ABSTRACT

Title of thesis: COUNTY AND CENSUS TRACT SOCIOECONOMIC ATTRIBUTES OF ESOPHAGEAL ADENOCARCINOMA CASES SEER 15 (2000-2007)

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Esophageal adenocarcinoma (EAC) incidence rates have increased among U.S. men. We examined associations between area-level socioeconomic attributes and stage at diagnosis, an important prognostic predictor of survival time. Logistic regression models were developed to estimate odds ratios (OR) adjusted for age, race, gender and year of diagnosis and 95% confidence intervals (CI) for localized and regional versus distant stage by census tract and county level socioeconomic attributes. At the county level, a high percent of foreign born population was associated with distant stage EAC: >15.4%-26.6%, (OR=1.15, 95% CI: 1.04–1.28) and >26.6% (OR 1.16, 95% CI: 1.03–1.31). Median household income from $40.8-$45.6K (OR=1.14, 95% CI: 1.01–1.28) was also associated with distant stage EAC. Conversely, residence in an urban county was associated with localized or regional stage EAC (OR=0.90, 95% CI: 0.82–0.98). Findings regarding area level disparities in EAC stage may inform cancer control efforts.

COUNTY AND CENSUS TRACT SOCIOECONOMIC ATTRIBUTES OF ESOPHAGEAL ADENOCARCINOMA CASES SEER 15 (2000-2007)

by

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Chapter 1: Introduction

Esophageal cancer is the twelfth leading incident cancer among men in the United States (US) (1). It is estimated that 16,640 men and women (13,130 men and 3,510 women) will be diagnosed with and 14,500 men and women will die of cancer of the esophagus in 2010 (1). The incidence rate for esophageal cancer increased from 1975 through 2007 in SEER 9 Registries (annual percent change greater than zero, $p < 0.05$). Furthermore, mortality rates significantly increased among US men from 1992 through 2006, for esophageal cancer is the seventh leading cause of cancer death (2). For the recent time period, 1999-2006, the five-year relative survival for EAC was 18.9 percent (2), far below the Healthy People 2010 objective 3.15, to increase the proportion of people who are living five years after cancer diagnosis to at least 70 percent (3). Most of the increasing incidence and death rates are attributed to the rising burden of EAC experienced among white males (4,5).

There are two major histological types of esophageal carcinoma, squamous cell carcinoma (SCC) and adenocarcinoma (EAC). EAC is defined as malignancy of the esophagus arising from glandular cells present at the junction of the esophagus and stomach (1). Over the past 2 decades, the incidence of esophageal adenocarcinoma (EAC) has increased more rapidly than any other cancer in the US (1,6). The specific reasons for this increase are not yet understood. Since the presence of Barrett's esophagus is essential for the development of most esophageal adenocarcinomas, the increasing incidence of esophageal adenocarcinoma may be related to an increasing prevalence of Barrett's esophagus, and its precursor, gastroesophageal reflux (7). In contrast, rates of SCC have remained relatively stable (6).

Associations between socioeconomic status (SES) and cancer (using measures such as income, education, and occupation) have been observed in several studies (8-12) based on widely accepted measures of social class (9-11). Although low SES has been associated with an increased risk of esophageal adenocarcinoma (9), few studies have investigated the basis by which socioeconomic factors are related to the disease. There are some indications that low SES may also increase the risk of EAC (9, 10, 12) but inconsistent results (9) and the use of different measures of SES make comparisons and interpretations difficult.

1.1. Diagnosis

It is thought that chronic inflammation of the esophagus can contribute to the mutations found in DNA which eventually lead to esophageal cancer (13). Factors that can cause inflammation in the cells of the esophagus include alcohol consumption, bile reflux, chewing tobacco, drinking very hot liquids, eating a diet low in fruits and vegetables, eating foods preserved in lye, and smoking. Symptoms of esophageal cancer usually do not show up until the cancer is fairly advanced (13). They may include pain, dysphagia (difficulty swallowing), weight loss, poor appetite with a preference for soft foods, pneumonia, and fatigue. A widely-used test in detecting esophageal cancer is esophagogastroduodenoscopy (EGD), in which a lighted, fiber-optic tube is passed from the mouth into the stomach to visualize abnormalities in the lining of the esophagus and stomach. Biopsies (samples of tissue) can be taken during an EGD. Another test in detecting esophageal cancer is a barium swallow. This is a radiographic test that can show unhealthy areas in the esophagus and stomach after the patient drinks a barium contrast agent. Chest radiography, computed tomography (CT), magnetic resonance imaging (MRI), blood testing, and positron emission tomography (PET) may also be part of the testing for esophageal cancer.

1.2. Stage at diagnosis

EAC is generally staged into three categories: localized, regional, or distant. In localized EAC, cancer has formed and spread beyond the innermost layer of tissue to the next layer of tissue in the wall of the esophagus. The cancer is contained to the esophagus and has not spread to lymph nodes or any other organs in the body. Localized EAC has the best treatment outcome of all three stages if detected early. In regional EAC, cancer has spread to the outer wall of the esophagus and may have spread to tissues and/or lymph nodes near the esophagus. In distant EAC, cancer has spread to distant lymph nodes and/or organs in other parts of the body. The distant stage of EAC has the worst treatment outcome and has the highest mortality rate.

1.3. Risk Factors

Risk factors for EAC include age, gender, race, family history, obesity, smoking, alcohol consumption, and diet (14). A summary of EAC risk factors found in previously published literature is located in Appendix I.

1.3.1. Age

Studies consistently show that the incidence of EAC increases with age (6, 14-16). Data from both SEER and the Danish Cancer Registry demonstrate that the incidence rate of EAC increases with age until it peaks at 75-79 years of age and declines thereafter (14).

1.3.2. Gender

Male gender is a well-recognized risk factor for EAC. It is estimated that the incidence of EAC is approximately six to eight fold greater in men than in women (14).

1.3.3. Race

White race has long been associated with EAC. Kubo and Corley found that the average annual incidence rate for EAC for white men was double that of Hispanic men (4.2 versus 2.0/100,000/year). This rate was also four times higher than that seen in black, Asian/Pacific Islanders, and Native Americans.

1.3.4. Family History

Several small studies suggest the possibility of an autosomal dominant inheritance pattern of EAC (14, 16). Larger case-control studies come to less clear-cut conclusions (14). Chak et al. found that a positive family history was higher among cases with Barrett's esophagus, EAC, or gastroesophageal junction carcinoma than among controls (24% versus 5%).

1.3.5. Obesity

The rapid increase in the incidence of EAC parallels the rise of obesity in the Western world (14). As a result, obesity has emerged as a leading candidate risk factor for EAC. Kubo and Corley found that a BMI greater than 25 was associated with an increased risk of EAC in both men (OR 2.2; 85% CI, 1.7 – 2.7) and women (OR 2.0; 95% CI 1.4 – 2.9) and higher levels of BMI were associated with increased risk.

1.3.6. Smoking

Several studies have identified current or past smoking as a risk factor for EAC (6, 14-17). The risk increases with increasing intensity and duration of smoking (14).

1.3.7. Alcohol Consumption

Most epidemiologic studies find no association between alcohol consumption and EAC (14). However, several studies do find a modest association of alcohol consumption and risk of EAC (6, 14, 18). Overall, alcohol does not seem to be a major risk factor for EAC (14).

