

Adenocarcinoma of the esophagus and esophagogastric junction in White men in the United States: alcohol, tobacco, and socioeconomic factors

Linda Morris Brown, Debra T. Silverman, Linda M. Pottern, Janet B. Schoenberg, Raymond S. Greenberg, G. Marie Swanson, Jonathan M. Liff, Ann G. Schwartz, Richard B. Hayes, William J. Blot, and Robert N. Hoover

(Received 6 December 1993; accepted in revised form 10 February 1994)

In the United States, the incidence of adenocarcinoma of the esophagus, including the esophagogastric (EG) junction, has been increasing rapidly over the past two decades. Except for an association with Barrett's esophagus, little is known about the etiology of these cancers. A population-based case-control interview study of 174 White men with adenocarcinoma of the esophagus and 750 controls living in three areas of the United States offered the opportunity to investigate the relationship of these cancers with smoking, alcohol drinking, socioeconomic factors, and history of ulcer. There were significantly elevated risks for men who smoked cigarettes (odds ratio [OR] = 2.1) or drank liquor (OR = 1.6). For both cigarette smoking and liquor drinking, there were significant dose gradients with amount consumed. No reduction in risk was observed following smoking cessation. Subjects who switched from nonfilter to filter cigarettes experienced half the risk of those who only smoked nonfilter cigarettes. Inverse risk gradients were seen with increasing recent annual income, with the highest risk (OR = 3.4) for the lowest category. The risk for a history of ulcer (OR = 1.7), especially of the duodenum (OR = 2.2), was also significantly elevated. These data suggest that tobacco and alcohol may be etiologic factors for adenocarcinoma of the esophagus and EG junction, but these factors do not appear to explain the rapid rise in incidence of these tumors. The associations with low social class and history of ulcer need to be explored in greater detail along with other factors that may account for the temporal trends in esophageal adenocarcinomas. *Cancer Causes and Control* 1994, 5, 333 - 340

Key words: Adenocarcinoma, alcohol, case-control study, esophagus, males, social class, tobacco, ulcer, United States.

Ms Brown, and Drs Silverman, Pottern, Hayes, Blot, and Hoover are with the Epidemiology and Biostatistics Program, National Cancer Institute, Bethesda, MD, USA. Ms Schoenberg is with the Special Epidemiology Program, New Jersey State Department of Health, Trenton, NJ, USA. Drs Greenberg and Liff are with the Division of Epidemiology, Emory University School of Public Health, Atlanta, GA, USA. Dr Swanson is with the College of Human Medicine, Michigan State University, East Lansing, MI, USA. Dr Schwartz is with the Department of Clinical Epidemiology and Family Medicine, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA. Address correspondence to Ms Brown, Epidemiology and Biostatistics Program, National Cancer Institute, National Institutes of Health, Executive Plaza North, Room 415, Bethesda, MD 20892, USA. This research was performed under contracts NO1-CP-51090, NO1-CP-51089, NO1-CP-51092, NO1-CN-05225, NO1-CN-31022, and NO1-CN-05227.

Introduction

In the United States, the incidence of adenocarcinoma of the esophagus and gastric cardia, including the esophagogastric (EG) junction, has been increasing rapidly over the past two decades.¹ Among White men, the race-gender group with the highest rates (rates are more than three times higher in White compared with Black men¹), the average annual age-adjusted incidence of adenocarcinoma of the esophagus tripled from 0.8/100,000 in 1976-78 to 2.5/100,000 in 1988-90.² Over the same time periods, the corresponding incidence rates for adenocarcinoma of the gastric cardia rose from 2.3/100,000 to 3.4/100,000. Except for an association with Barrett's esophagus, a recognized precursor lesion for adenocarcinoma of the esophagus,^{3,4} little is known about the etiology of these cancers. As part of a case-control study designed to evaluate reasons for the excess incidence of esophageal cancer (largely squamous cell carcinomas) among Black compared with White men, data were collected on subjects with adenocarcinoma of the esophagus and EG junction. Because of the sudden increase in incidence of adenocarcinomas of the esophagus and EG junction in White men, these were ascertained in much greater numbers than originally expected and provided an ideal opportunity to investigate risk factors for these previously rare cell types.

