



Epidemiologic trends in esophageal and gastric cancer in the United States

Linda Morris Brown, DrPH*, Susan S. Devesa, PhD

*Biostatistics Branch, Division of Cancer Epidemiology and Genetics,
National Cancer Institute, 6120 Executive Blvd, Room 8026,
MSC 7244, Bethesda, MD 20892-7244, USA*

Esophageal cancer is known for its marked variation by geographic region, race, ethnicity, and gender [1]. In the United States, esophageal cancer accounts for only 1% of all newly diagnosed cancers; however, it is the seventh leading cause of death from cancer among men [2]. Stomach cancer is the second leading cause of cancer deaths worldwide, although it ranks tenth among US women and eleventh among US men. According to estimates provided by the American Cancer Society, approximately 9500 men and 3000 women were expected to die from esophageal cancer and 7400 men and 5400 women from gastric cancer in the United States during 2001 [2].

Historically, esophageal and gastric cancers have been considered as two cancers. Esophageal cancers were predominately squamous cell carcinomas, stomach cancers were adenocarcinomas, tumors arose throughout each of the two organs, and rates for each were higher among African Americans than whites. Recent observations suggest that there may be at least three, if not four, distinct epidemiologic and potentially etiologic entities: squamous cell carcinoma of the esophagus (SCE), adenocarcinoma of the esophagus (ACE) (arising in the distal region), proximal stomach or gastric cardia adenocarcinoma (GCA), and noncardia gastric adenocarcinoma (NGA). This article will review the descriptive patterns of these four major tumor types of esophageal and gastric cancer. Because ACE and GCA comprised only a small fraction of esophageal and gastric cancers until recently, results from most epidemiologic studies of these tumors mainly reflect the risk factors for SCE and NGA. Recently, special attention has focused on ACE and GCA in view of the rising incidence rates of these tumors [3–5]. This article will also explore the role of race and ethnicity in lifestyle practices

* Corresponding author.

E-mail address: brownl@mail.nih.gov (L.M. Brown).

and its possible impact on rates of esophageal and gastric cancer in the United States.

Demographic features

Mortality patterns

Based on data from the National Center for Health Statistics and Bureau of the Census, mortality rates for esophageal cancer almost doubled among nonwhites (ie, African Americans, Asian Americans, Pacific Islanders, American Indians, Alaskan Natives) between 1950 through 1954 and 1980 through 1984, reaching a high of 14.1 per 100,000 among nonwhite men and 3.6 per 100,000 among nonwhite women (Fig. 1A). Since 1985, however, there have been steady decreases, with rates for nonwhite men and women falling to 9.3 per 100,000 and 2.5 per 100,000, respectively, in 1995 to 1998. Mortality rates among whites changed little during the time periods from 1950 to 1954 and 1980 to 1984, however, a striking increase in rates among men occurred during the period from 1985 to 1989 and 1995 to 1998. Mortality rates among white men and women in 1995 to 1998 were 5.9 per 100,000 and 1.3 per 100,000, respectively. Rates specifically for African Americans, available since the early 1970s, are higher than rates for all nonwhites combined. In 1995 to 1998, mortality rates for African American men and women were 11.6 per 100,000 and 3.1 per 100,000, respectively.

Mortality rates for stomach cancer show a strikingly different pattern. Between 1950 through 1954 and 1995 through 1998 rates declined steadily among all race-sex groups (Fig. 1B). Rates for nonwhite men and women were 30.1 per 100,000 and 14.5 per 100,000, respectively; in 1950 to 1954, dropping to 10.7 per 100,000 among nonwhite men and 5.2 per 100,000 among nonwhite women for 1995 to 1998. Rates for whites consistently were lower at each period than for nonwhites but also dropped from highs of 22.4 per 100,000 for white men and 12.1 per 100,000 for white women in the earliest period to lows of 5.0 per 100,000 and 2.3 per 100,000, respectively, in the most recent period. Rates for African Americans were similar to rates for all nonwhites combined. In 1995 to 1998, mortality rates for African American men and women were 11.3 per 100,000 and 5.1 per 100,000, respectively.

Survival patterns

Survival data based on follow-up of newly diagnosed cases since the 1970s are available from the Surveillance, Epidemiology, and End Results (SEER) program [6]. In this article, data are presented from nine SEER population-based cancer registries surveying approximately 10% of the US population. The 5-year relative survival rates for patients diagnosed during 1990 to 1997 were similar for SCE (12.5%), ACE (13.7%) and CGA (14.3%) but substantially higher for NGA (26.0%) because of the notably higher

Fig. 1. Trend years, age-stat 1950 to 1954 Health Statist

al and gastric cancer in the

Health Statistics and Bureau of the Census. Esophageal cancer almost doubled among African Americans, Pacific Islanders, and Alaska Natives from 1950 through 1954 and 1980 through 1984 among nonwhite men and women (Fig. 1A). Since 1985, however, rates have declined steadily among nonwhite men and women, respectively, in 1995 to 1998. During the time periods from 1950 to 1954 and 1980 to 1984, there was a marked increase in rates among whites, specifically for African American men (11.3 per 100,000, respectively). In 1995 to 1998, mortality rates for African American men were 11.3 per 100,000, respectively. A strikingly different pattern was seen for white men. In 1998 rates declined steadily from 5.9 per 100,000 in 1950 to 5.2 per 100,000 in 1998. Rates for whites consistently declined from high rates of 11.3 per 100,000 for white women in 1950 to 5.1 per 100,000 in 1998. Mortality rates for African Americans were similar to those for whites in 1998, mortality rates for African American men were 11.3 per 100,000 and 5.1 per 100,000, respectively.

diagnosed cases since the 1970s. In 1998, approximately 10% of the US patients diagnosed during 1995 to 1998 (3.7%) and CGA (14.3%) were of the notably higher