1.3.8. Diet

A diet high in carbohydrates may be linked to EAC. A recent ecologic study found a correlation between the rise in carbohydrate consumption with the increase in EAC rates (19). On the contrary, a diet rich in fruits and vegetables is consistently associated with a decrease in the risk of EAC (19).

1.4. Main EAC Risk Factors: GERD and BE

Gastroesophageal reflux disease (GERD) is the first disease present in the EAC pathway. GERD exhibits the same symptoms as heartburn, leaving the affected individual with an uncomfortable burning feeling in the chest area (20). Individuals with GERD may choose to either temporarily ignore their symptoms, self-medicate, or take secondary preventive measures such as proton-pump inhibitors (20). For example, the prescription Nexium is an inexpensive, proton-pump inhibitor which is covered by most basic health insurance. Those without health insurance may still be able to afford the inexpensive medication or obtain low-cost generic versions. If left untreated, GERD can evolve into Barrett's esophagus (BE), a much more serious disease where normal esophageal cells change into gland-like adenomatous cells. BE is defined as metaplasia in the cells of the inferior portion of the esophagus (18). Epidemiological studies conducted in the US suggest that the prevalence of BE in the general population is approximately 1%, however, only a small number of these cases are actually diagnosed within a patient's lifetime (21).

BE is more difficult to detect and requires more complex screening methods. At this stage of disease progression, health insurance is almost mandatory to cover the high costs of screening procedures. Without health insurance, it would be very difficult to meet the financial burden presented by these screening methods; therefore, those who are uninsured usually ignore or cope with symptoms. Over-time, symptoms progress into more unbearable pain, difficulty swallowing, etcetera. At this point, patients who have not received previous screening are more likely to get screened due to the intensity of their symptoms. By this time, it is too late for most cases as the disease has spread to the distant stage and will not only require more aggressive treatment, but will have a worse prognosis.

1.5. Screening

Because the esophagus is located near other vital anatomic structures, EAC is most manageable when detected early. Several screening techniques are currently in use to help detect both EAC and its precursor (BE) including esophagoscopy, biopsy, brush and balloon cytology, chromoendoscopy, and fluorescence spectroscopy (22). Esophagoscopy is a procedure in which an esophagoscope is inserted through the mouth or nose to look inside the esophagus for abnormal areas (22). Tissue samples may be removed (biopsied) using this procedure for further analysis in the laboratory. Brush and balloon cytology are techniques in which cells from the lining of the esophagus are collected and observed under a microscope to check for abnormalities (22). Chromoendoscopy is a procedure used in conjunction with esophagoscopy. A dye is sprayed onto the lining of the esophagus and observations are made based upon the amount of staining present. Increased staining may suggest early BE (22). Fluorescence spectroscopy uses a special light to view tissue in the lining of the esophagus. The light given off by the cells in the lining of the esophagus is measured. Malignant tissue gives off less light than normal tissue (22), thus confirming the presence of absence of carcinoma.

1.6. Socioeconomic Contributors to Disease

The most commonly used SES variables in cancer research include educational attainment, employment, income, geographical location, and marital status (6, 9, 15, 16). Educational attainment relates to EAC in that unskilled workers may be prone to more work-place exposures (i.e.: mining) and have less healthy habits, such as smoking (15). Unemployment and lower income generally result in lower SES levels, which has been linked to higher EAC risk (17). Geographical location (urban vs. suburban environment) is also used in predicting cancer prevalence. Studies suggest those living in more urban environments are prone to greater environmental pollutants, raising their exposure levels to certain cancers (12). A summary of socioeconomic contributors of EAC found in previously published literature is located in Appendix I.

1.7. Role of Socioeconomic Status in Stage at Diagnosis

The National Center of Educational Statistics defines socioeconomic status as an economic and sociological combined total measure of an individual's or family's economic and social position relative to others, based on determinants such as income, education, and occupation (26). Lower SES is known to be associated with worsened survival and increased incidence of cancer in the US (6, 9, 15, 16). Additionally, several studies conducted in the US have confirmed an association between SES and stage of disease diagnosis (9, 16). Several hypotheses to explain survival differences between social groups have been proposed including differences in tumor biology, patient co-morbidity, stage of disease at diagnosis, access to therapy, and treatment practices (16).

Of these hypotheses, the most commonly cited as a potential mechanism for the observed relation between SES and cancer outcomes is differences in stage of disease (16). Woods et al. conclude in their review of literature that stage of disease at diagnosis and access to optimal treatment explain a portion of disparity in survival of patients with cancer (16).

Previous cancer studies have shown a positive association between low socioeconomic status (specifically poverty) and later stage of cancer diagnosis (10-12, 23-25). One study found that a lack of health insurance explained some of the observed differences in stage at diagnosis (10). Several studies have directly or indirectly addressed the effect of health insurance on stage at the time of cancer diagnosis (11, 23-25). However, health insurance alone is unlikely to be the only explanation as the issue is most likely multi-factorial (25). A majority of studies that examined the impact of poverty on stage of cancer diagnosis used registry data, such as SEER Program data, that were then linked to census-tract indicators of socioeconomic status (10-12). This is the same approach that will be used in this study. In most of these studies, adjustment for socioeconomic indicators explained the majority of the observed differences in stage at diagnosis (11, 12).

1.8. Area Socioeconomic Attributes

Area socioeconomic status is defined as a "group" measure of socioeconomic status (such as a neighborhood or defined geographical unit). Common measures of area SES include unemployment rate, median household income, percent of persons below poverty threshold, percent of persons foreign born, percent of persons living in an urban area, and percent of persons with less than a high school diploma. Several studies use area SES because data on area SES are available for most cancer registries, however, individual SES is not collected to protect patient confidentiality (27). A recent study conducted by the National Cancer Institute (NCI) linked five area socioeconomic categories to county mortality data. The socioeconomic categories were based on factors such as education, occupation, median family income, unemployment rate, family poverty rate, and housing condition. The study found that between 1950 and 1960, male cancer mortality was nearly 50% greater in the highest area socioeconomic group than in the lowest area socioeconomic group (15). However, by 1998, cancer mortality was 19% higher in the lowest area socioeconomic group than in the highest area socioeconomic group (15). The authors conclude that the socioeconomic patterns in male cancer mortality trends are consistent with socioeconomic patterns in cigarette smoking, a commonly accepted contributing factor of EAC (15). Given the latency period between the start of regular smoking and cancer death, it is predicted that socioeconomic disparities in male cancer mortality will continue to widen in the near future (15).

1.9. Other Influences of SES on EAC

Socioeconomic status greatly influences the type of preventive care one receives in the precancerous stages of EAC along with obtaining the recommended screening techniques (9). Even in countries with equal access to health care (such as Canada and Sweden), low SES is still strongly related to an increased risk of esophageal adenocarcinoma (9). A common pattern could be social hierarchies where it is relative social position or social networks within countries that matters most (9). Addressing risk factors such as obesity, smoking, and alcohol consumption are all primary preventive measures which can be taken while the disease is still in its precancerous stages. In addition, having good social support may lead to the prevention of these adverse health behaviors (10). There is a consistent link between SES and marriage, an important form of social support. While marriage is hypothesized to increase income and SES (9), higher SES individuals also are more likely to get married (9) and hence receive social support from this marital partner (9). Therefore, individuals with higher SES are more likely to receive the social support needed to reduce risky health behaviors and stress, all of which contribute to better health including lower risk of factors that drive EAC.