This paper investigates the possible role of smoking, alcohol drinking, socioeconomic factors, and history of ulcer in the etiology of these cancers.

Materials and methods

Concurrent population-based case-control interview studies of four cancers that occur in excess among Blacks—esophagus, prostate, pancreas, and multiple myeloma—were conducted during 1986-89 in three areas of the US. For efficiency, one large control group was chosen for all four cancer types. It was decided to include only male esophageal cancer cases because the number of female cases available would have been too few for analysis (the number of affected females is about one-third the number of affected males).

Selected for the esophageal cancer component were all histologically confirmed cases of esophageal cancer (International Classification of Diseases for Oncology [ICD-O] site code 150) or cancer of the EG junction (ICD-O code 151.0) newly diagnosed between 1 August 1986 and 30 April 1989 among White and Black men aged 30 to 79 years. Cases were residents of geographic areas covered by three population-based cancer registries: the Georgia Center for Cancer Statistics (DeKalb or Fulton counties), the Metropolitan Detroit Cancer Surveillance System (Macomb, Oak-

land, or Wayne counties in Michigan), and the New Jersey State Cancer Registry (10 counties). Because survival for this disease is unfavorable, a rapid reporting system was established to facilitate ascertainment and interview of esophageal cancer patients within six weeks of diagnosis. The median number of days between date of diagnosis and interview was 49 days. Cases were identified from pathology and outpatient records at hospitals in the catchment areas. Pathology records were used to divide the esophageal cancer cases (ICD-O code 150) into three histologic groups: squamous cell carcinoma (ICD-O codes 8050 to 8082); adenocarcinoma (ICD-O codes 8140 to 8573), and all other histologic types including carcinoma not otherwise specified.

For each geographic area, registry data for all four cancer types were used to estimate the race- and age-specific (five-year age groups) numbers of cases anticipated in order to construct a sampling frame for controls. Two sources were utilized for control selection: a random-digit dialing (RDD) technique⁵ for controls aged 30-64 years, and random sampling from computerized listings of Medicare recipients provided by the Health Care Financing Administration (HCFA) for controls aged 65-79 years.

Sixty-minute in-person interviews with the cases and controls were conducted by trained interviewers, usually in the homes of the respondents. Detailed information was obtained on the use of alcohol and tobacco, usual adult diet, usual occupation, medical and dental history, and sociodemographic factors.

Of the 317, White, esophageal/EG-junction cancer cases interviewed, 174 were adenocarcinomas (113 were EG junction cancers), 124 were squamous cell cancers, and 19 were other or type not specified. Among the 270 Black cases interviewed, there were 10 adenocarcinomas (eight were EG junction cancers), 249 squamous cell cancers, and 11 other or not otherwise specified. Herein we limit analyses to adenocarcinomas of the esophagus and EG junction. Due to the small number of these tumors among Black men, for statistical considerations it was decided to restrict the analysis to the 174 White male cases of adenocarcinoma of the esophagus and EG junction, and 750 pooled White male controls.

The response rates at the interview phase were 74 percent for the adenocarcinoma and EG junction cases, 72 percent for the HCFA controls, and 76 percent for the RDD controls. Eighty-six percent of the households contacted through RDD provided a household census which was used to sample controls under 65 years of age. Among all White controls, refusal to be interviewed was the most common reason for nonresponse (18 percent), followed by too ill or deceased

(four percent). Reasons for case nonresponse included deceased (12 percent), too ill (eight percent), and refusal to be interviewed (five percent).