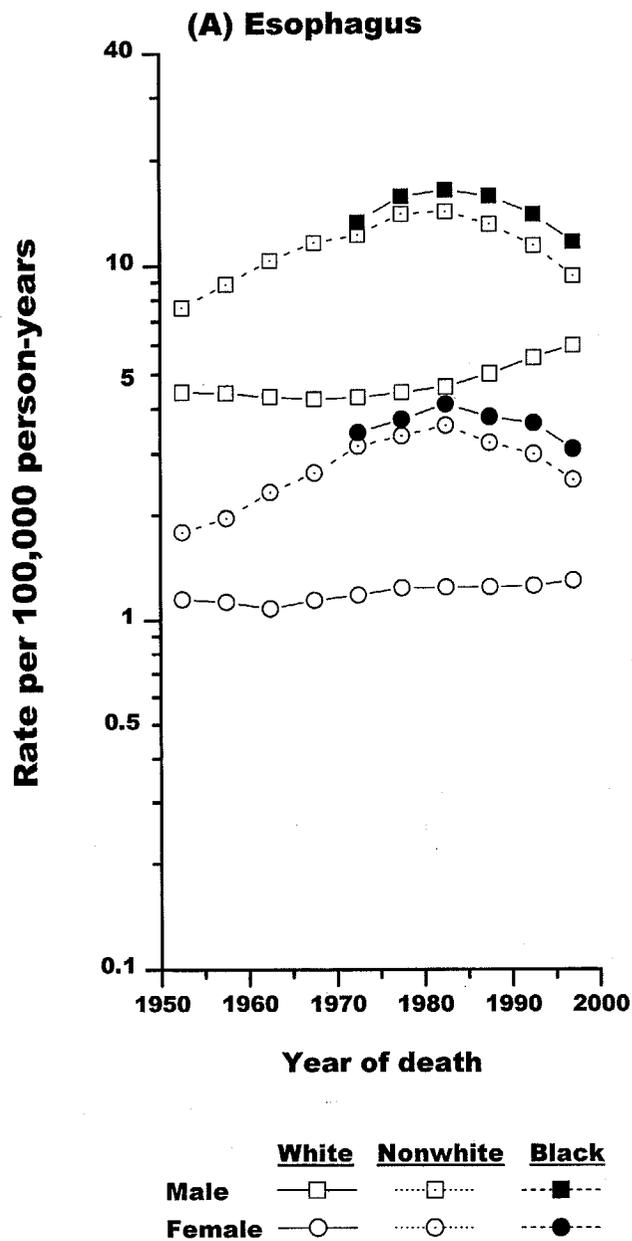


Fig. 1. Trends in esophageal (A) and gastric (B) cancer mortality rates (per 100,000 person-years, age-standardized to the 1970 US population) in the United States by race and gender, 1950 to 1954 through 1995 to 1998. (Based on unpublished data from the National Center for Health Statistics and the Bureau of the Census.)

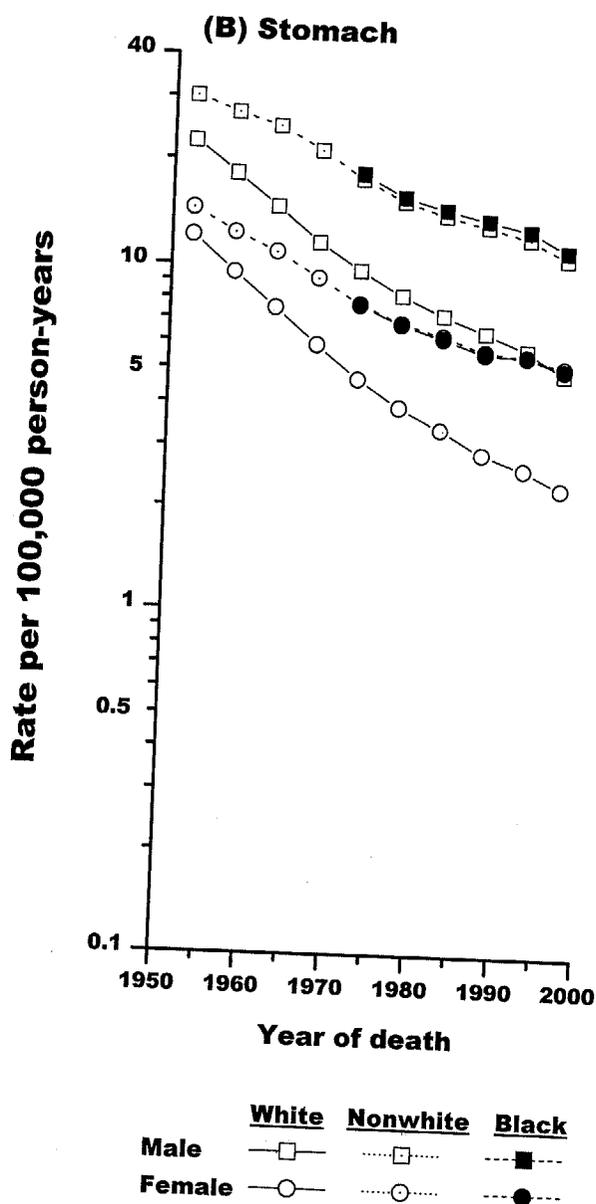


Fig. 1 (continued)

rates of survival for patients with localized (68.5%) and regional (24.6%) disease (Table 1). There is a strong decreasing gradient in patient survival with increasing extent of disease for all esophageal and gastric cancer types/sites, with patients with distant disease having uniformly poor survival. The stage distribution of SCE and ACE tumors is fairly evenly divided among the four

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Table 1
Esophageal and gastric cancer 5-year relative survival rates* by type/site and stage, and stage distribution percentage—1990-1997

Stage	SCE		ACE		GCA		NGA	
	Survival rate	Stage distribution						
All stages	12.5	100%	13.7	100%	14.3	100%	26.0	100%
Localized	20.4	29%	33.9	25%	40.5	19%	68.5	24%
Regional	13.2	26%	11.0	26%	13.6	33%	24.6	34%
Distant	3.0	20%	0.9	28%	2.3	33%	1.4	31%
Unstaged	10.7	25%	13.0	21%	12.8	16%	13.8	12%

* Rates are relative rates expressed as percentages.

Abbreviations: SCE, squamous cell esophageal cancer; ACE, adenocarcinoma of the esophagus; GCA, gastric cardia adenocarcinoma; NGA, noncardia gastric adenocarcinoma.

Based on unpublished data from Surveillance, Epidemiology, and End Results (SEER), National Cancer Institute, from nine population-based registries in Connecticut, New Mexico, Utah, Iowa, Hawaii, Atlanta, Detroit, Seattle-Puget Sound, and San Francisco-Oakland, as described in [6]. Rates are based on follow-up of patients through 1998.

extent-of-disease categories (localized, regional, distant, and unstaged), whereas for CGA and NCA, a higher percentage of tumors are regional or distant and a lower percentage are unstaged. Although survival rates among patients diagnosed with esophageal and gastric cancers are relatively poor, over the past two decades there have been dramatic improvements in the 5-year relative survival rates for SCE (167%), ACE (158%), and GCA (87%), and modest improvements for NCA (31%) (Table 2).

Incidence patterns

Data from nine SEER registries [6] were also used to generate age-adjusted incidence rates for total esophageal and gastric cancers and for the four types/sites (Figs. 2-4). Incidence rates for total esophageal cancer

Table 2
Esophageal and gastric cancer 5-year relative survival rates* by type/site by diagnosis year

Diagnosis year	SCE rate	ACE rate	GCA rate	NGA rate
1974-1979	4.6	5.3	7.9	20.3
1980-1985	7.7	7.8	10.9	21.2
1986-1991	9.6	11.1	12.9	24.9
1992-1997	12.3	13.7	14.8	26.5

* Rates are relative rates expressed as percentages.

Abbreviations: SCE, squamous cell esophageal cancer; ACE, adenocarcinoma of the esophagus; GCA, gastric cardia adenocarcinoma; NGA, noncardia gastric adenocarcinoma.