A temporal shift toward earlier stage diagnosis does not explain the increasing incidence rate of EAC (15). Because a better prognosis is associated with earlier stage diagnosis, we looked at predictors of early stage disease. In this study, we examined the association between EAC stage and area-level SES measures including educational attainment, employment status, median household income, place of birth, and geographical location. We hypothesized that lower SES would be associated with later stage diagnosis.

Chapter 2: Methods

2.1. Aims

Prior studies have demonstrated an association between SES and EAC incidence and prevalence (6, 9, 15, 16). The purpose of this study is to expand the literature on SES and EAC by improving understanding of the ways in which SES may contribute to late stage EAC diagnosis. Since early detection of EAC is the best predictor of treatment success, the study would be significant in finding which socioeconomic disparities predict a later diagnosis. These disparities can be targeted by public health organizations or researchers to implement special programs which can help lead to earlier EAC detection.

2.2. Hypothesis

We hypothesize that area-level SES indicators (educational attainment, employment, income, place of birth, and geographical location) will be associated with elevated odds of late stage EAC diagnosis. In addition, we hypothesize that area-level median household income and unemployment will be the two strongest predictors of later EAC detection, possibly due to the high costs associated with EAC screening. This is in accordance with prior literature that indicates the importance of income and unemployment status on EAC outcomes. Hebert et al. found a positive association between area-level measures of employment status and income with the risk of EAC (17), while Berki et al. determined that "lack of health insurance is directly related to the length of unemployment" (28).

2.3. Study Design

The design for this study is cross-sectional, using data collected between the years 2000 and 2007 from the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute. SEER is a coordinated system of population-based registries strategically located across the United States. These registries monitor cancer trends and provide timely, accurate, and continuous data on cancer incidence, the extent of disease at diagnosis, therapy, and patient survival. SEER gathers data on all incident cancers occurring in 18 geographic areas in the United States. There are nine states (New Mexico, Hawaii, Utah, Iowa, Connecticut, Greater California, Kentucky, Louisiana, New Jersey), five metropolitan areas (metropolitan Atlanta plus a sample of rural Georgia, the Greater Bay area [San Francisco-Oakland and San-Jose Monterey], Los Angeles, Seattle, Detroit), and the Alaska Tumor Registry, which together represent approximately 26 percent of the United States population in the SEER registry (29). The SEER program registries routinely collect data on patient demographics, primary tumor site, tumor morphology and stage at diagnosis, first course of treatment, and follow-up for vital status. Cases are identified by reviewing hospital pathology reports and discharge diagnoses, death certificates, and records from pathology laboratories, oncologists, and radiotherapists. Vital status is determined through contact with physicians and patients, review of death certificates and local obituaries, and matching against the National Death Index and records of the Health Care Financing Administration (30).

Census tract- and county-level socioeconomic attributes were obtained from the Bureau of Census through a custom data agreement with NCI. Direct linkage between SEER data and Bureau of Census data was made possible through unique Federal Information Processing Standard (FIPS) geo-coding, a unique code that matches individual-level data to both census tract- and county-level attributes.

2.4. FIPS Geo-coding

FIPS geo-coding allowed for the linkage of SEER 15 data to Bureau of Census data. All SEER 15 cases belonged to census-tracts which were reported and recorded in SEER data collection. The standard FIPS code of residence was used when this information was collected. The census-tract data taken from The Bureau of Census used the same standard FIPS code, therefore, linkage of census data to SEER data was made possible through this standard coding.

2.5. Description of the Participants and Criteria for Selection

The analysis was based on EAC cases in 12 states within the SEER 15 Registries (California, Connecticut, Metropolitan Detroit, Hawaii, Iowa, New Mexico, Seattle (Puget Sound), Utah, Georgia, Kentucky, Louisiana, New Jersey). Case definition site and type categories were based on International Classification of Diseases for Oncology (ICD-O) (3rd edition) codes: esophagus (C15.0-C15.9) and adenocarcinoma (8140-8573). This definition identified 14,264 EAC cases in SEER 15 registries during the surveillance period.

Of these 14,264 identified EAC cases, only 11,233 had a single primary tumor. Only cases with a single primary tumor were included in the analysis as they were considered newly onset and not previously diagnosed. From these 11,233 EAC cases with a single primary tumor, 1,134 cases were missing data on stage at diagnosis or were reported as unstaged. These cases were deleted for missing information necessary for analysis. After deleting these cases, we were left with 10,099 total cases reporting to have localized, regional, or distant stage EAC at initial diagnosis, based on SEER summary stage definitions.

After further review of the data, it was found that 319 cases were missing census-tract attributes. Additionally, all 27 cases from Whatcom County, Washington were missing county-level attributes, and 23 more cases from various registries were missing data for census-tract level median family income. A total of 17 cases were missing county population data. Two cases were missing census-tract level data on educational attainment and one case is missing census-tract level unemployment data. After excluding these discrepancies, an analytic dataset was created consisting of 9,710 single primary EAC cases with local area socioeconomic attributes (Figure 1). The figure yields 68% of the original 14,264 EAC cases in the SEER dataset and includes 96% of 10,099 EAC cases with specific stage at diagnosis data.

2.6. Human Subjects

Approval was obtained from the University of Maryland, College Park (UMCP) Institutional Review Board (IRB). The study met requirements for "exempt review." SEER data is publicly available after submitting a signed user agreement form which ensures the investigator will use the data in such manner that subjects cannot be identified, directly or indirectly through identifiers linked to the subjects. Approval for the analysis was also obtained from the NCI, SEER Custom Data User Committee.

2.7. Description of Variables

2.7.1. County- and Census- Tract Socioeconomic Variables

Census-tracts are the smallest territorial unit for which population data are available in many countries (31). They comprise of approximately 2,500 people who share similar demographic attributes, such as income, employment status, home ownership, and location. Census-tracts tend to be more discrete about the population they contain compared to counties due to demographic similarities shared among residents. On the other hand, county-level data is more of an aggregate. Demographic attributes are aggregated and are more diverse since counties do not focus on smaller sub-populations. More affluent counties have less cancer cases. A study done by Ezzati et al. confirmed that counties are the smallest unit for which mortality data are routinely available, allowing consistent and comparable long-term analysis of trends in health disparities (31). County-level data gives more of an aggregate which is generalizable to a larger population compared to census-tract data, which is limited in its generalizaibliltiy. Due to the smaller sample size, census-tract data are more discrete. Both census tract- and county-level data are used in the analysis as census-tract data provides more localized data that is homogeneous in nature (people residing in the same census-tract tend to have similar SES). Conversely, counties are much larger and much more socioeconomically heterogeneous. They account for a wider range of data since more individuals are present in counties than census-tracts. As a result, this may help drive statistically significant associations due to the increased population size.

The analysis linked EAC cases to census tract- and county-level socioeconomic attributes. A list of variables used in the analysis is found in Table 1. The census-tract data taken from The Bureau of Census used the same standard FIPS code, therefore, linkage of census data to SEER data was made possible through this standard coding.

2.7.2. Individual Case-Level Variables

Six individual (case) level variables that have been shown to be associated with EAC were explored as possible confounders. A description of these variables is found in

Table 2. These variables all came from SEER 15 data provided by NCI. Dummy variables were created to better categorize age at diagnosis.

2.7.3. Main Outcome Variable

The main outcome variable of interest is stage at diagnosis, specifically the distant stage. The distant stage of EAC has the worst treatment outcome and has the highest mortality rate, therefore, examining SES attributes which predict distant stage diagnosis may help better target these disparities in future studies.