The distributions of the cases and controls by the selection factors, age and geographic area, are presented in Table 1. The median age was 63 years for cases and 61 years for controls. The majority of both interviewed (68 percent) and noninterviewed (77 percent) cases were residents of Detroit. The paucity of cases of adenocarcinoma of the esophagus and EG junction from New Jersey (19 percent of those interviewed and 10 percent of those not interviewed) was particularly striking. Although the reason for such a low percentage from New Jersey is unclear, it may be related to underascertainment of cases or to the demographics of the counties which were selected to provide a large number of Black cases to investigate their high rate of esophageal cancer. The controls were more evenly distributed over the three areas, reflecting the combined distributions of the four cancer types which utilized the same controls.

Statistical analysis

Data were analyzed using unconditional logistic regression.⁶ Adjusted odds ratios (OR) and 95 percent confidence intervals (CI) were obtained using the EPI-CURE programs for personal computers.⁷ Tobacco smokers were defined as subjects who reported smoking at least one cigarette per day or one cigar or pipe per week for six months or longer. For each type of tobacco, questions were asked on the age at first and last use, also the number of years and usual amount smoked. Detailed information was also collected for users of filtered and nonfiltered cigarettes.

Alcohol drinkers were defined as subjects who reported drinking at least one drink of beer, wine, or hard liquor per month for at least six months. For drinkers, usual weekly consumption of each type of beverage was ascertained. Total alcohol consumption was estimated by summing the contribution from each type of alcohol, where one drink was equivalent to 12 oz of beer, four oz of wine, or 1½ oz of hard liquor.

Information was sought concerning a history of duodenal or stomach ulcer diagnosed by a doctor before one year ago. Subjects were also asked to report their total income before taxes for the past calendar year, the number of persons supported by this income, the highest grade level or schooling completed, and the occupation they had worked at the longest during their adult life. A socioeconomic status (SES) level was assigned to each occupational code using a three-level scale (low, medium, high) based on income and education levels required for that particular occupation.

Table 1. Numbers of interviewed White male cases of adenocarcinoma of the esophagus and esophagogastric junction and controls according to age and location

Factor	Case		Control	
	<i>n</i>	%	<i>n</i>	%
Age				
< 50	17	9.8	125	16.6
50-59	43	24.7	218	29.1
60-69	69	39.7	224	29.9
≤ 70	45	25.9	183	24.4
Location				
Atlanta (GA)	22	12.6	167	22.3
Detroit (MI)	119	68.4	277	36.9
New Jersey	33	19.0	306	40.8
Total	174		750	

All models included the selection factors of age and geographic area. Other variables included where indicated were: number of cigarettes smoked per day, number of drinks of liquor per week, recent annual income, and number of people supported by the income. Adjustment for other social class variables such as education and marital status, dietary variables, such as fruit and vegetable consumption, and history of ulcer did not substantially alter any of the risk estimates and thus were not included in the final models. To test for linear trend, categorical variables were entered as continuous variables in the logistic models.

Results

Cigarette smoking was reported by 84 percent of the cases and 70 percent of the controls (Table 2). Compared with non-tobacco smokers, the risk among those who smoked cigarettes was significantly elevated (OR = 2.1) and that among those who smoked only pipes or cigars was nonsignificantly elevated (OR = 1.5). There was a significant trend ($P < 0.01$) of increasing risk with increasing number of cigarettes smoked per day, with the OR reaching 2.6 for cigarette smokers of at least two packs a day. No gradients in risk were seen with duration of smoking or age started smoking cigarettes. These patterns remained when the analysis was limited to cigarette smokers, and intensity, duration, and age started were each adjusted for the other two. There was no protective effect of smoking cessation. Most subjects who had stopped smoking cigarettes had stopped more than 10 years prior to interview, with over 23 percent of the cases and 19 percent of the controls having stopped for 30 or more years. These effects remained when the analysis was restricted to cigarette smokers and ORs were adjusted

Table 2. Risk of adenocarcinoma of the esophagus and esophagogastric junction in White men according to smoking characteristics