Based on unpublished data from Surveillance, Epidemiology, and End Results (SEER), National Cancer Institute, from nine population-based registries in Connecticut, New Mexico, Utah, Iowa, Hawaii, Atlanta, Detroit, Seattle-Puget Sound, and San Francisco-Oakland, as described in [6]. Rates are based on follow-up of patients through 1998.

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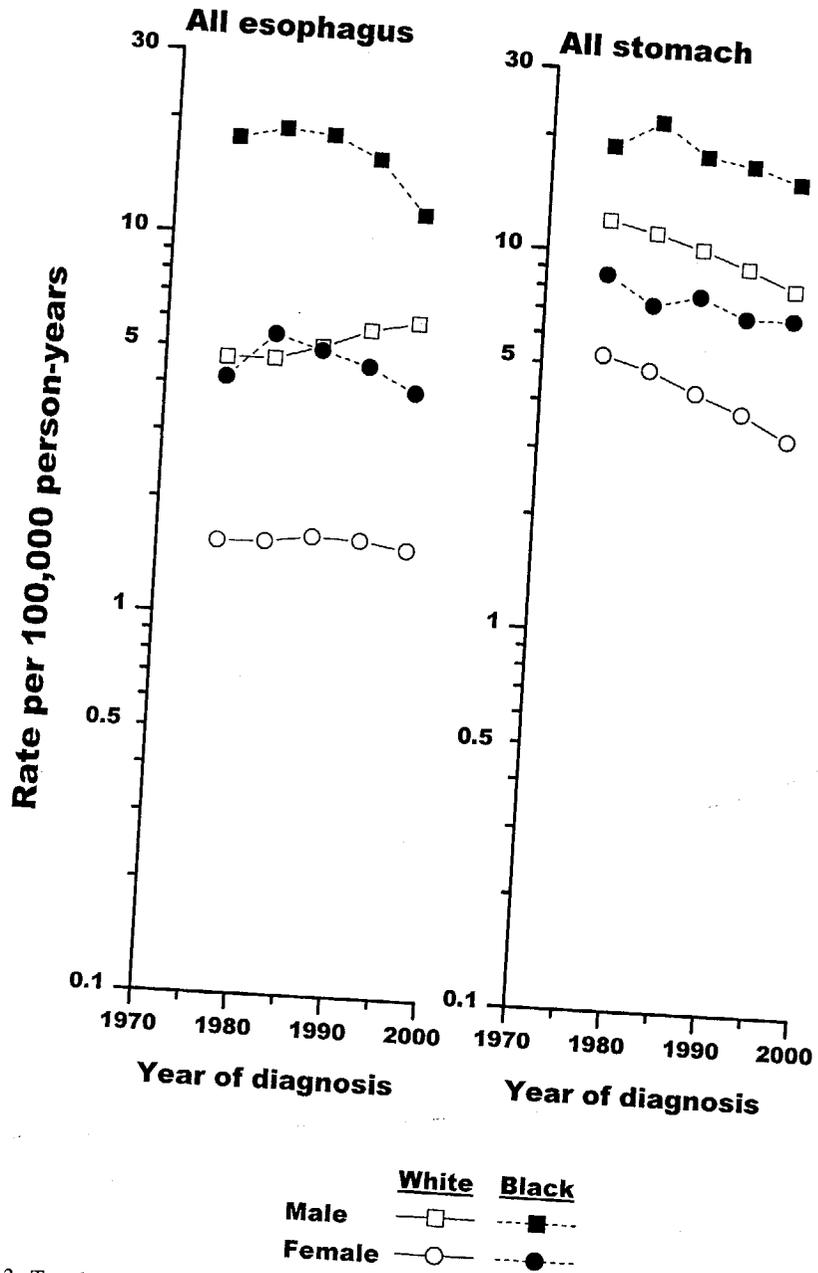


Fig. 2. Trends in esophageal and gastric cancer incidence rates (per 100,000 person-years, age-standardized to the 1970 US population) in nine SEER areas in the United States by race and gender from 1974 to 1978 through 1994 to 1998. (Based on unpublished data from Surveillance, Epidemiology, and End Results (SEER), National Cancer Institute, as described in [6].)

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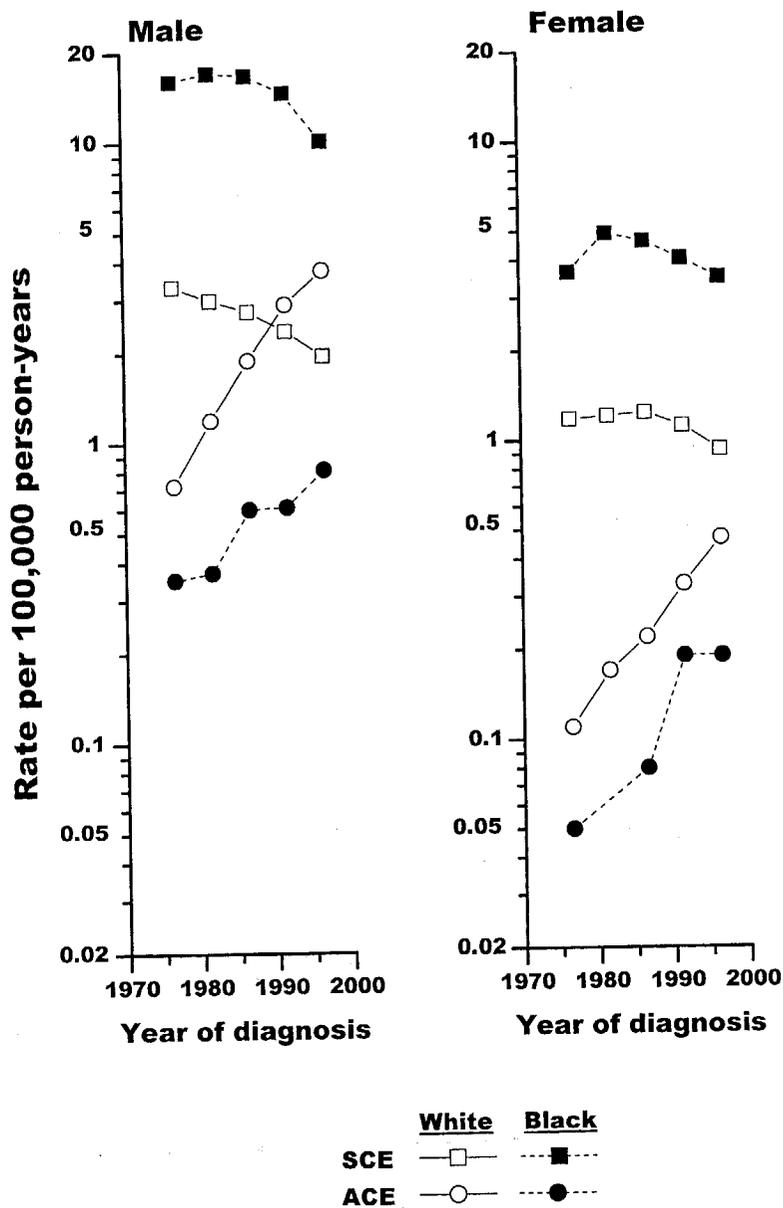


Fig. 3. Trends in esophageal cancer incidence rates (per 100,000 person-years, age-standardized to the 1970 US population) in nine SEER areas in the United States by gender, race, and cell type from 1974 to 1978 through 1994 to 1998. SCE, squamous cell esophageal cancer; ACE, adenocarcinoma of the esophagus. (Based on unpublished data from Surveillance, Epidemiology, and End Results (SEER), National Cancer Institute, as described in [6].)