Determining the best base model to use for data analysis was one of the primary focuses early on in the study. The optimal referent group for logistic regression is important to determine due to "stage shift" in the SEER data. A higher proportion of EAC cases were classified as localized, however over time, there was only a small decrease observed in survival time. A possible explanation could be misclassification of localized cases as regional due to histological similarities. To ensure a clear distinction between stages, it was necessary to group localized and regional cases together. This presented as a more appropriate referent group when conducting data analysis. Another model that could be informative is comparing localized stage versus distant stage only due to the extreme histological differences. This approach, however, reduced statistical power due to the elimination of the regional stage and thus was not used in the analysis. Combining stages when conducting analyses yielded more significant results and was therefore worth examining while establishing a base model.

2.8. Variable Coding

After selecting the base model, the data was further explored to determine the best method to code variables. In preliminary analysis, it was determined that the study would yield more meaningful results if variables were dichotomized. There is evidence of a monotonic relationship between certain variables; however, a referent group is not standardized in this approach. The study benefited from the use of dichotomized variables since a referent group was established. Certain variables, such as age, could not be analyzed monotonically in SAS. Dummy variables were created (which can only be performed in a dichotomized analysis). The outcome variable (distant stage EAC) was coded with the value of zero (0) in the analysis, while the referent group (localized and regional EAC) was coded with the value of one (1).

2.9. Statistical Analysis

All statistical analyses were conducted using SAS statistical software, Version 9.2. The distribution of EAC cases by individual, census-tract, and county-level attributes was explored in general and by stage of diagnosis (local/regional and distant). Additionally, EAC cases were explored by each SEER 15 registry included in the study. Because of the significant findings in the individual-level analysis (Table 3), these variables were used as controls in the logistic regression.

Logistic regression models were developed to estimate odds ratios and 95% confidence intervals for EAC cases to determine which area-level SES attributes were associated with late stage EAC diagnosis. A crude model along with an adjusted model controlling for age group (20 to 49, 50 to 69, 70 to 84, 85+ years), year of diagnosis (2000 to 2007), sex (male or female), and race (white or other) were created. We did not control for registry effects as only modest differences in localized and regional EAC rates were observed (Table 4).

Chapter 3: Results

3.1. Demographic and Registry Distributions

Table 5 displays individual case-level demographic data for esophageal adenocarcinoma cases diagnosed in SEER 15 registries from 2000 to 2007, by stage at diagnosis. Regardless of stage at diagnosis, the vast majority of cases (> 80%) were male. Similarly, approximately 95% of cases were white. Approximately 64% of cases were married and nearly one-third were missing data on marital status. The peak age groups of diagnosis were 50-69 years of age (53%) followed by 70-84 years of age (33%). A small increase in the number of newly diagnosed EAC cases was observed between 2000 to 2007.

The registries with the highest rates of EAC (at least 3 per 100,000 or above) included Iowa, Kentucky, and Seattle (Table 4). These registries accounted for approximately 15% of the SEER 15 registry. The registries with the lowest rates of EAC (2 per 100,000 or below) included Los Angeles and Atlanta. These two registries accounted for approximately 17% of the SEER 15 registry. The remaining 10 registries (California, New Jersey, San Francisco-Oakland, Louisiana, Detroit, Connecticut, Utah, San Jose-Monterey, New Mexico, and Hawaii) all had EAC rates that were roughly around 2 per 100,000. Additionally, all registries (except Los Angeles) had half of their EAC cases categorized in the localized/regional stage.

3.2. Census tract- and County-Level Attributes

Tables 6 and 7 display census- tract and county- level area socioeconomic attributes for esophageal adenocarcinoma cases diagnosed in SEER 15 registries from 2000 to 2007 by stage at diagnosis, respectively.

For both census- tract and county- level data, the highest percentage of cases were seen in the lower strata for the following area socioeconomic attributes: (1) percent of persons ages 25 and over that are less than a high school graduate, (2) percent of persons ages 16 and over who are unemployed, and (3) percent of persons below poverty threshold. The census- tract estimate for all three variables was around 44% for all cases of distant stage disease. The county- level estimate for all three variables was approximately 30% for all cases of distant stage disease.

At the census- tract level, approximately 73% of distant EAC cases lived in urban environments, as similar to the county- level data. Additionally, 44% of distant EAC cases had a median household income less than or equal to $40,800, whereas the county-level data was more evenly distributed amongst the four strata. Both census- tract and county- level data shared a similar distribution for percent of persons that were foreign born.

3.3. Logistic Regression

Results from the crude and adjusted models for census-tract and county-level SES variables are presented in Tables 8 and 9, respectively. At the census-tract level, the only area-level SES variable that was significantly different from its referent group was percent of individuals who were foreign born. Cases living in census-tracts with > 26.6% foreign born individuals had statistically significant higher odds ratios of distant stage EAC (adjusted odds ratio (OR) = 1.14, 95% confidence interval (95% CI) from 1.02 to 1.27) when compared with EAC cases living in census-tracts with ≤ 6.7% foreign born individuals.

At the county-level, there were three area-level SES variables that were significantly different from the referent group, including percent of individuals foreign born, percent of individuals living in an urban environment, and median household income.

In both crude and adjusted models, cases living in counties with >15.3% foreign born individuals had statistically significant higher odds ratios of distant stage EAC (adjusted odds ratio (OR) = 1.16, 95% confidence interval (95% CI) from 1.03 to 1.31) compared to cases living in counties with ≤ 6.7% of foreign born individuals.

Additionally, cases living in counties with >89% of individuals living in an urban environment had statistically significant lower odds ratios of distant stage EAC (adjusted odds ratio (OR) = 0.90, 95% confidence interval (95% CI) from 0.82 to 0.98) compared to cases living in counties with ≤ 89% of individuals living in an urban environment.

Finally, cases living in counties with a median household income between $40,800 and $45,600 had statistically significant higher odds ratios of distant stage EAC (adjusted odds ratio (OR) = 1.14, 95% confidence interval (95% CI) from 1.01 to 1.28) compared to cases living in counties with a median household income less than or equal to $40,800.

Chapter 4: Discussion

4.1. Discussion of Results

The principal findings of this study were observed at the county-level. Cases who lived in counties with higher percentages of foreign born residents, higher percentages of residents living in urban settings, and lower median household income had slightly elevated odds of late stage EAC. The only significant association at the census-tract level for late stage EAC was the place of birth variable; cases who lived in census-tracts with greater than 26.6% foreign born residents had higher odds of developing distant stage EAC.

It was hypothesized that lower SES would be a predictor of later stage EAC diagnosis. Most of the socioeconomic variables used in the study are interrelated and may suggest possible pathways leading to later detection. For example, persons with lower educational attainment are more likely to be unemployed, which can result in a lower household income. Lower SES individuals may not be able to afford the high costs associated with EAC screening, therefore further delaying the detection process until symptoms become much more aggressive (when it may be too late). Out of all SES variables, it was expected that median household income and unemployment would be the two strongest predictors of later EAC detection. The analysis did find one level of median household income to be significant at the county-level, but unemployment was not associated with later stage EAC diagnosis in the present study.