Characteristic	No. of cases	No. of controls	OR ^{a,b}	(CI) ^c
Tobacco status				
Nonsmoker	16	160	1.0	—
Pipe/cigar only	11	65	1.5	(0.6-3.6)
Cigarettes	146	517	2.1	(1.2-3.8)
Cigarettes Intensity (no/day)				
<20	18	125	1.1	(0.5-2.4)
20-39	91	271	2.4	(1.3-4.4)
≥40	37	119	2.6**	(1.3-5.0)
Duration (yrs)				
<30	60	223	2.5	(1.3-4.7)
30-39	38	122	2.5	(1.3-4.9)
≥40	48	156	1.6	(0.8-3.2)
Age started (yrs)				
≥21	55	75	2.4	(0.5-3.2)
16-20	68	273	1.9	(0.9-3.2)
<16	23	168	2.5	(0.9-3.6)
Smoking status				
Current smoker	47	186	1.7	(0.9-3.2)
Stopped 1-9 yrs	26	97	2.0	(1.0-4.1)
Stopped 10-19 yrs	28	92	2.4	(1.2-4.9)
Stopped 20-29 yrs	21	78	2.2	(1.0-4.7)
Stopped ≥30 yrs	23	64	3.1	(1.5-6.6)
Filter status				
Filters only	10	71	1.4	(0.6-3.3)
Nonfilters only	53	137	2.9	(1.5-5.4)
Both	75	273	2.0	(1.1-3.7)

^a All estimates relative to the 16 cases and 160 controls who never smoked tobacco.

^b Estimates are adjusted for age, area, liquor use, and income.

^c (CI) = 95% confidence interval.

**P* for trend < 0.05.

***P* for trend < 0.01.

for cigarette smoking intensity. A marked difference in risk by filter status was seen, with subjects who smoked only nonfilter cigarettes (OR = 2.9) having twice the risk of subjects who smoked only filter cigarettes (OR = 1.4). The risk for the subset of subjects who had switched from nonfilters to filters was 1.6 (0.9-3.0). Among smokers who used only nonfilter cigarettes, the ORs rose to 4.0 (1.3-5.9) for those who smoked at least two packs per day and to 3.4 (1.7-7.0) for those who inhaled. These risks remained elevated when the analysis was restricted to smokers of nonfilter cigarettes, and inhalation and intensity were each adjusted for the effect of the other.

Use of alcoholic beverages was reported by 82 percent of the cases and 79 percent of the controls (adjusted OR = 0.9) (Table 3). Risk was nonsignifi-

Table 3. Risk of adenocarcinoma of the esophagus and esophagogastric junction in White men according to type of alcohol^a

Type of alcohol	No. of cases	No. of controls	OR ^{b,c}	(CI) ^d
Never drank alcohol	32	155	1.0	—
Drank alcohol	142	595	0.9	(0.6-1.4)
Drinks/week ^a				
<8	38	222	0.7	(0.4-1.3)
8-21	42	204	0.8	(0.4-1.3)
22-56	43	132	1.1	(0.6-1.9)
≥56	18	37	1.5	(0.7-3.1)
Never drank liquor	64	342	1.0	—
Drank liquor	110	408	1.6	(1.1-2.4)
Drinks/week ^a				
<8	50	257	1.3	(0.8-2.0)
8-1	24	78	1.8	(1.0-3.2)
15-28	21	50	2.1	(1.1-4.0)
≥29	13	22	2.8*	(1.2-6.3)
Never drank beer	60	275	1.0	—
Drank beer	114	475	0.6	(0.4-0.9)
Drinks/week ^a				
<8	46	254	0.6	(0.4-1.0)
8-14	26	97	0.7	(0.4-1.2)
15-28	21	71	0.6	(0.3-1.1)
≥29	50	20	0.6	(0.3-1.3)
Never drank wine	127	492	1.0	—
Drank wine	47	258	0.9	(0.6-1.4)
Drinks/week ^a				
<3	19	119	0.9	(0.5-1.5)
3-13	17	101	0.8	(0.4-1.5)
≥14	11	35	1.6	(0.7-3.8)

^a 1 drink is equal to 12 oz of beer, 4 oz of wine, 1.5 oz of liquor.