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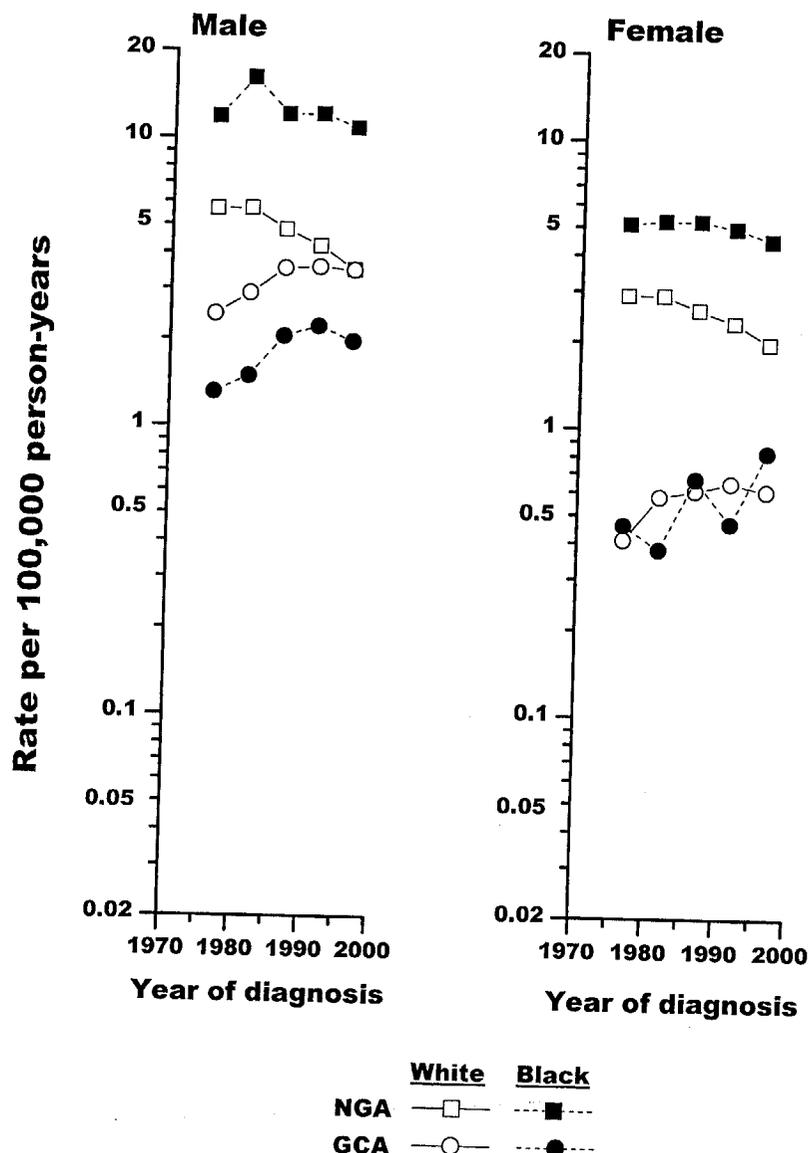
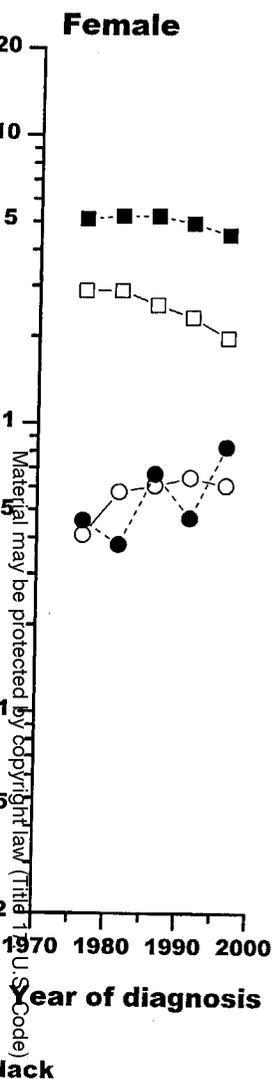


Fig. 4. Trends in gastric cancer incidence rates (per 100,000 person-years, age-standardized to the 1970 US population) in nine SEER areas in the United States by gender, race, and subsite from 1974 to 1978 through 1994 to 1998. GCA, gastric cardia adenocarcinoma; NGA, noncardia gastric adenocarcinoma. (Based on unpublished data from Surveillance, Epidemiology, and End Results (SEER), National Cancer Institute, as described in [6].)

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among African American men peaked at 19.1 per 100,000 in 1979 to 1983 and then began a marked decline, reaching 11.7 per 100,000 in 1994 to 1998 (Fig. 2). Rates among white men increased consistently from 1974 to 1978 through 1994 to 1998, with rates approaching 6.1 per 100,000 in 1994 to 1998. Rates among white women changed little over time, whereas rates among African American women have declined since the mid-1980s. Age-adjusted rates for total gastric cancer among African American men also peaked in 1979 to 1983 (22.1 per 100,000), before decreasing to 15.8 per 100,000 in 1994 to 1998 (Fig. 2). Rates among white men and women declined steadily, from highs of 12.0 and 5.3, respectively, per 100,000 in 1974 to 1978 to lows of 8.3 and 3.3, respectively per 100,000 in 1994 to 1998. Rates among African American women generally declined, but the pattern was less striking.

The dramatic decrease in total esophageal cancer rates of African American men was driven by the concurrent drop in rates for SCE (Fig. 3). Indeed, the SCE rate decreased after 1988 for all race-gender groups. Among white males, the incidence of ACE rose from 0.72 per 100,000 in 1974 to 1978 to 3.7 per 100,000 in 1994 to 1998, an increase of more than 400%. With the decrease in SCE and the increase in ACE, rates of ACE among white men surpassed those of SCE after 1988. Rates of ACE among white females, although much lower than those among white males, increased more than 300%, from 0.11 per 100,000 in 1974 to 1978 to 0.47 per 100,000 in 1994 to 1998. In addition, ACE rates increased more than 100% among African American males, from 0.35 per 100,000 in 1974 to 1978 to 0.81 per 100,000 in 1994 to 1998; however, the rates of SCE remain considerably higher. Rates of ACE also showed an upward trend for African American women during this period; however, the rates remain low at present.