Living in counties with a low median household income, but not the lowest, was associated with later stage EAC diagnosis in this analysis. Cases living in counties with a median household income between $40,800 and $45,600 had statistically significant higher odds ratios of distant stage EAC diagnosis compared to cases living in counties with a median household income less than or equal to $40,800. Hebert et al. found a positive association between lower income and EAC risk (17). Patients with lower income are less likely to get screened due to the expensive cost associated with EAC screening. This could explain why those with lower income are more prone to distant stage EAC. When comparing the second strata of median household income (40.8 to 45.6K) with the referent group (≤ 40.8K), it was found that cases in the second strata (40.8 to 45.6K) had 14% greater odds of developing late stage EAC compared to cases who are in the referent group (≤ 40.8K). One would expect the referent group to have greater odds of developing late stage EAC, since income in this group is far less than the second strata. A possible explanation could be the poverty threshold of the geographical area. Certain individuals have a median household income which is slightly above the poverty threshold, placing them at a great disadvantage since they do not qualify for Medicaid and other government benefits. Those who make slightly below the poverty threshold may qualify for Medicaid and other government benefits such as health insurance (which may promote healthy screening behaviors). This could provide a possible explanation as to why the association at the second strata was significant. Taplin et al. supports the findings of the current study as the research team found a positive association between poverty and later stage cancer diagnosis (33).

The analysis suggest that cases living in counties with greater than 15.3% persons being foreign born have a higher odds of developing distant stage EAC. Previous studies have noted that immigrants tend to have lower SES than native born Americans (16). Additionally, lower SES is linked to later stage cancer diagnosis (6, 9, 15, 16). This may explain a possible pathway of later stage cancer diagnosis in foreign born EAC patients. Immigrants may also have a more difficult time adjusting to life in the US compared to native born Americans, which can directly or indirectly affect SES. Additionally, the findings of Hongo et al. suggest that the development of esophageal adenocarcinoma appears to be strongly influenced by ethnic factors (34). This supports the findings of the current study.

Living in an urban environment appeared to be associated with earlier diagnosis of EAC in this sample. Cases living in counties with >89% of individuals living in an urban environment had statistically significant lower odds ratios of distant stage EAC compared to cases living in counties with ≤ 89% of individuals living in an urban environment. Falk et al. found that people living in more urban environments have a higher risk of developing EAC (35). The present study finds no such association for EAC, as living in an urban environment was protective of distant stage EAC. Falk explains that people living in urban environments are exposed to more environmental pollutants, thus raising their risk for certain cancers. A possible explanation for the contradictory findings of the present study could be that urban areas tend to have more hospitals and/or clinics, making screening readily available and accessible to residents of urban areas compared to cases living in suburban areas.

The analysis examined both census tract- and county-level SES factors. There was a notable difference in the findings between these two levels, such that census-tract SES variables were not significantly associated with later stage diagnosis of EAC. Differences in association between county and census-tract data may be due to the homogeneity of SES in census-tracts and the heterogeneity of SES in counties. Census-tracts are much smaller than counties and generally comprise of individuals who share similar SES attributes. This homogeneity may mask any significant socioeconomic association, if present. Conversely, counties are much larger and much more socioeconomically heterogeneous. They account for a wider range of data since more individuals are present in counties than census-tracts. As a result, this may help increase statistical confidence and narrow confidence intervals, which may drive more statistically significant associations.

Islami et al. found that various dimensions of SES, such as education, wealth, and being married were all inversely related to esophageal cancer (32). The strongest inverse association was found with education. Compared with no education, the adjusted odds ratios for primary education and high school or beyond were 0.52 and 0.20, respectively. The present study did not find any significant associations between education and late stage EAC, however, wealth (defined as median household income) was significant at the county-level. The social support provided by a life partner may explain why Islami et al. found that those who are married are less likely to develop EAC. Additionally, a statistically significant association between being married and earlier stage diagnosis was found in the individual-level analysis of the current study which further supports the findings of Islami.

Jansson et al. found that the risk of esophageal adenocarcinoma increased with decreasing SES; unskilled workers had 3.7-fold and 2.1-fold increased risks, respectively, compared with age- and sex-comparable professionals (9). Jansson et al. defines SES as the type of skill one possessed (professional, intermediate, assistant, skilled, and unskilled). Due to the difference in SES definitions, Jansson et al. cannot be used to show consistency with the current study.

4.2. Strengths

A major strength of the study is the large sample size provided by SEER. SEER data accounts for a large sub-set of the US population, making it one of the largest cancer databases available for public use. SEER data can also be accessed through the Internet, making it very convenient for researchers. The large sample size allowed for several deletions of individuals having incomplete data records. This strengthened the quality of the analytic data set since each data entry had a complete list of research variables. Furthermore, the large sample size allowed for narrower confidence intervals in statistical analyses, suggesting a truer association among odds ratios.

4.3. Limitations

A major limitation of the study would be the cross-sectional design, as it prevents us from deriving causality between SES variables and EAC. Additionally, the study is restricted to area-level SES measures and does not account for individual-level SES. Most registry based studies do not use individual SES measures since the cancer registry does not capture this information. Most individual-level data comes from medical records which are required by law to de-identify patients to protect their privacy and confidentiality. Using individual-level data can compromise patient confidentiality; therefore, area SES serves as a good proxy since people who live in the same neighborhood/area tend to share similar SES levels. Conversely, area SES does not serve as a reliable proxy for individual data. SES measures at the census tract- and county-level may operate in different ways than at the individual-level. County X may comprise primarily of residents whose median household income is below the poverty threshold. There may be a small number of individuals who reside in the same county whose income is significantly greater than the poverty threshold, therefore, area SES measures cannot be generalized to these individuals. Thus, generalizing area SES measures at the individual-level is inaccurate and should be avoided.

Although adjustment for sex, race, and year of diagnosis had no effect on statistically significant associations with place of birth, income, and population density, we cannot dismiss the possibility of residual confounding due to individual-level attributes such as income, health insurance status, and smoking status. Additionally, we cannot dismiss the possibility of residual confounding due to registry effects, although none were observed in the present study.

The present study only examined the association between area-level SES and late stage EAC diagnosis. However, low SES also influences risk factors of EAC (which then ultimately leads to disease). Future follow-up studies would benefit from separate sub-analyses looking at individual-level SES data (if available) as well as the influence of low SES on EAC risk factors.

4.4. Public Health Significance

This study provides insight into area-level attributes associated with stage at diagnosis for esophageal adenocarcinoma. The information in this report may inform cancer control efforts if area-level income, population density, and nativity can be used as a basis to target EAC screening, prevention, and early treatment resources, which could help reduce the burden of this disease. More research is recommended to determine if these finding can be replicated at the individual-level.

Although the outcome for advanced stage esophageal adenocarcinoma is poor, the early detection and treatment of early stage disease is usually associated with a much better outcome (13). Until recently, esophagectomy has been the treatment of choice in fit patients, however, morbidity is significant and has encouraged the development of newer endoscopic treatments that preserve the esophagus such as ablation and mucosal resection (13). Promising results are foreseen, and endoscopic methods may provide as an alternative treatment for early esophageal adenocarcinoma. Minimally invasive techniques for esophageal resection have also been shown to be feasible, although there is only limited evidence that they reduce postoperative morbidity (13). Further data is needed to demonstrate improved outcomes from the above two methods.