^b Estimates are adjusted for age, area, smoking, and income.

^c Each type of alcoholic beverage is adjusted for amount of the other two.

^d (CI) = 95% confidence interval.

**P* for trend < 0.05.

cantly elevated (OR = 1.5) for the highest consumption category (more than 56 drinks per week). When ORs were calculated for use of specific types of alcoholic beverages adjusted for amount of the other two, a significant increase in risk was associated with drinking liquor (OR = 1.6). There was no risk for use of wine (OR = 0.9) and the risk for beer consumption was significantly reduced (OR = 0.6). Use of moonshine (home brewed liquor) was not included in the analysis because it was reported by only six cases (3.4 percent) and 31 controls (4.1 percent). A significant dose gradient was seen for number of drinks of liquor consumed, the OR reaching 2.8 in the highest category (more than four drinks per day). When the analysis was restricted to liquor drinkers and ORs were adjusted for amount of liquor consumed, risk was not related to the

Table 4. Risk of adenocarcinoma of the esophagus and esophagogastric junction in White men according to the combined effects of cigarettes and hard liquor^a

Drink	Cigarette smoking							
	< 1 pack/day				≥ 1 pack/day			
	No. of cases	No. of controls	OR	(CI) ^b	No. of cases	No. of controls	OR	(CI) ^b
< 8/week	32	309	1.0	—	82	288	2.4	(1.5-3.8)
≥ 8/week	13	38	2.4	(1.1-5.1)	45	102	3.8	(2.2-6.4)

^a Estimates are adjusted for age, area, and income.

^b (CI) = 95% confidence interval.

age at first consumption, the number of years liquor was consumed, or the use of mixers. Among liquor drinkers, risk was nonsignificantly elevated for subjects who usually drank gin or vodka (OR = 1.7, 95 percent confidence interval [CI] = 0.9-3.3) or whiskey (OR = 1.3, CI = 0.7-2.4) compared with subjects who usually drank bourbon, scotch, or rye.

The risks from combined exposure to cigarettes and liquor are presented in Table 4, where separate effects of each are seen. Although it was not possible to distinguish statistically between additive, multiplicative, or intermediate models, risk was greatest (OR = 3.8) for subjects who smoked at least one pack of cigarettes per day and drank at least eight drinks of liquor per week.

A history of ulcer was reported by 24 percent of the cases and 14 percent of the controls (OR = 1.7, CI = 1.1-2.6). The risk remained significantly elevated (OR = 1.7, CI = 1.1-2.8) when the analysis was restricted to the 35 cases and 91 controls who had had their ulcer diagnosed by a doctor more than five years before interview. For this latter group, risk was greatest for ulcers of the duodenum (OR = 2.2, CI = 1.0-4.6), followed by the stomach and duodenum (OR = 1.4, CI = 0.2-8.3), and stomach (OR = 1.3, CI = 0.7-2.5). All ORs were adjusted for smoking, liquor use, and income.

Results from the analysis of the socioeconomic variables (recent annual income, highest level of schooling completed, and SES derived from usual occupation) are presented in Table 5. Inverse risk gradients were seen with both increasing income and SES based on occupation, with smoking- and drinking-adjusted ORs reaching 3.4 and 1.6, respectively, for the lowest income and SES categories. A similar pattern was not seen for level of education, with a nonsignificantly lower risk among those with less than a high school education. When risk estimates for the socioeconomic variables were recalculated without adjustment for smoking and drinking (two factors which may be

Table 5. Risk of adenocarcinoma of the esophagus and esophagogastric junction in White men according to socio-demographic characteristics^a