The decline in the total gastric cancer rates among whites primarily reflects the steady downward trends in incidence of NGA among both men (from 5.7/100,000 in 1974-78 to 3.5 per 100,000 in 1994-98) and women (from 2.9 per 100,000 in 1974-78 to 2.0 per 100,000 in 1994-98) (Fig. 4). NGA time trends for African Americans also resemble total gastric cancer incidence patterns, with rates for men peaking at 16.1 per 100,000 in 1979 to 1983 and declining to 10.9 per 100,000 in 1994 to 1998 and rates for women declining modestly. Similar to ACE, rates of GCA increased from the 1974 to 1978 period to the 1984 to 1988 period, although to a lesser extent. GCA rates among white men stabilized at 3.5 per 100,000 in 1989 to 1993, whereas rates for African American men peaked at 2.2 per 100,000 in 1989 to 1993 before falling slightly, to 2.0 per 100,000 in 1994 to 1998. With the decrease in NGA rates and the increase, then stabilization, in GCA rates, rates of GCA and NGA among white men were similar (3.5 per 100,000) in 1994 to 1998. GCA rates for white women also peaked in 1989 to 1993 and declined in 1994 to 1998, whereas rates among African American women rose inconsistently over time.

person-years, age-standardized to rates by gender, race, and subsite cardia adenocarcinoma; NGA, from Surveillance, Epidemiology, and in [6].)

Data from 11 SEER registries were available to calculate type/site-specific incidence rates by race, ethnicity, and gender for 1992 to 1998 (Table 3) [6]. Among males, the incidence of SCE among African Americans (10.1 per 100,000) was more than five times the rate among whites (2.0 per 100,000). Rates among Asian Americans were higher than those among whites (3.5 per 100,000), whereas rates among Native Americans and Hispanics were similar. Incidence rates for ACE among males showed a different pattern. The rate among whites (3.4 per 100,000) was more than four times the rates among African Americans (0.8 per 100,000), Asian Americans (0.7 per 100,000), and Native Americans (0.6 per 100,000) and almost twice the rate among Hispanics (1.9 per 100,000). Rates of GCA were almost twice as high in white men (3.5 per 100,000) as in African American men (1.9 per 100,000). Rates among Asian American (2.3 per 100,000) and Hispanic (2.4 per 100,000) men were slightly higher than rates among African American men, and rates among Native American/men (1.1 per 100,000) were lowest. Rates of NGA among African American (10.7 per 100,000) and Hispanic (9.6 per 100,000) men were more than two times those among white (4.1 per 100,000) or Native American (4.3 per 100,000) men, the highest rates were observed among Asian American/men (14.1 per 100,000). Among females, rates of SCE were one half to one third those among males, and rates of ACE were extremely low (less than 0.5 per 100,000) in all ethnic groups. Rates of NGA among women were about half of those among men, but the ethnic patterns were similar. None of the GCA rates among women exceeded 0.7 per 100,000.

Risk factor profiles and trends by race and ethnicity

The remainder of this article will explore whether the established or suspected risk or protective factors for SCE, ACE, GCA, and NGA listed in Table 4 can explain the trends in incidence and mortality and the racial and ethnic patterns observed.

Alcohol use

Although consumption of alcoholic beverages is strongly related to risk of SCE in the United States [7-11], the mechanisms responsible for the carcinogenicity of alcohol 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].

In a recent study among US 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 [14]. In the United States, use of alcoholic beverages has not been found to be consistently related to the risk of ACE, GCA, or NGA [8,10,15-17].

calculate type/site-specific rates from 1992 to 1998 (Table 3) [6]. Rates among African Americans (10.1 per 100,000) were higher than those among Caucasians and Hispanics. Males showed a difference in rates (10.0) was more than four times that of whites (per 100,000), Asian Americans (per 100,000) and almost twice that of African Americans. Rates of GCA were higher in African American men (2.3 per 100,000) and higher than rates among African American/men (1.1 per 100,000) and African American (10.7 per 100,000) were more than two times that of African American/men (4.3 per 100,000) and African American/men (14.1 per 100,000) were about half that of African American/men (less than 0.5 per 100,000). None of the GCA

the established or sustained, and NGA listed in Table 3 and the racial and

strongly related to risk factors responsible for the disease. Alcohol itself may be an irritant, by enhancing the risk of cancer by promoting dietary

and whites, the percentage of alcohol a day. For African American men, the percentage has not been found to be significantly different, or NGA [8,10,15-17].

Table 3 Age-adjusted esophageal and gastric cancer incidence rates by type/site* 1992-1998, race/ethnicity, and gender

Race/ethnicity	Males												Females											
	SCE		ACE		GCA		NGA		SCE		ACE		GCA		NGA									
	n	Rate	n	Rate	n	Rate	n	Rate	n	Rate	n	Rate	n	Rate	n	Rate								
White	1871	2.0	3333	3.4	3397	3.5	4127	4.1	1261	1.0	571	0.4	882	0.7	3336	2.3								
Hispanic	220	2.2	193	1.9	253	2.4	974	9.6	62	0.5	33	0.3	94	0.7	758	5.3								
NonHispanic	1645	1.9	3132	3.6	3135	3.6	3144	3.5	1195	1.0	538	0.4	788	0.7	2569	1.9								
African American	936	10.1	69	0.8	177	1.9	979	10.7	423	3.5	26	0.2	84	0.6	643	4.7								
Asian American	368	3.5	74	0.7	251	2.3	1506	14.1	92	0.7	12	0.1	99	0.7	1092	8.0								
Native American	11	1.7	4	0.6	10	1.1	32	4.3	5	0.6	0	0.0	3	0.4	28	3.1								

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

Abbreviations: SCE, squamous cell esophageal cancer; ACE, adenocarcinoma of the esophagus; GCA, gastric cardia adenocarcinoma; NGA, noncardia gastric adenocarcinoma.

Based on unpublished data from Surveillance, Epidemiology, and End Results (SEER) Program, National Cancer Institute, from 11 SEER population-based registries (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey and Los Angeles, as described in [6]).

Table 4
Risk and protective factors for esophageal and gastric cancers in the United States by type/site

Factors	SCE	ACE	GCA	NGA
Alcohol use	+++	0 ^a	0	0
Tobacco use	+++	++	++	++
Diet (fruit and vegetable intake)	--	--	--	--
Obesity	--	+++	++	0
Low socioeconomic status	++	+	+	+
Gastroesophageal reflux disease	0	+++	++	0
<i>Helicobacter pylori</i> prevalence	0	--	--	+++

Risk factor: +++ (strong and well documented); ++ (medium); + (weak/not well documented). Protective factor: --- (strong and well documented); -- (medium); - (weak/not well documented).

^a No relationship: 0.

Abbreviations: SCE, squamous cell esophageal cancer; ACE, adenocarcinoma of the esophagus; GCA, gastric cardia adenocarcinoma; NGA, noncardia gastric adenocarcinoma.

