,000. Although EAC incidence continues to increase, a slowing of the rate of increase occurs around 1997. EAC IB mortality follows a similar pattern of a continued rise, with a slowing of the rate of increase occurring around 1998. In addition, a divergence of the incidence and IB mortality curves is evident; the IB mortality curve gradually becomes flatter than the incidence curve.

Trends by Sex

When sex-specific trends were explored, we found a continued increase in both incidence and IB mortality in men, with inflection points occurring in the mid to late 1990s, indicating the beginning of a reduction in the rate of increase for both (Fig. 3A). Although a joinpoint was found in IB mortality for women in the late 1990s, similar to the IB mortality in men, no joinpoint was observed in incidence in women (Fig. 3B). Although annual EAC incidence and IB mortality rates in men are approximately 6 times that of the rates in women (4.87 versus 0.68 cases per 100,000 in men versus women in 2009; and 0.71 versus 0.26 in 1975), the trends have similar slopes; the overall average annual rates of increase (AAPC) for incidence and IB mortality over the study period are approximately the same for both men and women (Tables 1 and 2). Over the study period, EAC incidence and IB mortality increased at an average rate of 6.1% and 5.4% per year, respectively, for men and 5.9% and 5.5%, respectively, for women.

Trends by Stage

The trends in localized and distant EAC reveal a narrower gap between incidence and IB mortality curves in advanced-stage EAC than in early-stage EAC. A change in APC occurs for both the incidence and IB mortality rates for localized EAC patients; however, the change in IB mortality rate occurs approximately 1 year after the decline in incidence in 2000 (Fig. 4A). Incidence initially increased at an APC of 9.8 (95% CI = 8.5-11.2) from 1975 to 1999 and then slowed to an annual increase of 0.1 (95% CI = -4.5 to 4.8) thereafter. In terms of IB mortality, the initial APC increased at a rate of 9.3 (95% CI = 7.8-10.8) from 1978 to 2000 but decreased from 2000 to 2009 (APC = -1.0, 95% CI = -6.1 to 4.5).

When regional and distant stages of EAC were analyzed, although some joinpoints were found (Fig. 4B,C), they were not readily interpretable. This may have resulted from a smaller number of cases, particularly during the earlier years of the study period, and could be due to aberrations in data collection procedures or other anomalies. However, the AAPC for the whole study period was 5.5 (95% CI = 1.9-9.2) for regional EAC incidence and 6.0 (95% CI = 5.3-6.7) for distant EAC cases. For IB mortality, the AAPC from 1978 to 2009 was 6.4 (95% CI = 4.5-8.8) and 8.1 (95% CI = 5.7-10.6) for regional and distant cases, respectively.

Trends by Sex and Stage

Comparisons of trends by sex and stage revealed a substantial change in the APC for localized EAC incidence in men occurring around 1997 (Table 1) followed by a change in localized EAC IB mortality in men around 1999 (Table 2). From 1975 to 1997, localized male EAC incidence increased sharply at an APC of 11.1 (95% CI = 9.4-12.8). However, after 1997, the APC slowed to 1.0 (95% CI = -2.8 to 4.9). A similar pattern is observed in localized EAC IB mortality where the APC was 9.8 from 1978 to 1999 (95% CI = 8.1-11.4); however, after 1999, IB mortality in men with localized EAC remained at a steady rate from year to year (APC = 0.0, 95% CI = -4.6 to 4.7). The trends for regional EAC in men (Tables 1 and 2) were similar to that in Fig. 4B. A change in trend in incidence occurred approximately 10 years earlier in distant EAC in men compared with localized EAC trends; however, these changes in slope have wide confidence intervals and it is therefore difficult to draw any conclusions from them.

