

THE ROLE OF RACE/ETHNICITY IN THE EPIDEMIOLOGY OF ESOPHAGEAL CANCER

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ABSTRACT Esophageal cancer is known for its marked variation by geographic region, race, ethnicity, and gender. In the United States, incidence rates for African Americans are more than twice the rates for whites, and rates for whites exceed those for Hispanics, Asian Americans, and Native Americans. In addition, decreases in incidence of squamous cell carcinoma of the esophagus and increases in esophageal adenocarcinoma have been observed over the past several decades. This paper will explore the role of race/ethnicity in the epidemiology of esophageal cancer and the extent to which alcohol, tobacco, diet, and social class may contribute to racial/ethnic differences in incidence and mortality.

Key Words: alcohol, diet, esophageal cancer, ethnicity, race, tobacco

INTRODUCTION

Esophageal cancer is known for its marked variation by geographic region, race, ethnicity, and gender. In the United States, esophageal cancer accounts for only 1% of all diagnosed cancers; however, it is the seventh leading cause of death from cancer among men.¹ According to estimates provided by the American Cancer Society, approximately 9200 men and 2900 women are expected to die from esophageal cancer in the United States during 2000.¹ Although the two major histologic types of esophageal cancer, squamous cell carcinoma of the esophagus (SCE) and adenocarcinoma of the esophagus (ACE), share a poor prognosis, they have rather distinct epidemiologic profiles. This paper will review the descriptive patterns of both tumor types and the major risk or protective factors (alcohol, tobacco, diet, and social class). It will also explore the role of race/ethnicity in lifestyle practices and its possible impact on rates of esophageal cancer.

MORTALITY PATTERNS IN THE UNITED STATES

Based on data from the National Center for Health Statistics, mortality rates for esophageal cancer almost doubled among nonwhites (ie, African Americans, Asian Americans, Pacific Islanders, American Indians,

Alaskan Natives) between 1950 and 1984, reaching a high of 14.1/100,000 among nonwhite men and 3.6/100,000 among nonwhite women (Figure 1). However, since 1985 there has been a steady decrease, with rates of nonwhite men and women falling to 9.8/100,000 and 2.5/100,000, respectively, in 1995–1996. Mortality rates among whites changed little during the time period 1950–1984, but a striking increase in rates among men occurred during the period 1985–1996. Mortality rates of white men and women in 1995–1996 were 5.9/100,000 and 1.3/100,000, respectively. Rates specific for African Americans, available since the early 1970s, are higher than rates for all nonwhites combined. In 1995–1996, mortality rates for African American men and women were 12.3/100,000 and 3.1/100,000, respectively.

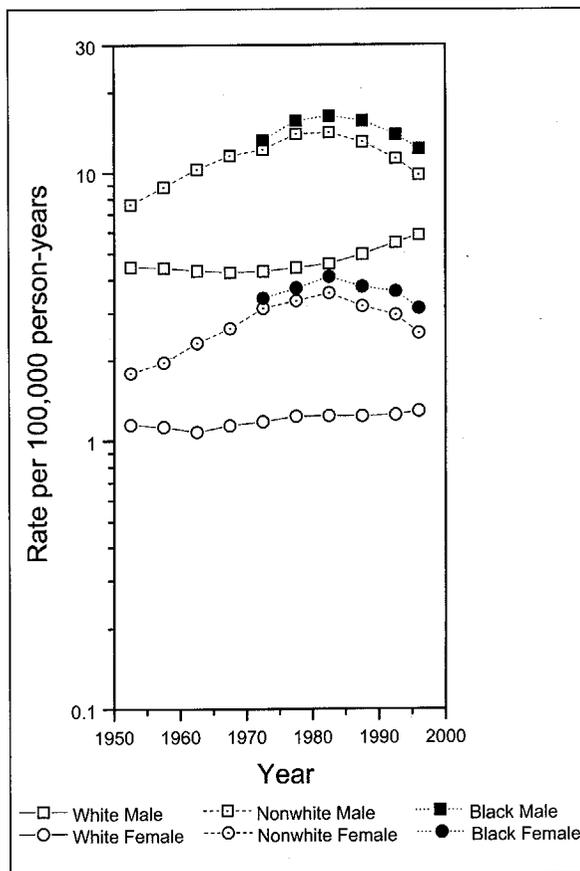


Figure 1
Trends in esophageal cancer mortality rates (per 100,000 person-years, age-standardized to the 1970 United States population) in the United States by race and sex, 1950–1996. Data from SEER, National Cancer Institute.