Based on data from the National Institute on Alcohol Abuse and Alcoholism [18], per capita alcohol consumption peaked in the United States in 1980 to 1981 (Fig. 5) and has declined recently because of higher rates of abstinence among African Americans and Hispanics and lower rates of heavy drinking among whites [19]. In addition, Asian Americans tend to have lower rates of drinking than the general population, and Native Americans tend to have higher rates [20]. Recent declines in SCE among men have mirrored decreases in liquor consumption, which peaked around 1969 (Fig. 5), and has been the form of alcoholic beverage most closely linked to SCE risk in the United States [21–24]. This decline in alcohol consumption, especially use of liquor, may explain part of the recent decreases in rates of SCE. Prevalence of use and frequency of heavy drinking do not consistently explain the observed racial and ethnic variability in SCE.

Tobacco use

Although several known or suspected carcinogens have been identified in tobacco smoke condensate, the specific agents responsible for esophageal and gastric cancer and mechanisms of action are unclear [25]. Regardless of form, tobacco use is a major risk factor for SCE in most US populations [10,14,21,24,26]. The percentage of SCE caused by 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 [14]. Most studies evaluating the effect of quitting smoking have noted a 50% reduction in risk among ex-smokers compared with current smokers, along with an inverse effect with time since cessation of smoking [10,21,24,26].

Although a less potent factor than for SCE, cigarette smoking is also a significant risk factor for ACE, GCA, and NGA, with a doubling of risk for

Fig. 5. Trends of beverage consumption (gallons) per capita in the United States, 1960–1995. Data Reference: Dufour MC, U.S. Alcoholism, Di

ancers in the United States by type/site

ACE	GCA	NGA
a	0	0
++	++	++
-	--	--
+++	++	0
+	+	+
+++	++	0
-	--	+++

++ (medium); + (weak/not well mented); -- (medium); - (weak/not

er; ACE, adenocarcinoma of the oncardia gastric adenocarcinoma.

Material Alcohol Abuse and Alco- and in the United States in because of higher rates of panics and lower rates of , Asian Americans tend to population, and Native Amer- cines in SCE among men which peaked around 1969 erage most closely linked to ngs in alcohol consumption, recent decreases in rates of y drinking do not consi- ability in SCE.

gs have been identified in responsible for esophageal re unclear [25]. Regardless CE in most US populations d by smoking cigarettes, tly been estimated at 65% en [14]. Most studies eval- a 50% reduction in risk ers, along with an inverse ,24,26].

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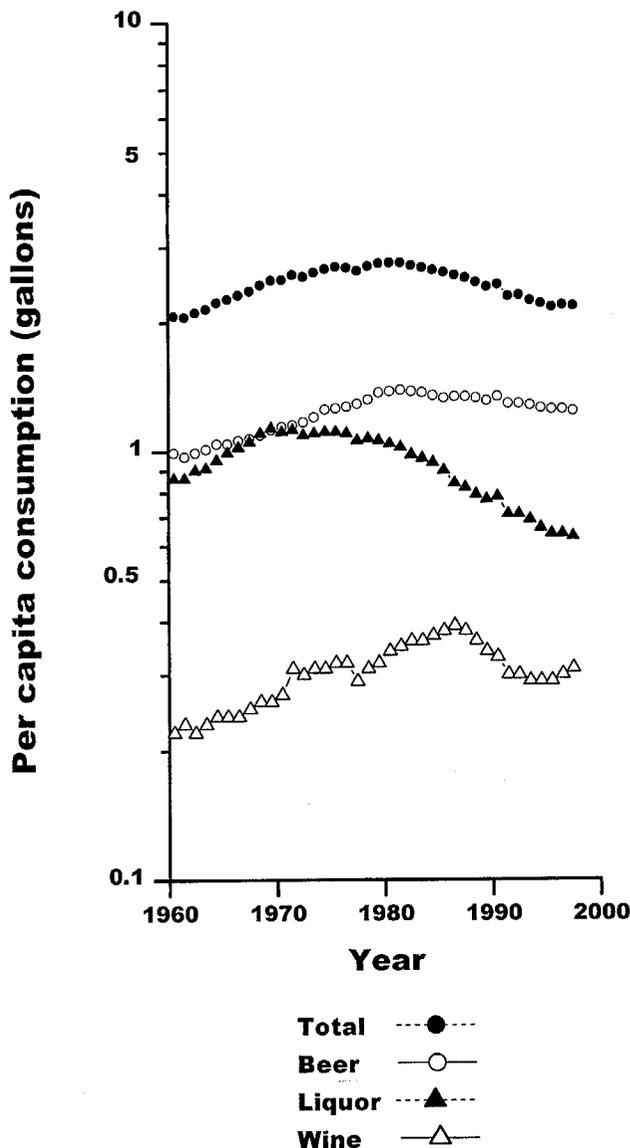


Fig. 5. Trends in per capita ethanol consumption (in gallons) in the United States by type of beverage consumed from 1960 to 1997. (Data from Stinson FS, Lane JD, Williams GD, Dufour MC. U.S. Apparent consumption of alcoholic beverages. U.S. Alcohol Epidemiologic Data Reference Manual. 3rd edition. Rockville (MD): National Institute on Alcohol Abuse and Alcoholism, Division of Biometry and Epidemiology; 1997. p. 1.)

those who smoke more than one pack a day [8,10,11,15–17,27,28]. A recent US study found that 41% of ACE and GCA is caused by cigarette smoking [16]. Unlike findings for SCE, being an ex-smoker does not appear to attenuate risks for ACE and, instead, the risks remain high for more than 30 years after smoking cessation [8,10,16].

The factors that determine smoking patterns include socioeconomic status (SES), traditional habits, and acculturation. Among adults during 1998, Native Americans had the highest prevalence of tobacco use (40%), and Asian Americans (14%) and Hispanics (19%) the lowest [29]. Although smoking prevalence among adults declined 40% between 1965 and 1998, it has remained consistently higher among African American men than among white men (Fig. 6; based on data from the National Center for Health Statistics [30]). Recently, smoking prevalence has been strongly inversely related to educational status, probably because of the greater decline among higher compared with lower educational groups, with older adults, men, whites, and college graduates leading other groups in their rates of smoking cessation [31,32]. Although it is likely that changes in smoking habits partly explain the overall decline in SCE and NGA, they do not fully account for the descriptive epidemiology of these tumors with regard to race and ethnicity. Because being an ex-smoker does not appear to attenuate risks for ACE, it is possible that smoking may affect an early stage of carcinogenesis for this cancer and thus may still contribute to the rising incidence of ACE in the face of recent downward trends in smoking prevalence in the United States.

Diet and nutrition

Although consumption of various foods, food groups, and nutrients has been related to risk of all four tumor types, the most consistent finding has been the protective effect of fruits and vegetables, especially those eaten raw [10,21,27,28,33–39]. Fruits and vegetables contain various micronutrients and dietary components with potential anticarcinogenic effects [40]. One of these micronutrients, Vitamin C, blocks the endogenous formation of N-nitroso compounds, which are linked to risk of esophageal and gastric cancers [1,27].