Figure 1. Exclusions, esophageal adenocarcinoma incident cases, SEER 15 registries, 2000-2007

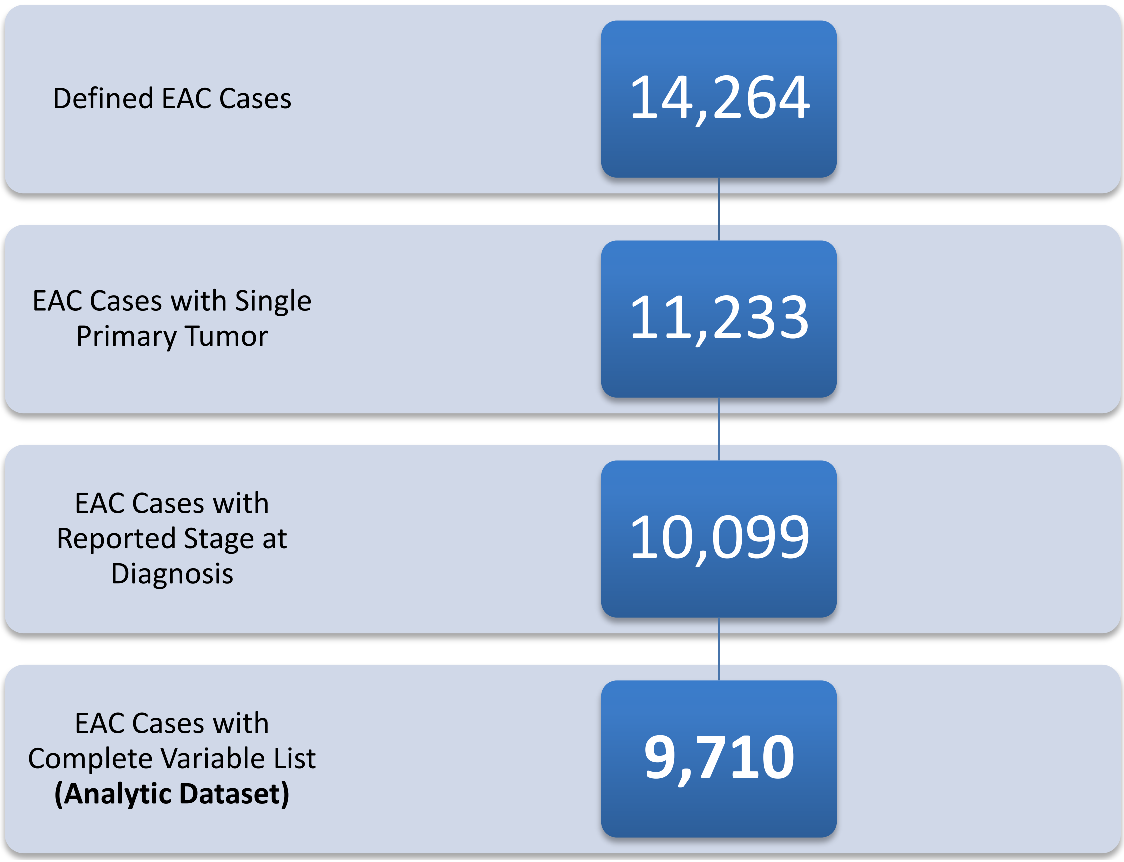

Table 1. County- and Census- Tract Socioeconomic Variables, esophageal adenocarcinoma incident cases, SEER 15 registries, 2000-2007

Variable	Format
Education	Percent of persons ages 25 and over that are less than a high school graduate > 26.7% > 19.3 to 26.7% 15.4 to 19.3% ≤ 15.4%
Employment	Percent of persons ages 16 and over who are unemployed > 8.2 > 6.0 to 8.2% 4.8 to 6.0% ≤ 6.0%
Income	Median household income > 54K > 45.6 to 26.6K 40.8 to 45.6K ≤ 40.8K
Poverty	Percent of persons below poverty threshold > 17.7% > 12.0 to 17.7% 8.4 to 12.0% ≤ 8.4%
Birthplace	Percent foreign born > 26.7% > 19.3 to 26.7% 15.4 to 19.3% ≤ 15.4%
Environment	Percent of people in an area that are living in an urban environment 100% 0 to < 100%

Table 2. Individual Case-Level Variables, esophageal adenocarcinoma incident cases, SEER 15 registries, 2000-2007

Variable	Description
Age at diagnosis	Categorized into 4 groups using dummy variables. Group 1 includes ages 20-49; Group 2 includes ages 50-69; Group 3 includes ages 70-84; and Group 4 includes ages 85 +
Race	White Non-Hispanic; all other races will be considered “other” for analyses as EAC is primarily a disease of white males
Gender	Male/Female
Year of diagnosis	SEER 15 covers years 2000-2007
Marital Status	Married, single, widowed, separated, divorced, unknown
Health Insurance Status	No insurance, some insurance, missing
Place of Birth	Born in US or US territory versus a foreign country

Table 3. Logistic regression model of the association between stage at diagnosis and individual-level attributes, esophageal adenocarcinoma incident cases, SEER 15 registries, 2000-2007

	No.	Crude OR	95% CI	Adj. OR†	95% CI
Age					
≥ 70	3642	0.64	0.59 - 0.70	0.64	0.59 - 0.70
≤ 69	6068	1.00	Referent	1.00	Referent
Marital Status					
Married	6210	0.80	0.73 - 0.87	0.81	0.74 - 0.88
Other^	3500	1.00	Referent	1.00	Referent
Race					
White	9239	0.72	0.60 - 0.87	0.73	0.60 -0.88
Other+	471	1.00	Referent	1.00	Referent
Sex					
Male	8355	0.94	0.83 - 1.05	0.93	0.82 - 1.06
Female	1355	1.00	Referent	1.00	Referent
*Health Insurance Status^*					
Some insurance	4025	0.82	0.65 - 1.03	0.89	0.70 - 1.12
No Insurance	325	1.00	Referent	1.00	Referent
Place of Birth					
Foreign Country	561	1.04	0.87 - 1.24	1.02	0.86 - 1.22
United States	6446	1.00	Referent	1.00	Referent

† Adjusted for age, sex, race, and year of diagnosis

^ Cases with missing data on marital status, place of birth, and health insurance not included in respective analyses

\+ Other race includes Black, Asian and Pacific Islander, and American Indian and Alaskan Native

Abbreviations: Adj. =Adjusted, CI=confidence interval

Table 4. Stage distribution and incidence rate by registry, SEER 15, 2000-2007

Registries	Population	All cases**	L/R**	Distant**	L/R Stage (%)	(%) of Total
ALL SEER 15	**605,071,719**	**2.5**	**0.7**	**0.8**	**52.0%**	**100%**
California*	152,115,563	2.5	0.7	0.9	52.0%	25.1%
Los Angeles	78,043,826	1.7	0.4	0.6	41.2%	12.9%
New Jersey	68,607,598	2.8	0.8	0.9	53.6%	11.3%
Seattle (Puget Sound)	33,772,761	3.0	1.0	0.9	63.3%	5.6%
San Francisco-Oakland	33,345,672	1.8	0.6	0.7	61.1%	5.5%
Louisiana	33,220,635	2.2	0.7	0.7	63.6%	5.5%
Kentucky	33,050,222	3.1	0.9	1.0	54.8%	5.5%
Detroit (Metropolitan)	32,399,937	2.7	0.8	1.0	55.6%	5.4%
Connecticut	27,687,944	3.0	0.9	0.9	56.7%	4.6%
Atlanta (Metropolitan)	25,544,166	1.9	0.6	0.6	57.9%	4.2%
Iowa	23,565,286	3.6	1.1	1.2	58.3%	3.9%
Utah	19,445,394	2.4	0.7	0.8	58.3%	3.2%
San Jose-Monterey	19,238,540	2.1	0.7	0.7	61.9%	3.2%
New Mexico	15,070,397	2.3	0.7	0.6	60.9%	2.5%
Hawaii	9,963,778	1.2	0.3	0.6	50.0%	1.6%