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INCIDENCE PATTERNS IN THE UNITED STATES

Because of the relatively unfavorable survival (the 5-year relative survival rates, 1989–1995, were 13.3% and 8.9% for whites and African Americans, respectively²), incidence and mortality patterns for esophageal cancer are quite similar. Based on data from the National Cancer Institute's Surveillance Epidemiology and End Results (SEER) Program,³ the overall rates for esophageal cancer among males and females combined were more than two times higher among African Americans (8.2/100,000) than whites (3.6/100,000) (Table 1). Rates among Hispanics, Asian/Pacific Islanders, and American Indians were lower than those among whites, although based on small numbers.

Presented in Figure 2 are the age-adjusted incidence rates of esophageal cancer, in total and by histologic type, among whites and African Americans in nine SEER registries. Detailed data from the SEER program are currently available only for whites and African Americans. Rates of esophageal cancer among African American men peaked at 19.9/100,000 in 1985–1987 and then began a marked decline, dropping to 13.3/100,000 in 1994–1996, whereas rates among white men increased steadily during the time period 1976–1996, with rates approaching 6.1/100,000 in 1994–1996. Rates among white women changed little, but declined among African American women after the mid-1980s. The dramatic decrease in total esophageal

Table 1
Age-Adjusted Esophageal Cancer SEER Incidence Rates*, 1990–1996, by Race/Ethnicity and Gender^a

| Race/ethnicity | Rate per 100,000 Persons | | |
|------------------------|--------------------------|-------|---------|
| | Total | Males | Females |
| All races | 3.8 | 6.3 | 1.8 |
| African American | 8.2 | 13.5 | 4.2 |
| White | 3.6 | 5.8 | 1.7 |
| Hispanic | 2.4 | 4.4 | — |
| Asian/Pacific Islander | 2.5 | 4.5 | 0.8 |
| American Indian | 1.3 | 2.5 | 0.4 |

*Rates per 100,000 person-years, age-adjusted using 1970 U.S. standard.

^aSEER, National Cancer Institute. Based on data from population-based registries in Connecticut, New Mexico, Utah, Iowa, Hawaii, Atlanta, Detroit, Seattle-Puget Sound, and San Francisco-Oakland.

cancer rates of African American males was driven by the concurrent drop in rates for SCE. Indeed, the SCE rate decreased after 1987 for all race-gender groups. Among white males, the incidence of ACE rose from 0.76/100,000 in 1976–1978 to 3.6/100,000 in 1994–1996, an increase of more than 350%. With the decrease in SCE rates and the increase in ACE rates, rates of ACE among white men have recently surpassed those of SCE. Rates of ACE among white fe-