Although the incidence rate of localized EAC in women was consistently higher than the IB mortality rate, the annual change in incidence and IB mortality of localized EAC in women occurred at approximately the same rate (6.60 [95% CI = 5.0-8.3] incidence versus 6.63 [95% CI = 4.7-8.5] IB mortality) (Tables 1 and 2). Because of the small number of cases for women, regional incidence and IB mortality curves were not plotted. Annual changes in incidence and IB mortality in distant EAC in women occurred at approximately the same rate. However, as evidenced by the spread of the data points, unlike localized EAC, incidence and IB mortality rates in distant EAC in women appear to be very similar.

Survival Trends

Examination of 5-year relative age-adjusted EAC survival trends by stage revealed that 5-year survival rates have been improving since 1975 (Fig. 5). The greatest improvement in survival trends occurred in people diagnosed with localized disease. Approximately 2.1% of patients diagnosed with EAC in 1975 survived 5 years after their diagnosis, whereas more than half of all patients diagnosed with localized EAC in 2004 had survived until 2009. In contrast, there were relatively modest improvements in 5-year survival in people diagnosed with regional EAC. Only 4.9% of patients diagnosed with regional staged EAC in 1975 were living 5 years after their diagnosis, whereas more than 20% of people diagnosed with regional staged EAC in 2004 were living in 2009. Five-year survival for patients diagnosed

with distant disease remained relatively flat over the study period. None of the people who were diagnosed with distant staged EAC in 1975 were recorded as surviving 5 years after diagnosis and by 2004, 5-year survival for distant staged disease had only risen to 2.8%. These findings are consistent with our comparative analysis of incidence and IB mortality which revealed a divergence of the incidence and IB mortality curves in localized disease and a faster overall increase in IB mortality than in incidence in the more advanced stages of EAC over the study period.

Discussion

Esophageal adenocarcinoma incidence and IB mortality continue to increase. Our analysis shows that there is a deceleration in both incidence and IB mortality in the 1990s, and that this finding was mostly driven by localized cases in males. For localized EAC, both incidence and IB mortality rates appear to have leveled off in the 1990s, although the striking feature is the divergence or separation that results due to IB mortality rates plateauing or possibly dropping more rapidly. This finding is further emphasized by our examination of 5-year survival by stage, which revealed that over the study period, the survival in the localized cancer groups appeared to improve dramatically.

In women, we observed absolute incidence and IB mortality rates that are approximately 6 times lower than those observed in men. However, both women and men have experienced a similar trend of a rapid increase in incidence and IB mortality rates over the past few decades. Although EAC mortality rates from 1975 to 2009 in women are fit by joinpoint using 1 inflection point, no joinpoint is found in EAC incidence at this time, despite the data indicating a possible slowing in female incidence. This is possibly due to the relatively small number of cases in women. A steady rise in incidence and IB mortality in women persists in the stage subset analysis where, because of a limited number of cases, regional stage trends were not examined. However, we suspect that no shift or joinpoint in EAC incidence or IB mortality was detected in women because of insufficient power resulting from a smaller number of cases.

Other studies support our findings of a leveling off of incidence for localized EAC cases compared to a continued increase in distant and regional stages of EAC.^{3,4,7} Localized EAC IB mortality seems to have decreased during the last decade, although it is not statistically significant. Although there was also a slowing in the increase of the incidence rate of regional and distant EAC, the change in APC was less pronounced for regional and distant cancers than for localized EAC. Similar trends in IB mortality were revealed, except in regional EAC IB mortality which may possibly be decreasing or slowing in rate of increase.

It is unclear why there is a slowing of the rate of increase of incidence of EAC; however, there are several theories that may possibly explain this trend. Some have suggested that risk factors such as acid reflux or adiposity might have already had their maximal impact on incidence⁵ or that the decrease in smoking rates as a moderate risk factor of EAC might have partially contributed to the slowing.¹⁶ It is also possible that increased surveillance through endoscopy of patients with Barrett's esophagus has been effective at identifying patients with dysplasia resulting in some patients undergoing cancer-preventing treatments such as endoscopic ablation.^{5,17} However, additional research is needed to further validate, explore, and explain this trend. Such research could be pivotal to understanding what possible interventions and programs could potentially be effective in diminishing the morbidity and mortality associated with EAC.