* Excludes San Francisco, San Jose-Monterey, and Los Angeles
** Rate per 100,000
Abbreviations: L/R = Localized/Regional

Table 5. Individual case-level demographic attributes by stage at diagnosis, esophageal adenocarcinoma incident cases, SEER 15 registries, 2000-2007

	Total (n = 9710)		Stage: Localized/Regional (n = 5876)		Stage: Distant (n = 3834)	
	No. Cases	%	No. Cases	%	No. Cases	%
Individual Level Attributes						
Gender						
Male	8355	86.0	5074	86.4	3281	85.6
Female	1355	14.0	802	13.6	553	14.4
Race						
White	9239	95.1	5627	95.8	3612	94.2
Other	471	4.9	249	4.2	222	5.8
Marital Status						
Married	6210	64.0	3859	65.7	2351	61.3
Other*	3155	32.5	1792	30.5	1363	35.6
Unknown	345	3.6	225	3.8	120	3.1
Age at Diagnosis						
20-49 years	972	10.0	488	8.3	484	12.6
50-69 years	5096	52.5	2949	50.2	2147	56.0
70-84 years	3164	32.6	2094	35.6	1070	27.9
≥ 85 years	478	4.9	345	5.9	133	3.5
Year of Diagnosis						
2000	1072	11.0	653	11.1	419	10.9
2001	1129	11.6	698	11.9	431	11.2
2002	1152	11.9	696	11.8	456	11.9
2003	1149	11.8	693	11.8	456	11.9
2004	1279	13.2	774	13.2	505	13.2
2005	1276	13.1	762	13.0	514	13.4
2006	1329	13.7	790	13.4	539	14.1
2007	1324	13.6	810	13.8	514	13.4

* Widowed, Separated, Divorced, and Single

Table 6. Census tract- area socioeconomic attributes by stage at diagnosis, esophageal adenocarcinoma incident cases, SEER 15 registries, 2000-2007

	Stage					
	Total (n = 9710)		Localized/Regional (n = 5876)		Distant (n = 3834)	
	No. Cases	%	No. Cases	%	No. Cases	%
Census Tract Attributes						
Percent Adults 25+ years of age, less than a high school education						
> 26.7%	3209	33.0	1945	33.1	1264	33.0
> 19.3 to 26.7%	1446	14.9	886	15.1	560	14.6
15.4 to 19.3%	955	9.8	601	10.2	354	9.2
≤ 15.4%	4100	42.2	2444	41.6	1656	43.2
Percent persons 16+ years of age, unemployed						
> 8.2%	2721	28.0	1663	28.3	1058	27.6
> 6.0 to 8.2%	1570	16.2	936	15.9	634	16.5
4.8 to 6.0%	1143	11.8	681	11.6	462	12.1
≤ 4.8%	4276	44.0	2596	44.2	1680	43.8
Percent persons below poverty line						
> 17.7%	2714	28.0	1631	27.8	1083	28.2
> 12.0 to 17.7%	1428	14.7	883	15.0	545	14.2
8.4 to 12.0%	1373	14.1	820	14.0	553	14.4
≤ 8.4%	4195	43.2	2542	43.3	1653	43.1
Percent foreign born						
> 26.6%	2213	22.8	1304	22.2	909	23.7
> 15.3 to 26.6%	1593	16.4	986	16.8	607	15.8
6.7 to 15.3%	2353	24.2	1394	23.7	959	25.0
≤ 6.7%	3551	36.6	2192	37.3	1359	35.4
Percent people in area, living in urban environment						
100.0%	7068	72.8	4256	72.4	2812	73.3
> 88.0 to < 100%	706	7.3	421	7.2	285	7.4
21.5 to 88.0%	969	10.0	588	10.0	381	9.9
≤ 21.5%	967	10.0	611	10.4	356	9.3
Median household income						
> 54K	3162	32.6	1892	32.2	1270	33.1
> 45.6 to 54K	1316	13.6	798	13.6	518	13.5
40.8 to 45.6K	898	9.2	528	9.0	370	9.7
≤ 40.8K	4334	44.6	2658	45.2	1676	43.7

Table 7. County- level area socioeconomic attributes by stage at diagnosis, esophageal adenocarcinoma incident cases, SEER 15 registries, 2000-2007

	Stage					
	Total (n = 9710)		Localized/Regional (n = 5876)		Distant (n = 3834)	
	No. Cases	%	No. Cases	%	No. Cases	%
County Level Attributes						
Percent Adults 25+ years of age, less than a high school education						
> 26.7%	1790	18.4	1076	18.3	714	18.6
> 19.3 to 26.7%	2070	21.3	1238	21.1	832	21.7
15.4 to 19.3%	2873	29.6	1743	29.7	1130	29.5
≤ 15.4%	2977	30.7	1819	31.0	1158	30.2
Percent persons 16+ years of age, unemployed						
> 8.2%	1696	17.5	1017	17.3	679	17.7
> 6.0 to 8.2%	2326	24.0	1378	23.5	948	24.7
4.8 to 6.0%	2790	28.7	1711	29.1	1079	28.1
≤ 4.8%	2898	29.8	1770	30.1	1128	29.4
Percent persons below poverty line						
> 17.7%	1752	18.0	1050	17.9	702	18.3
> 12.0 to 17.7%	2572	26.5	1550	26.4	1022	26.7
8.4 to 12.0%	2201	22.7	1326	22.6	875	22.8
≤ 8.4%	3185	32.8	1950	33.2	1235	32.2
Percent foreign born						
> 26.6%	1619	16.7	950	16.2	669	17.4
> 15.3 to 26.6%	2862	29.5	1690	28.8	1172	30.6
6.7 to 15.3%	1995	20.5	1223	20.8	772	20.1
≤ 6.7%	3234	33.3	2013	34.3	1221	31.8
Percent people in area, living in urban environment						
> 99.3%	1223	12.6	703	12.0	520	13.6
> 95.7 to 99.3%	3440	35.4	2067	35.2	1373	35.8
89.0 to 95.7%	1853	19.1	1099	18.7	754	19.7
≤ 89.0%	3194	32.9	2007	34.2	1187	31.0
Median household income						
> 54K	2476	25.5	1501	25.5	975	25.4
> 45.6 to 54K	2520	26.0	1517	25.8	1003	26.2
40.8 to 45.6K	1942	20.0	1144	19.5	798	20.8
≤ 40.8K	2772	28.5	1714	29.2	1058	27.6

Table 8. Logistic regression model of the association between stage at diagnosis and census tract attributes, esophageal adenocarcinoma incident cases, SEER 15 registries, 2000-2007