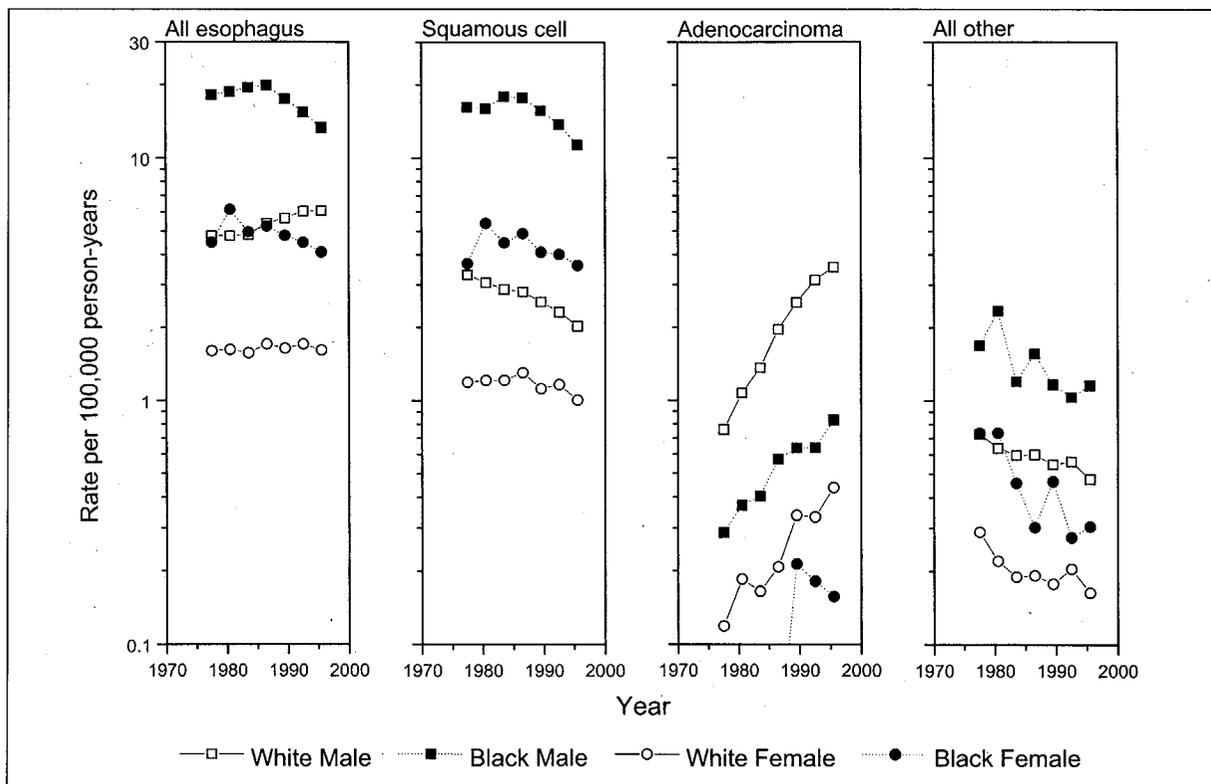


Figure 2
Trends in esophageal cancer incidence rates (per 100,000 person-years, age-standardized to the 1970 United States population) in nine SEER areas combined in the United States by cell type, race, and sex, 1976–1996. Data from SEER, National Cancer Institute.

Table 2
Case-control Studies of Squamous Cell Esophageal Cancer (SCE) in the United States with at least 10% Minority Representation that Assessed Risks for Alcohol, Tobacco, or Dietary Factors

| Study No. | Authors (Year Published) | Location | Number of Cases | % African American | % Female |
|-----------|--|----------------------|-----------------|--------------------|----------|
| 1 | Wynder, Bross (1961) ¹¹ | New York City, NY | 150 | 14 | 0 |
| 2 | Pottern, Morris, Blot, et al. (1981) ¹⁰ Ziegler, Morris, Blot, et al. (1981) ²⁹ | Washington, DC | 120 | 100 | 0 |
| 3 | Kaul, Nidiry, Charles-Marcel, et al. (1986) ⁵⁵ | Washington, DC | 23 | 100 | 52 |
| 4 | Brown, Blot, Schuman, et al. (1988) ⁸ | Coastal SC | 207 | 77 | 0 |
| 5 | Yu, Garabrant, Peters, et al. (1988) ⁹ | Los Angeles, CA | 275 | <33 ^a | 32 |
| 6 | Barone, Taioli, Hebert, Wynder (1992) ³¹ | 4 major cities | 133 | 24 | 0 |
| 7 | Brown, Hoover, Greenberg, et al. (1994) ²² Brown, Hoover, Gridley, et al. (1997) ²⁰ Brown, Swanson, Gridley, et al. (1998) ³⁰ | Atlanta, Detroit, NJ | 373 | 67 | 0 |
| 8 | Vaughan, Davis, Kristal, Thomas (1995) ¹⁷ | Western WA | 106 | 15 | 40 |
| 9 | Gammon, Schoenberg, Ahsan, et al. (1997) ²³ Chow, Blot, Vaughan, et al (1998) ⁴¹ | CT, NJ, WA | 589 | 22 | 20 |

^aAuthors did not present separate percentages for Hispanic whites, African Americans, and Asians.

males, although much lower than among white males, also increased more than 350%, from 0.12/100,000 in 1976–1978 to 0.44/100,000 in 1994–1996. In addition, ACE rates increased almost 200% among African American males, from 0.29/100,000 in 1976–1978 to 0.83/100,000 in 1994–1996; however, the rates of SCE remain considerably higher. Rates of ACE over the 21-year time period were more variable for African American females, since they were based on only 34 cases. Decreases in the reported incidence of esophageal cancers not attributed to SCE or ACE were also seen over the 21-year time period. Even if some cases of ACE were previously misclassified as other or undefined histology, the small decrease (0.25/100,000) from 1976–1978 to 1994–1996 in rates for esophageal cancer of other or undefined histology could not account for the large increase among white males (2.8/100,000) observed between these two periods.