There are several possible explanations for the separation of the incidence and IB mortality incidence curves in early-stage EAC and relatively parallel course of the incidence and IB

mortality curves in late-stage EAC. Treatments for EAC have been improving through advancements in imaging, surgical techniques, and adjuvant therapy for patients.^{9,18} Some studies have suggested that access to surgery¹⁸ or esophagectomy⁹ have also contributed to improvements in survival. Furthermore, the increased use of upper endoscopy specifically for gastroesophageal reflux disease screening and for other diagnostic purposes^{19–21} could have diagnosed an increasing number of EAC cases earlier, making them more likely to receive and benefit from treatment. Although there does not seem to be an obvious stage shift over the study period, because the SEER summary stage categories are broad, there could have been intrastage effect (eg, diagnosing more surgically curable localized EAC than incurable localized EAC).

In addition, endoscopies performed in a screening context, even if they target higher risk individuals, are more likely to diagnose cancers that are less aggressive or indolent than diagnostic endoscopies performed for signs or symptoms.²² In support of our hypotheses, Dubecz et al found that the median survival for patients with localized EAC has improved from 11 months in the 1970s to 35 months in the 2010s, whereas the median survival for patients with distant EAC has improved from 4 to only 6 months over the same period.¹⁸

Our analysis has numerous strengths, including the comparison of incidence and IB mortality trends and ability to examine trends by sex and stage. However, there are also limitations to our study. First, because of limited numbers of cases in race/ethnicities other than white, we were unable to compare trends by race/ethnicity. Second, some analyses of sex were limited due to the lower number of EAC cases in women. Finally, this analysis aimed to examine trends in EAC incidence and IB mortality and was not designed to examine factors that influence these trends or might explain the slowing of the rate of increase in EAC incidence. Future research should examine screening, incidence, survival, and treatment trends by various population subgroups such as sex, race/ethnicity, and stage in a larger population. Such studies would help explore these hypotheses regarding changes in incidence and mortality trends by stage and sex.

In conclusion, our results indicate a continued increase in the incidence and IB mortality rates of EAC, although both are increasing at a slower rate since the 1990s. In early-stage cancers, IB mortality and incidence rates have diverged primarily because IB mortality rates have plateaued in more recent years; however, the opposite is true for late-stage cancers. These findings warrant further investigation and characterization, because such research could inform future cancer prevention and intervention programs aimed at curbing the morbidity and mortality associated with EAC. Although EAC continues to be significantly less common in women by approximately a 6-fold difference when compared with men, the rate of increase or trend in EAC incidence and mortality is similar in both sexes over the study period.

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Figure 1. Graph depicts stage distribution of incident cases of esophageal adenocarcinoma showing unstaged cases, 1975 to 2009.

Figure 2.

Graph shows SEER 9 esophageal adenocarcinoma incidence and incidence-based mortality, 1975 to 2009. From 1975 to 1997, EAC incidence increased at an annual percentage change (APC) of 8.4 (95% confidence interval [CI] = 7.7-9.1), whereas the APC was 1.6 (95% CI = 0.0-3.3) from 1997 to 2009. For incidence-based mortality, the APC was 8.0 from 1978 to 1998 (95% CI = 7.2-8.8) and 1.1 from 1998 to 2009 (95% CI = -0.7 to 2.9). All rates were age-adjusted to the 2000 Standard population using 19 age groups.

Figure 3.