Characteristic	No. of cases	No. of controls	OR ^b	(CI) ^c
Recent annual income (\$)				
≥ 50,000	22	179	1.0	—
25,000-49,999	46	215	1.6	(0.9-2.9)
10,000-24,999	62	242	1.7	(0.9-3.3)
< 10,000	26	53	3.4*	(1.5-7.4)
Education				
> High school	68	344	1.0	—
High school	44	210	0.7	(0.4-1.1)
< High school	62	190	0.7	(0.4-1.2)
SES from occupation				
High	29	165	1.0	—
Medium	74	362	1.1	(0.7-1.9)
Low	70	220	1.6	(0.8-3.0)

^a Estimates are adjusted for age, area, smoking, liquor use, and number supported.

^b Each sociodemographic characteristic is adjusted for the other two.

^c (CI) = 95% confidence interval.

*P for trend < 0.05.

partly determined by socioeconomic factors), the ORs changed only slightly.

When risks for selected smoking, alcohol, and SES variables were analyzed separately for esophageal and EG junction cases, patterns of risk were similar for the two anatomic categories. The ORs, however, tended to be somewhat higher for the esophageal cases.

Discussion

Previous studies in the US and other Western countries have consistently shown that consumption of cigarettes and alcoholic beverages are the major risk factors for esophageal cancer.^{8,9} The large majority of the tumors studied, however, have been squamous cell car-

cinomas, until recently the predominant cell type of esophageal cancer in both races.² Prior research has also shown that smoking is linked to a modest increase in stomach cancer risk, while alcohol intake has generally not been found to be a stomach cancer risk factor.^{10,11} Nearly all the stomach cancers have been adenocarcinomas, typically located in the lowest portions of the stomach and not near the EG junction. Thus, it was not clear at the start of our investigation whether risk factors for adenocarcinomas of the esophagus would more closely resemble those for squamous cell cancers of the esophagus or adenocarcinomas of the stomach, or would show unique features. Similar to the finding of Gray *et al*¹² our data suggest that the risk associated with tobacco and alcohol use is closer in magnitude to the risk for lower stomach cancers than to the risk for squamous cell cancers of the esophagus.

We found that use of cigarettes was significantly related to risk of adenocarcinoma of the esophagus and EG junction, with a doubling of risk for smokers of more than one pack a day. Risk was also related to type of cigarette smoked. Smokers of nonfilter cigarettes showed the highest risks and the strongest patterns of dose-response with intensity and inhalation. Subjects who switched from nonfilter to filter cigarettes experienced half the risk of those who only smoked nonfilter cigarettes, suggesting that filters may block some of the components of cigarette smoke carcinogenic to the esophagus. Unlike findings for squamous cell carcinoma of the esophagus,^{13,14} cessation of smoking conferred no protective effect, even for subjects who had stopped for more than 20 years. The lack of an association with smoking cessation helps explain why trends in esophageal adenocarcinoma do not parallel the trends in smoking prevalence (which is declining¹⁵) in the United States. The absence of a cessation effect also suggests that smoking acts at a relatively early stage in the development of esophageal adenocarcinomas and that the effects of smoking in adolescence and early adulthood may be permanent. These findings are consistent with those of Kabat *et al*¹⁶ who reported that risk for esophageal adenocarcinoma was significantly elevated for ex-smokers. They also found a relative risk of around 2.0 for cigarette smokers and a dose-response with intensity of use. Limited data from other countries have reported smoking to be a risk factor for gastric cardia cancer in Japan¹⁷ and China,¹⁸ but not Italy.¹⁹

Our results for alcoholic beverage consumption were less clear. Only the trend for use of liquor was significant, with the OR approaching 3.0 among the heaviest drinkers. Trends of rising risk with increasing intake were not significant for all types of alcoholic beverages combined, or for use of beer or wine. In fact, the