DIFFERENCES IN RISK FACTOR PROFILES BY RACE/ETHNICITY

The estimated percentage distribution of the United States population by race/ethnicity for 1999 was white, 71.7%; African American, 12.2%; Hispanic, 11.6%; Asian American/Pacific Islander (Asian Americans), 3.8%; and American Indian/Alaskan Native (Native Americans), 0.7%.⁴ Despite this, only nine case-control studies of esophageal cancer conducted in the United States had minority participation of at least 10%. These studies are presented in Table 2. Two of these studies had only African American subjects (study numbers 2 and 3). The remaining seven studies had both African American and white subjects; however, only one study presents results for African Amer-

icans and whites separately (study number 7). There are no case-control studies that present results for other minorities separately, and only one study (study number 5) includes Asian Americans and Hispanics. However, 35 cases of esophageal cancer were included in a cohort study among Japanese American men from Hawaii that assessed risk factors for cancer of the upper aerodigestive tract.⁵ Also, no studies have been conducted among females alone, and limited data have been presented for females separate from males. Consequently, the etiologic data available for esophageal cancer in the United States for minorities and females are limited. Most of the epidemiology studies in the past have referred to SCE. Although attention has recently centered on ACE in view of the rising incidence rates of this tumor, the number of minorities included in these studies was minimal. Therefore, the discussion of risk factors will focus on SCE.

Alcohol

There are clear-cut epidemiologic data indicating that alcoholic beverages are a major cause of SCE in the United States.⁶ In a recent study among U.S. African Americans and whites, the percentage of SCE attributable to intake of more than one drink of alcohol a day was estimated at 77% for white men and 82% for African American men.⁷ Variability in risks by type of alcoholic beverage may reflect culturally or economically determined drinking habits. In most United States studies, the risk was highest among users of hard liquor.^{8–11} A study of esophageal cancer in a high-risk area of coastal South Carolina revealed an increased risk associated with use of moonshine (home-brewed) whiskey, particularly among African Americans,⁸ fur-

ther suggesting that regional variation in type of alcoholic beverage consumed may contribute to the excess risk in some geographic areas. Although alcohol is strongly related to risk of esophageal cancer, the components or mechanisms responsible for its carcinogenicity have not been identified. Alcohol itself may enhance cancer development by acting as a chronic irritant, by enhancing susceptibility to tobacco and other carcinogens, or by promoting dietary deficiencies.^{12,13} A recent study from Japan suggests that acetaldehyde, a metabolite of alcohol and a recognized animal carcinogen, may play a critical role in the mechanism by which alcohol causes esophageal cancer.¹⁴ In this study, a significantly higher frequency of the mutant acetaldehyde dehydrogenase 2 (ALDH2*2) allele was found among cancer patients than among controls with similar levels of alcohol consumption,¹⁴ thus blocking the metabolism of acetaldehyde to acetate. While several case-control studies have suggested an association between alcohol intake and risk of ACE, the risks are much lower than for SCE.¹⁵⁻¹⁷

In the United States, there has been an overall decline in alcohol use over the past several years caused by higher rates of abstinence among African Americans and Hispanics and lower rates of heavy drinking among whites.¹⁸ This decline in alcohol consumption may explain part of the recent decreases in rates of SCE. In addition, Asian Americans tend to have lower rates of drinking than the general population, whereas Native Americans tend to have higher.¹⁹ Prevalence of use and frequency of heavy drinking do not consistently explain the observed racial/ethnic variability in esophageal cancer incidence rates.