SEER 9 esophageal adenocarcinoma incidence and incidence-based mortality is shown in men and women, 1975 to 2009. **(A)** SEER 9 esophageal adenocarcinoma incidence and incidence-based mortality is shown in men, 1975 to 2009. From 1975 to 1996, the APC in EAC incidence in men was 9.0 (95% CI = 8.1-9.8) whereas from 1996 to 2009, the change was 1.7% per year (95% CI = 0.1-3.3). The APC in incidence-based EAC mortality was 8.1 (95% CI = 7.3-8.9) from 1978 to 1998, whereas after 1998, the rate of increase in mortality slowed to an APC of 0.8 (95% CI = -1.0 to 2.6) from 1998 to 2009. **(B)** SEER 9 esophageal adenocarcinoma incidence and incidence-based mortality in women, 1975 to 2009. The APC in EAC incidence in women was 5.9% (95% CI = 5.1-6.7) from 1975 to 2009. From 1978 to 1997, EAC incidence-based mortality in women increased at an APC of 7.8 (95% CI = 5.8-9.8) and slowed to an APC of 2.1 (95% CI = -1.5 to 6.0). All rates were age-adjusted to the 2000 Standard population using 19 age groups.

Figure 4.

SEER 9 esophageal adenocarcinoma incidence and incidence-based mortality is shown by stage, 1975 to 2009. **(A)** Local esophageal adenocarcinoma incidence and incidence-based mortality. Incidence of localized EAC increased at an annual percentage change (APC) of 9.8 (95% confidence interval [CI] = 8.5-11.2) from 1975 to 1999. From 1999 to 2009, there was a slowing of the increased incidence to 0.1% per year (95% CI = -4.5 to 4.8). A similar pattern is also evident in localized EAC incidence-based mortality; from 1978 to 2000, the APC was 9.3 (95% CI = 7.8-10.8), whereas from 2000 to 2009 the incidence-based mortality trend decreased with an APC of -1.0 (95% CI = -6.1 to 4.5). **(B)** Regional esophageal adenocarcinoma incidence and incidence-based mortality. Incidence of regional EAC decreased at an APC of -2.4 from 1975 to 1981 (95% CI = -8.3 to 3.8), rose to an APC of 28.2 (95% CI = -11.3 to 85.3) from 1981 to 1984, but slowed to an APC of 7.7 (95% CI = 6.2-9.2) from 1984 to 2001 then decreased at an APC of -0.6 (95% CI = -4.5 to 3.5) from 2001 to 2009. Incidence-based mortality in this group increased at an APC of 9.2 (95% CI = 7.5-10.9) from 1978 to 1999, and slowed to an APC of 0.7 (95% CI = -3.9 to 5.6), from 1999 to 2009. **(C)** Distant esophageal adenocarcinoma incidence and incidence-based mortality. From 1975 to 1987, the incidence of distant EAC increased at an APC of 9.5 (95% CI = 7.4-11.7) but then slowed to an APC of 5.4 (95% CI = 4.6-6.3) from 1987 to 2009. In terms of incidence-based mortality, there was a sharp increase from 1978 to 1980 at an APC of 48.5 (95% CI = 3.9-112.3) whereas from 1980 to 2009 the APC was 5.8 (95% CI = 5.2-6.3). All rates were age-adjusted to the 2000 Standard population using 19 age groups.

Figure 5. Five-year relative age-adjusted survival is shown for esophageal adenocarcinoma, 1975 to 2004. Dashed lines indicate imputed data points for those years for which values were not available.

Table 1
SEER 9 Esophageal Adenocarcinoma Incidence Annual Percentage Change (APC) and Average Annual Percentage Changes (AAPC) by Sex and Stage^a