OR for beer consumption was significantly less than 1.0. In contrast, risks of squamous esophageal cancers have been reported to be sharply elevated among heavy drinkers of all types of alcoholic beverages.^{13,14,20-22} Indeed, several clusters of exceptional esophageal cancer mortality have been linked to consumption of specific alcoholic beverages, *e.g.*, apple brandies in France,²³ cachaca in Brazil,²⁴ moonshine in South Carolina (USA),¹³ and whiskeys and beer in Washington, DC.²⁰ Alcohol use has been unrelated to risk of stomach cancers in most studies, including those focusing on gastric cardia tumors,^{11,17-19} but there are some exceptions.²⁵ Few studies have evaluated the role of alcohol in esophageal adenocarcinomas, but in Canada, risks associated with drinking were stronger for lower esophagus and EG junction adenocarcinomas than for stomach cancers.¹² Kabat *et al*¹⁶ reported a significant increase among hard liquor drinkers, similar to our finding. Although whiskey may contain compounds besides ethanol which are carcinogenic,^{11,26} it is not clear why an association with cancers of the esophagus and EG junction would be limited to liquor drinkers. Consistent with findings by Kabat *et al*,¹⁶ we found that the risk for exposure to both smoking and alcohol was greater than to either one alone. The interaction in our study appeared to be most consistent with an additive model, however, we lacked the power to distinguish statistically between an additive and a multiplicative model.

Even though we did not collect information on Barrett's esophagus, a recognized precursor lesion for adenocarcinoma of the esophagus,^{3,4} we did find that risk was significantly elevated among those with a history of ulcer, especially those located in the duodenum. MacDonald and MacDonald²⁷ reported a similar finding: 27 percent of their cases had peptic ulcer, with the majority located in the duodenum. Our finding is unlikely to be a result of early clinical disease since the excess risk persisted when the analysis was restricted to subjects whose ulcer preceded their cancer diagnosis by more than five years. Unfortunately, we did not obtain data on ulcer medication or medical conditions related to Barrett's esophagus, such as esophageal reflux.^{28,29} Therefore, we were unable to determine more specifically the role of ulcer in these tumors. It is of interest, however, that *Helicobacter pylori* infection appears to be related to duodenal ulcer, but not to adenocarcinoma of the EG junction.³⁰

A significantly elevated risk was found for subjects with recent annual incomes of less than \$10,000. Although not significant, subjects whose usual job was classified as low SES were also at excess risk. Inverse associations with social class are commonly found for both squamous esophageal cancer and stomach cancers,^{8,9,31} but have not previously been reported for

esophageal adenocarcinomas. In addition, others have noted that a higher percentage of cases of adenocarcinoma of the esophagus were in professional and managerial occupations than were cases of squamous cell carcinoma of the esophagus.³² In contrast to the findings with income and SES, our study found educational status to be positively associated with risk of adenocarcinoma of the esophagus and EG junction. A similar finding was seen in Los Angeles County (CA) men with gastric cardia cancer.²⁵

When risk factors were analyzed separately for esophageal adenocarcinomas and EG junction cancers the patterns were similar, but the strength of the associations with smoking and drinking appeared to be slightly greater for adenocarcinoma of the esophagus than for cancer of the EG junction. These two groups have been found to be nearly identical clinically and pathologically.²⁷

The results from our population-based case-control study suggest that both tobacco and alcohol may be etiologic factors for adenocarcinomas of the esophagus and EG junction in White men, whereas the findings related to low social class and history of ulcer need to be explored further to determine what specific practices may be related to risk. It is unlikely, however, that smoking and drinking are strong enough risk factors to account for the rapid rise in the incidence of these tumors. It is also doubtful that changes in tobacco and alcohol use were substantial enough to have caused such dramatic increases in the risk of these tumors in such a short time period. In fact, during this time-period use of cigarettes by White men actually decreased.¹⁵ Further, these two factors do not appear to explain the White excess of these tumor types, because the frequency of use of liquor and cigarettes is similar for Black and White men.^{33,34} Additional study, therefore, is needed to explain the rapid rise in incidence of these tumors and to clarify etiologic factors for these emergent cancers.