	No.	Crude OR	95% CI	Adj. OR†	95% CI
Percent Adults 25+ years of age, less than a high school education					
> 26.7%	3209	0.96	0.87 - 1.05	0.96	0.87 - 1.05
> 19.3 to 26.7%	1446	0.93	0.83 - 1.06	0.94	0.83 - 1.06
15.4 to 19.3%	955	0.87	0.75 - 1.01	0.87	0.75 - 1.01
≤ 15.4%	4100	1.00	Referent	1.00	Referent
Percent persons 16+ years of age, unemployed					
> 8.2%	2721	0.98	0.89 - 1.09	0.99	0.89 - 1.09
> 6.0 to 8.2%	1570	1.05	0.93 - 1.18	1.06	0.94 - 1.19
4.8 to 6.0%	1143	1.05	0.92 - 1.20	1.05	0.92 - 1.20
≤ 4.8%	4276	1.00	Referent	1.00	Referent
Percent persons below poverty line					
> 17.7%	2714	1.02	0.93 - 1.13	1.02	0.93 - 1.13
> 12.0 to 17.7%	1428	0.95	0.84 - 1.07	0.96	0.85 - 1.08
8.4 to 12.0%	1373	1.04	0.91 - 1.18	1.04	0.92 - 1.18
≤ 8.4%	4195	1.00	Referent	1.00	Referent
Percent foreign born					
> 26.6%	2213	1.12	1.01 - 1.25	1.14	1.02 - 1.27
> 15.3 to 26.6%	1593	0.99	0.88 - 1.12	1.01	0.89 - 1.14
6.7 to 15.3%	2353	1.11	1.00 - 1.23	1.11	1.00 - 1.23
≤ 6.7%	3551	1.00	Referent	1.00	Referent
Percent people in area, living in urban environment					
100.0%	7068	1.05	0.96 - 1.15	1.06	0.96 - 1.16
0 to < 100%	2642	1.00	Referent	1.00	Referent
Median household income					
> 54K	3162	1.07	0.96 - 1.29	1.07	0.97 - 1.17
> 45.6 to 54K	1316	1.03	0.91 - 1.17	1.03	0.91 - 1.17
40.8 to 45.6K	898	1.11	0.96 - 1.29	1.11	0.96 - 1.29
≤ 40.8K	4334	1.00	Referent	1.00	Referent

† Adjusted for age, sex, race, and year of diagnosis

Abbreviations: Adj. = Adjusted, CI = Confidence Interval

Table 9. Logistic regression model of the association between stage diagnosis and county level attributes, esophageal adenocarcinoma incident cases, SEER 15 registries, 2000-2007

	No.	Crude OR	95% CI	Adj. OR†	95% CI
Percent Adults 25+ years of age, less than a high school education					
> 26.7%	1790	1.04	0.93 - 1.18	1.02	0.91 - 1.16
> 19.3 to 26.7%	2070	1.06	0.94 - 1.18	1.05	0.94 - 1.18
15.4 to 19.3%	2873	1.02	0.91 - 1.13	1.02	0.92 - 1.13
≤ 15.4%	2977	1.00	Referent	1.00	Referent
Percent persons 16+ years of age, unemployed					
> 8.2%	1696	1.05	0.93 - 1.18	1.04	0.92 - 1.17
> 6.0 to 8.2%	2326	1.08	0.97 - 1.21	1.07	0.96 - 1.20
4.8 to 6.0%	2790	0.99	0.89 - 1.10	1.00	0.89 - 1.11
≤ 4.8%	2898	1.00	Referent	1.00	Referent
Percent persons below poverty line					
> 17.7%	1752	1.06	0.94 - 1.19	1.04	0.92 - 1.17
> 12.0 to 17.7%	2572	1.04	0.94 - 1.16	1.03	0.93 - 1.15
8.4 to 12.0%	2201	1.04	0.93 - 1.16	1.03	0.92 - 1.15
≤ 8.4%	3185	1.00	Referent	1.00	Referent
Percent foreign born					
> 26.6%	1619	1.16	1.03 - 1.31	1.16	1.03 - 1.31
> 15.3 to 26.6%	2862	1.14	1.03 - 1.27	1.15	1.04 - 1.28
6.7 to 15.3%	1995	1.04	0.93 - 1.17	1.05	0.94 - 1.18
≤ 6.7%	3234	1.00	Referent	1.00	Referent
Percent people in area, living in urban environment					
> 89.0%	6634	0.89	0.82 - 0.97	0.90	0.82 - 0.98
89.0 or less	3076	1.00	Referent	1.00	Referent
Median household income					
> 54K	2476	1.05	0.94 - 1.18	1.06	0.95 - 1.19
> 45.6 to 54K	2520	1.07	0.96 - 1.20	1.08	0.97 - 1.21
40.8 to 45.6K	1942	1.13	1.00 - 1.27	1.14	1.01 - 1.28
≤ 40.8K	2772	1.00	Referent	1.00	Referent

† Adjusted for age, sex, race, and year of diagnosis

Abbreviations: Adj. = Adjusted, CI = Confidence Interval

Appendix 1: Literature Review Summary

Variable	Level	Risk Factor	Conclusion	References
Age	Individual	Yes	Studies consistently show that the incidence of EAC increases with age. Data from both SEER and the Danish Cancer Registry demonstrate that the incidence rate of EAC increases with age until it peaks at 75-79 years of age and declines thereafter.	Bollschweiler et al. Singh et al. Woods et al. Falk et al.
Education	County Census	No	The strongest inverse association between EAC risk and various SES variables was found to be education. There are indications that low SES, based on measures of education, might increase the risk of EAC, but inconsistent results and the use of different measures of socioeconomic status makes comparisons and interpretations difficult.	Islami et al. Janson et al.
Employment	County Census	No	Unemployment generally results in lower SES levels, which has been linked to higher EAC risk.	Hebert et al.
Environment	County Census	No	One study suggests those living in more urban environments are prone to greater environmental pollutants, raising their exposure levels to certain cancers.	Falk et al. Downing et al.
Gender	Individual	Yes	It is estimated that the incidence of EAC is approximately six to eight fold greater in men than in women.	Falk et al.
Health Insurance Status	Individual	No	One study found that a lack of health insurance explained some of the observed differences in stage at EAC diagnosis. Several studies have directly or indirectly addressed the effect of health insurance on stage at the time of cancer diagnosis. However, health insurance alone is unlikely to be the only explanation. Additionally, unemployed individuals are less likely to have health insurance, which would further delay screening efforts. One study determined that "lack of health insurance is directly related to the length of unemployment."	Berki et al. Taplin et al. Bradley et al. Roetzheim et al. Ayanian et al. Garmon et al.
Income	County Census	No	Lower income generally results in lower SES levels, which has been linked to higher EAC risk.	Hebert et al.
Marital Status	Individual	No	One study found a greater than two-fold increase in risk of EAC in individuals without a life partner compared to individuals who had a life partner. Another study found that the social support provided by a life partner may explain why those who are married are less likely to develop EAC. Additionally, marriage is hypothesized to increase social support and income and reduce risky behavior and stress, all factors contributing to better health.	Janson et al. Hebert et al. Islami et al.

Place of Birth	Individual County Census	No	Development of esophageal adenocarcinoma appears to be strongly affected by ethnic factors, with populations resident at the west end of the Eurasian continent, such as Anglo-Celtics, being more prone to the condition.	Hongo et al.
Poverty	County Census	No	Previous cancer studies have shown a positive association between low SES (specifically poverty) and later cancer diagnosis. A majority of studies that examined the impact of poverty on stage of cancer diagnosis used registry that were then linked to census tract indicators of socioeconomic status. In most of these studies, adjustment for socioeconomic indicators explained the majority of the observed differences in stage at diagnosis.	Taplin et al. Bradley et al. Lannin et al. Roetzheim et al. Ayanian et al. Garmon et al.
Race	Individual	Yes	The average annual incidence rate for EAC for white men was double that of Hispanic men (4.2 versus 2.0/100,000/year). This rate was also four times higher than that seen in black, Asian/Pacific Islanders and Native Americans.	Kubo et al.
Year of Diagnosis	Individual	No	Despite efforts to increase screening of all risk individuals, no temporal improvement in stage at diagnosis profile for EAC has been seen.	Cooper et al. Wong et al.

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