	Joinpoint Location ^b	APC1 (95% CI)	APC2 (95% CI)	APC3 (95% CI)	APC4 (95% CI)	AAPC, 1975-2009 (95% CI)
All	1997	8.4 (7.7-9.1)	1.6 (0.0 - 3.3)			6.0 (5.3-6.7)
Localized	1999	9.8 (8.5-11.2)	0.1 (-4.5 to 4.8)			6.9 (5.2-8.5)
Regional	1981, 1984, 2001	-2.4 (-8.3 to 3.8)	28.2 (-11.3 to 85.3)	7.7 (6.2-9.2)	-0.6 (-4.5 to 3.5)	5.5 (1.9-9.2)
Distant	1987	9.5 (7.4-11.7)	5.4 (4.6-6.3)			6.9 (6.0-7.7)
Male						
All Stages	1996	9.0 (8.1-9.8)	1.7 (0.1-3.3)			6.1 (5.3-6.9)
Localized	1997	11.1 (9.4-12.8)	1.0 (-2.8 to 4.9)			7.4 (5.7-9.1)
Regional	1981, 1984, 2001	-3.2 (-10.3 to 4.5)	31.0 (-16.7 to 106.0)	7.6 (5.7-9.4)	-0.9 (-5.7 to 4.1)	5.4 (1.0-9.9)
Distant	1987	10.6 (8.3-12.9)	5.2 (4.4-6.1)			7.1 (6.1-8.0)
Females						
All Stages		5.9 (5.1-6.7)				5.9 (5.1-6.7)
Localized		6.6 (5.0-8.3)				6.6 (5.0-8.3)
Regional		No data				No data
Distant		6.1 (4.7-7.5)				6.1 (4.7-7.5)

Abbreviations: AAPC, average annual percentage change; APC, annual percentage change; CI, confidence interval.

^aRates are based on incidence data age-adjusted to the 2000 Standard Population with 19 age groups.

^bThe strata analyzed may have different numbers of joinpoints occurring in different calendar years and corresponding to different APC periods. For example, for overall esophageal adenocarcinoma incidence, there is 1 joinpoint occurring in 1997 corresponding to 2 APC periods, 1975-1997 and 1997-2009.

Table 2
SEER 9 Esophageal Adenocarcinoma Incidence-Based Mortality Annual Percentage Change (APC) and Average Annual Percentage Change (AAPC) by Sex and Stage^a

	Joinpoint Location ^b	APC1 (95% CI)	APC2 (95% CI)	APC3 (95% CI)	APC4 (95% CI)	AAPC, 1978-2009 (95% CI)
All	1998	8.0 (7.2-8.8)	1.1 (-0.7 to 2.9)			5.5 (4.7-6.3)
Localized	2000	9.3 (7.8-10.8)	-1.0 (-6.1 to 4.5)			6.2 (4.3-8.1)
Regional	1999	9.2 (7.5-10.9)	0.7 (-3.9 to 5.6)			6.4 (4.5-8.3)
Distant	1980	48.5 (3.9-112.3)	5.8 (5.2 to 6.3)			8.1 (5.7-10.6)
Male						
All Stages	1998	8.1 (7.3-8.9)	0.8 (-1.0 to 2.6)			5.4 (4.7-6.2)
Localized	1999	9.8 (8.1-11.4)	0.0 (-4.6 to 4.7)			6.5 (4.7-8.4)
Regional	1980, 1985, 2000	-37.8 (-58.8 to -6.1)	24.7 (9.4-42.1)	7.6 (5.5-9.7)	0.5 (-3.3 to 4.3)	4.2 (0.7-7.9)
Distant	1980	48.7 (-0.1 to 121.5)	5.8 (5.2-6.5)			8.2 (5.5-10.9)
Female						
All Stages	1997	7.8 (5.8-9.8)	2.1 (-1.5 to 6.0)			5.5 (3.7-7.4)
Localized		6.6 (4.7-8.5)				6.6 (4.7-8.5)
Regional		No data				No data
Distant		5.9 (4.5-7.2)				5.9 (4.5-7.2)

Abbreviations: AAPC, average annual percentage change; APC, annual percentage change; CI, confidence interval.

^aRates are based on incidence-based mortality data age-adjusted to the 2000 Standard Population with 19 age groups.

^bThe strata analyzed may have different numbers of joinpoints occurring in different calendar years and corresponding to different APC periods. For example, for overall esophageal adenocarcinoma incidence-based mortality, there is 1 joinpoint occurring in 1998 corresponding to 2 APC periods, 1978-1998 and 1998-2009.