Dietary differences may account for at least some of the disparity in esophageal cancer incidence among racial and ethnic groups. Some of the higher incidence in squamous cell carcinoma among African Americans may be caused by their poor nutritional status and inadequate dietary patterns [41]. Diets of African Americans are generally high in dark yellow and dark green leafy vegetables (especially sweet potatoes and southern greens), pork, and fish [41]. 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, however [42]. Compared with whites, African Americans consume more preserved and processed meats, which are likely to be high in N-nitroso compounds, and less raw fruits and vegetables, fiber, and dietary supplements

Fig. 6. Trends in smoking prevalence by race and gender in the United States.

10,11,15-17,27,28]. A recent caused by cigarette smoking does not appear to remain high for more than

include socioeconomic sta- Among adults during 1998, of tobacco use (40%), and the lowest [29]. Although between 1965 and 1998, it American men than among International Center for Health has been strongly inversely of the greater decline among s, with older adults, men, os, in their rates of smoking es, in smoking habits partly do not fully account for regard to race and ethnic- O attenuate risks for ACE, e of carcinogenesis for this incidence of ACE in the leace in the United States.

groups, and nutrients has most consistent finding has especially those eaten raw atious micronutrients and c effects [40]. One of these s formation of N-nitroso and gastric cancers [1,27]. some of the disparity in mic groups. Some of the g African Americans may dequate dietary patterns in dark yellow and dark d southern greens), pork, ne extensive use of frying ables in large amounts of nts), are less favorable, icans consume more pre- high in N-nitroso com- and dietary supplements

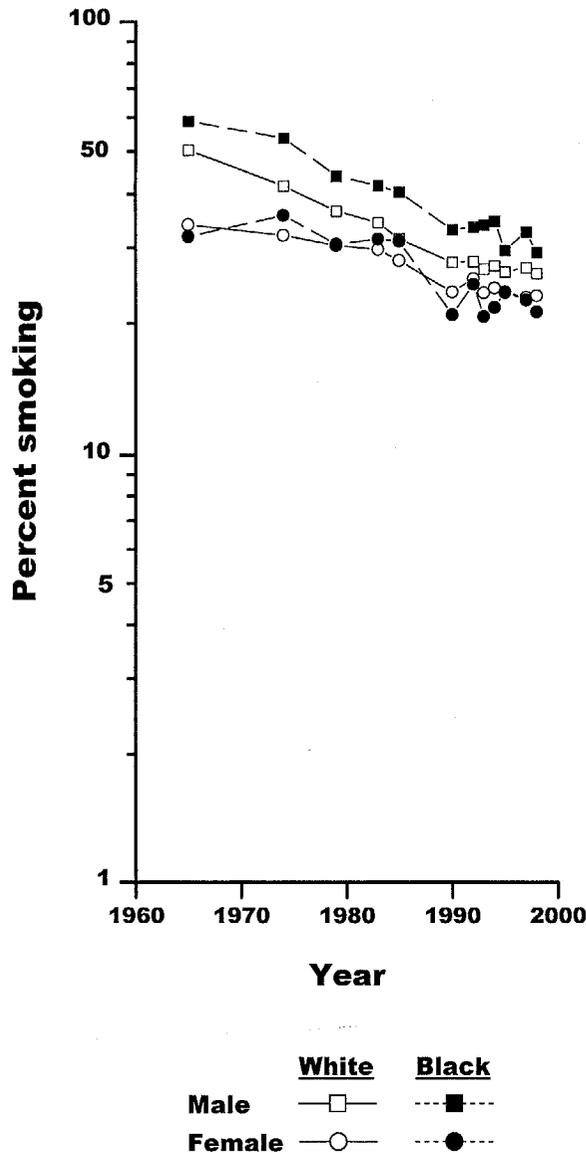


Fig. 6. Trends in percent of US adult (18 years of age and over) current cigarette smokers by race and gender from 1965 to 1998. (Data from National Center for Health Statistics. Health, United States, 2000 with Adolescent Health Chartbook. Hyattsville (MD); NCHS 2000.)

[42]. However, increases in the per capita consumption of fresh fruits (31%) and vegetables (24%) from the early 1970s to the late 1990s may contribute to the downward trends of SCE and the NGA in both whites and African Americans [43].

It is difficult to disentangle the influence of dietary and nutritional factors from the potent effects of alcohol and tobacco. In particular, heavy consumption of alcoholic beverages can interfere with the consumption and use of a variety of nutrients, including vitamins A, C, and D, the B vitamins, zinc, and protein [12,13], and smokers appear to have lower intake of several nutrients, including vitamin C, than do nonsmokers [44].

Obesity

In contrast to findings for SCE (which indicate that high-risk populations are generally poorly nourished and that risk tends to increase as body mass index [BMI] decreases [10,21,35,39]), risks for ACE tend to increase as BMI increases, with subjects in the upper quartile of BMI having three to seven times the risk of subjects in the lowest quartile [10,11,34,45]. Although the mechanism by which obesity affects the risk of ACE is unclear, it may be linked to the predisposition of obese individuals to gastroesophageal reflux disease (GERD) [11,34]. Risk of GCA was also increased for excess weight, but to a lesser extent than for ACE; and no association was seen for NGA [45,46].

Overall, the prevalence of obese adults (BMI \geq 30) increased notably from 12.8% in 1960 to 1962 to 22.6% in 1988 to 1994 [30]. Similar patterns of increasing prevalence were observed for each of the four race-gender groups (Fig. 7; based on data from the National Center for Health Statistics [30]). Therefore, it seems likely that obesity has contributed to the upward trend in ACE and GCA rates. Because African American women are the most obese and white men the least, obesity does not explain the gender and racial patterns observed for ACE and GCA. The pattern of increasing obesity over the past several decades does not appear to be related to recent reductions in SCE and GCA.

Socioeconomic status (SES)

Low SES—whether measured by income, education, or occupation—is a surrogate for a set of lifestyle and other environmental factors (eg, poor housing, unemployment, workplace hazards, limited access to medical care, stress, poor nutrition, and exposure to infectious agents) [47]. In the United States, elevated risks of esophageal cancer have been associated with low levels of income and education and with low-status occupations [16,23,47,48]. The percentage of SCE associated with low annual income in the United States was recently estimated at 39% for white men and 69% for African American men [14]. Low income and education have also been related to excess risk of ACE, GCA, and NGA; however, the effects are less pronounced than for SCE [8,16,17,27].