Tobacco

Tobacco use, regardless of form, is a major risk factor for SCE in most United States populations.^{8,9,16,17,20} The percentage of SCE attributable to smoking cigarettes, cigars, or pipes for 6 months or longer has recently been estimated at 65% for white men and 57% for African American men.⁷ A number of known or suspected carcinogens have been identified in tobacco smoke condensate, but the specific agents responsible for esophageal cancer and mechanisms of action are unclear.²¹ Most studies evaluating the effect of quitting smoking observed a 50% reduction in risk among ex-smokers compared to current smokers along with an inverse effect with time since stopped smoking.^{8,9,16,22} Cigarette smoking is also a significant risk factor for ACE, although it is a less potent risk factor for ACE than for SCE.^{15-17,23} Unlike findings for SCE, being an ex-smoker does not appear to attenuate risks, but instead the risks remain elevated for more than 30 years after smoking cessation.^{15,16,23,24}

Patterns of smoking are determined by multiple factors, including socioeconomic status, traditional habits,

and acculturation. Among adults, Native Americans have the highest prevalence of tobacco use and Asian Americans and Hispanics the lowest.²⁵ In addition, smoking prevalence is consistently higher among African Americans than whites, although the proportion of heavy smokers (20 cigarettes or more per day) has been consistently higher among whites.²⁶ Except for Native Americans, the prevalence of smoking has declined in all racial/ethnic groups since 1978.²⁵ Smoking prevalence is strongly inversely related to educational status, probably due to the greater decline among higher compared to lower educational groups, with older adults, men, whites, and college graduates leading other groups in their rates of smoking cessation.²⁶ It is likely that changes in smoking habits explain part of the overall decline in SCE. However, neither the prevalence of tobacco smoking nor the prevalence of heavy smoking fully accounts for the descriptive epidemiology of this tumor with regard to race/ethnicity.

Diet and Nutrition

A number of studies have indicated that dietary insufficiencies contribute to the varying incidence of SCE around the world.^{27,28} High-risk populations for this tumor are generally malnourished, and risk tends to increase as body mass index (BMI) decreases.^{8,16,29,30} In the United States, a number of case-control studies have suggested a protective effect of fruits and vegetables, especially those eaten raw, and of vitamin C from supplements and food sources, especially citrus fruits.^{8,29-32} Fruits and vegetables contain a variety of micronutrients and other dietary components with potential anticarcinogenic effects.³³ One of these micronutrients, Vitamin C, blocks the endogenous formation of N-nitroso compounds, which are thought to contribute to the incidence of esophageal cancer in some high-risk areas of the world.^{34,35}

Elevated risks associated with barbecued or fried meats have been noted in some case-control studies of esophageal cancer.^{8,9,29,36,37} Heterocyclic amines are potent mutagens and carcinogens formed during the cooking of red meat, with the highest mutagenic activity produced by pan frying, broiling, and barbecuing.³⁸ In addition, the higher esophageal cancer risks associated with red meat (especially cured or processed meat) suggest an effect of N-nitroso compounds or their precursors (nitrates and amines).^{34,36,39} These compounds may contribute to the development of esophageal tumors, particularly when accompanied by low intake of vitamins C and E, which interfere with the nitrosation process.³⁵

In contrast to findings for SCE indicating that high-risk populations are generally poorly nourished, risks for ACE tend to increase as body mass index (BMI) increases.^{14,15,38,39} The mechanism by which obesity affects the risk of ACE is unclear, although it may be linked to

the predisposition of obese individuals to gastroesophageal reflux disease (GERD).^{17,40} Whatever the process, it seems likely that obesity contributes to the upward trend in ACE rates because the prevalence of overweight adults increased 30% from 1976 to 1991.⁴² Various foods, food groups, and nutrients also have been related to risk of ACE, but most consistent is a protective effect of fruits and vegetables as well as fiber.^{16,40}

Dietary differences may account for at least some of the disparity in esophageal cancer incidence among racial and ethnic groups. Some of the excess in squamous cell carcinoma among African Americans may be due to their poor nutritional status and inadequate dietary patterns.⁴³ Diets of African Americans are generally high in dark yellow and dark green leafy vegetables (especially sweet potatoes and southern greens), pork, and fish. However, their cooking habits, which include the extensive use of frying and barbecuing meat and extended heating of vegetables in large amounts of water (which may leach out water-soluble nutrients), are less favorable.^{44,45} Compared with whites, African Americans consume more preserved and processed meats likely to be high in *N*-nitroso compounds and less raw fruits and vegetables, fiber, and dietary supplements.⁴⁵ African Americans also have poorer nutritional status and a greater percentage of African American males are underweight compared with white males.⁴³ Hispanic populations usually have diets that are high in fiber but low in calcium, iron, and vitamin C.⁴⁴ Traditional Asian-American diets are high in fish, fruits, and vegetables and low in meats and dairy.⁴⁴ Diets of Native Americans tend to be high in carbohydrates and low in meat and dairy products.⁴⁴

Disentangling the influence of dietary and nutritional factors from the potent effects of alcohol and tobacco is difficult. In particular, heavy consumption of alcoholic beverages can interfere with the consumption and utilization of a variety of nutrients, including vitamins A, C, D, the B vitamins, zinc, and protein.^{12,13} Also, since poor nutrition is a risk factor for esophageal cancer, it is conceivable that alcohol increases risk, in part, by reducing nutrient intake. Alcoholic beverages provide a share of the daily caloric needs and consequently reduce appetite but provide almost none of the daily requirements for micronutrients and protein. Smokers appear to have lower intake of several nutrients, including vitamin C, than do nonsmokers,^{46,47} even though the amount of vitamin C needed to achieve steady-state plasma concentrations is approximately 40% greater in smokers than nonsmokers.⁴⁸ In addition, tobacco products and some alcoholic beverages are sources of *N*-nitroso compounds that may elevate the risk of esophageal cancer.³⁴

Low Socioeconomic Status

The highest rates of SCE are generally found in areas of the world where the population is impover-

ished.⁴⁹ Within populations, the risk of esophageal cancer is greatest among those with the lowest socioeconomic status (SES).⁵⁰ In the United States, elevated risks of esophageal cancer have been associated with low levels of income and education and with low-status occupations.^{10,23,51-53} Low SES, whether measured by income, education, or occupation, is obviously a surrogate for a set of lifestyle and other environmental factors such as poor housing, unemployment, workplace hazards, limited access to medical care, stress, poor nutrition, and exposure to infectious agents.⁵¹ The percentage of SCE attributable to low annual income in the United States was recently estimated at 39% for white men and 69% for African American men.⁷ Low income has been related to excess risk of ACE in two United States studies, but the effect is less pronounced than for SCE.^{15,23}

According to data from the Current Population Survey, Bureau of the Census,⁵⁴ the median household incomes of African Americans and Hispanics have consistently been well below those of Asian Americans and whites. In 1997, the median household income of African Americans (\$25,050) was 6% lower than that of Hispanics (\$26,628), 56% lower than that of whites (\$38,972), and 81% lower than that of Asian Americans (\$45,249). A similar racial/ethnic differential has been observed for the poverty rate. Whites exhibit the lowest poverty rate of all racial/ethnic groups (approximately 10%), followed closely by Asian Americans (approximately 13%). The poverty rate of African Americans has remained near 30% over the past 25 years, while the rate for Hispanics has averaged slightly lower, around 27%. Differences in SES measured by income likely explain some of the excess esophageal cancer incidence in African Americans compared to whites. However, the role of SES is less clear for Asian Americans and Hispanics, who have similar rates of esophageal cancer but vastly different rates of poverty and household incomes.

SUMMARY

Use of tobacco, moderate/heavy alcohol ingestion, infrequent consumption of raw fruits and vegetables, and low income accounted for over 98% of the SCE rates among both African American and white men and for 99% of the excess incidence among African Americans over whites in a case-control study in three areas of the United States.⁷ Thus, it is likely that declines in the prevalence of smoking and drinking, especially among men, may have contributed to the downward incidence and mortality rate trends reported for SCE. In addition, it seems plausible that obesity contributes to the upward trend in ACE rates, and possibly to the downward trend in SCE rates, in view of the sharply increasing prevalence of individuals classified as overweight.

The higher incidence rates observed among African Americans following exposure to the same risk factors as whites may reflect a susceptibility state conditioned by genetic traits or by nutritional or other factors associated with social and cultural influences. Although similar estimates of attributable risk are not available for Hispanics, Asian Americans, or Native Americans, it is evident that lifestyle modifications, including a continued reduction in the use of alcoholic beverages and tobacco as well as improvements in diet (particularly increased consumption of raw fruits and vegetables) would markedly lower the incidence of SCE in all racial/ethnic groups.

ACKNOWLEDGMENTS

The author thanks Susan Devesa, PhD of NCI for preparation and presentation of descriptive data, John Lahey of IMS, Inc. for data tabulations and figure development, and B.J. Stone, PhD of NCI for editing.

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