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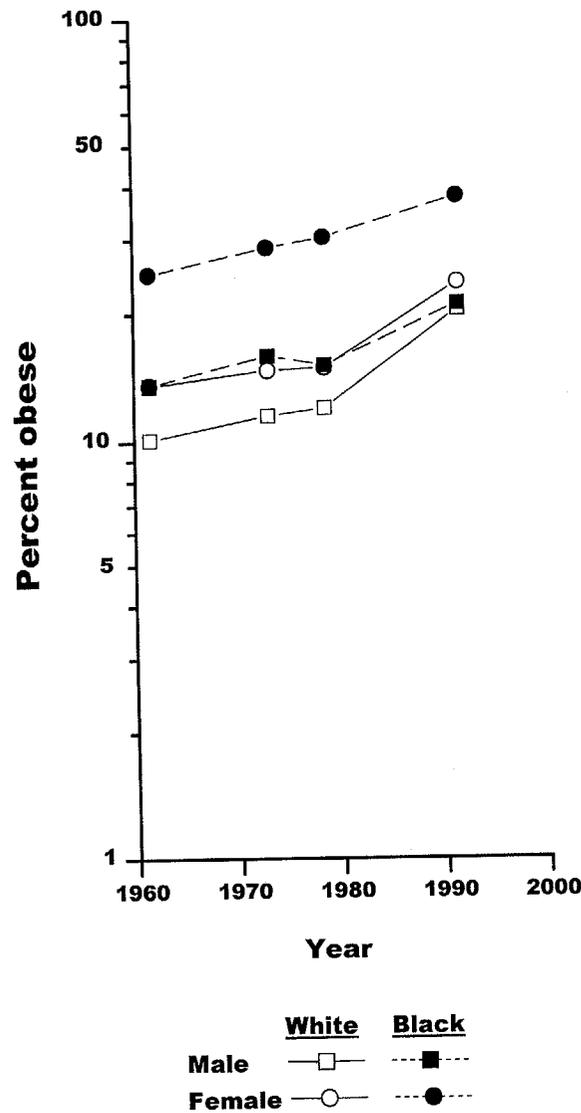


Fig. 7. Trends in prevalence of obesity in US adults (20 years of age and over) by race and gender from 1960 to 1962 and 1988 to 1994. (Data from National Center for Health Statistics. Health, United States, 2000 with Adolescent Health Chartbook. Hyattsville (MD); NCHS 2000.)

Based on data from the Current Population Survey published by the Bureau of the Census [49], whites have the lowest poverty rate of all racial and 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, and the rate for Hispanics has

averaged approximately 27%. Differences in SES probably explain some of the excess incidence of SCE and NGA in African Americans compared with whites, but not the excess incidence of ACE and GCA among whites. The role of SES in these tumors is even less clear for Asian Americans and Hispanics.

Gastroesophageal reflux disease (GERD)

GERD predisposes the esophagus to the development of metaplastic columnar epithelium, which is characteristic of Barrett's esophagus—the precursor lesion of ACE and GCA [50,51]. Barrett's esophagus is found in almost all patients with ACE and approximately one half of the patients with GCA [52]. Significant twofold or greater risks of ACE and GCA have been associated with the presence of GERD symptoms, with risk increasing with increasing frequency of symptoms [53,54]. No clear relationship has been shown between medications to treat this condition and ACE or GCA risk [53,54]. No association between GERD and risk of SCE or NGA has been reported [54].

According to discharge diagnoses calculated from a database obtained from the US Veterans Administration, the age-adjusted incidence rate of reflux disease per 1000 person years increased 250% in African American men, from 0.6 in 1970 to 1974 to 2.1 in 1990 to 1994, and 275% in white men, from 0.8 to 3.0 during the same periods (Fig. 8). These trends are consistent with the increasing rates of ACE and GCA and with the higher rates of these tumors in whites compared with African Americans.

Helicobacter pylori (H. pylori)

Infection with *H. pylori* is a risk factor for NGA and for its precursor state, chronic atrophic gastritis [55-57]. On the other hand, it has been suggested that *H. pylori* infection, particularly cagA+ strains, is associated with a reduced risk of ACE and GCA [56,58]. No apparent association exists between *H. pylori* infection and risk of SCE.

Current evidence suggests that the incidence and prevalence of *H. pylori* infection has been steadily declining in the United States, probably because of a combination of smaller family size, better hygiene, and increased use of antibiotics during childhood [59]. This decline has probably contributed to the downward trend in NGA. Further investigations are needed to determine whether the decreasing prevalence of *H. pylori* infection in the US population may contribute in some way to the upward trend for ACE and GCA.

Summary

Use of tobacco, moderate to heavy alcohol ingestion, infrequent consumption of raw fruits and vegetables, and low income accounted for more

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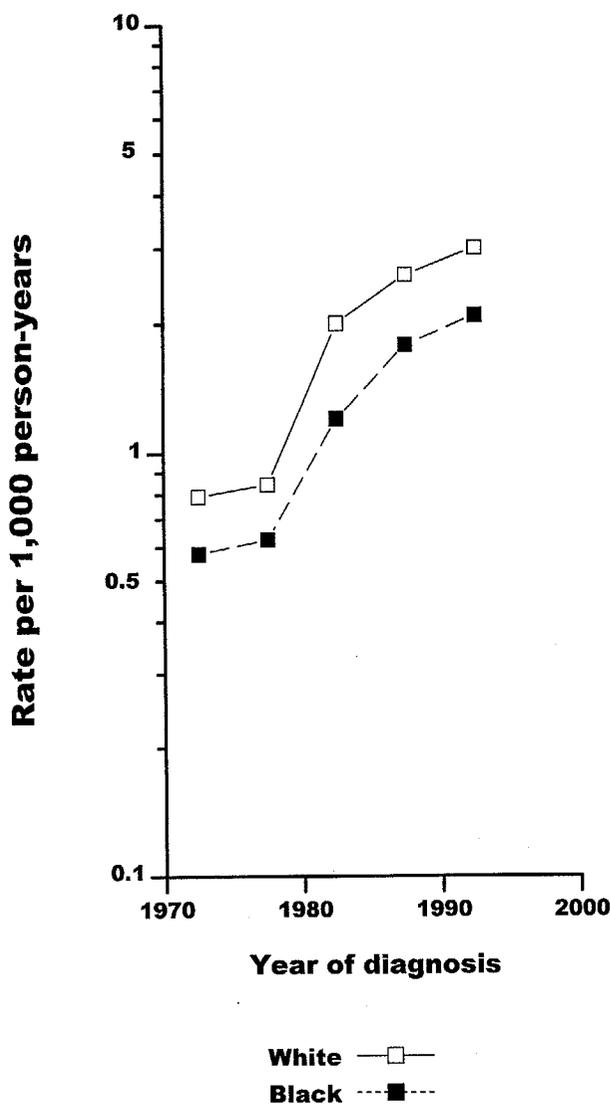


Fig. 8. Trends in gastroesophageal reflux disease incidence rates (per 1000 person-years, age-standardized to the 1970 US population) among male veterans in the United States by race from 1970 to 1974 and 1990 to 1994. (Based on unpublished data from the United States Veterans Administration.)

than 98% of the SCE rates among both African American and white men and for 99% of the excess incidence among African Americans compared to whites in a case-control study in three areas of the United States [14]. Thus, it is likely that declines in the prevalence of smoking and drinking, especially among men, and increased intake of fresh fruits and vegetables

may have contributed to the downward incidence and mortality rate trends reported for SCE. In addition, it seems plausible that obesity, GERD, and possibly reductions in *H. pylori* prevalence have contributed to the upward trends in ACE rates. Reductions in smoking, improved diet, and reductions in *H. pylori* prevalence probably have contributed to the consistent reductions observed for NGA. Contributing factors are less clear for the rising incidence rates of GCA during the 1970s and 1980s. These incidence rates have not continued to rise in recent years.

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