Acknowledgements—The authors wish to thank Ruth Thomson of Westat, Inc. for her assistance in study management and coordination, Roy Van Dusen of Information Management Systems, for computer support; study coordinators, interviewers, and support staff in each study area for their diligent work; and the many physicians, hospitals, and study participants who cooperated in this study.

References

1. Blot WJ, Devesa SS, Kneller RW, Fraumeni JF Jr. Rising incidence of adenocarcinoma of the esophagus and gastric cardia. *JAMA* 1991; 265: 1287-9.
2. Blot WJ, Devesa SS, Fraumeni JF Jr. Continuing climb in rates of esophageal adenocarcinoma: an update. *JAMA* 1993; 270: 1320.
3. Garewal HS, Sampliner R. Barrett's esophagus: a model premalignant lesion for adenocarcinoma. *Prev Med* 1989; 18: 749-56.
4. Spechler SJ, Goyal RK. Barrett's esophagus. *N Engl J Med* 1986; 315: 362-71.
5. Waksberg J. Sampling methods for random digit dialing. *J Am Stat Assoc* 1978; 73: 40-6.
6. Breslow NE, Day NE. *Statistical Methods in Cancer Research, Vol I. Analysis of Case-Control Studies*. Lyon, France: International Agency for Research on Cancer, 1980: 192-246.
7. Preston DL, Lubin JH, Pierce D. *EPICURE: Risk Regression and Data Analysis Software*. Seattle, WA (US): HiroSoft International Corporation; 1992.
8. Day NE, Muñoz N. Esophagus. In: Schottenfeld D, Fraumeni JF, Jr, eds. *Cancer Epidemiology and Prevention*. Philadelphia, PA (US): W.B. Saunders 1982: 596-623.
9. Schottenfeld D. Epidemiology of cancer of the esophagus. *Semin Oncol* 1984; 11: 92-100.
10. International Agency for Research on Cancer. *Tobacco Smoking, IARC Monographs on the Evaluation of the Carcinogenic Risk to Humans, Vol. 38*. Lyon, France: IARC, 1986.
11. International Agency for Research on Cancer. *Alcohol Drinking, IARC Monographs on the Evaluation of the Carcinogenic Risk to Humans, Vol. 44*. Lyon, France: IARC, 1988.
12. Gray JR, Coldman AJ, MacDonald WC. Cigarette and alcohol use in patients with adenocarcinoma of the gastric cardia or lower esophagus. *Cancer* 1992; 69: 2227-31.
13. Brown LM, Blot WJ, Schuman SH, et al. Environmental factors and high risk of esophageal cancer among men in coastal South Carolina. *JNCI* 1988; 80: 1620-5.
14. Yu MC, Garabrant DH, Peters JM, Mack TM. Tobacco, alcohol, diet, occupation, and carcinoma of the esophagus. *Cancer Res* 1988; 48: 3843-8.
15. Pierce JP, Fiore MC, Novotny TE, Hatziandreu EJ, Davis RM. Trends in cigarette smoking in the United States. Projections to the year 2000. *JAMA* 1989; 261: 61-5.
16. Kabat GC, Ng SKC, Wynder EL. Tobacco, alcohol intake, and diet in relation to adenocarcinoma of the esophagus and gastric cardia. *Cancer Causes Control* 1993; 4: 123-32.
17. Unakami M, Hara M, Fukuchi S, Akiyama H. Cancer of the gastric cardia and the habit of smoking. *Acta Pathol Jpn* 1989; 39: 420-4.
18. Li J-Y, Ershow AG, Chen Z-J, et al. A case-control study of cancer of the esophagus and gastric cardia in Linxian. *Int J Cancer* 1989; 43: 755-61.
19. Palli D, Bianchi S, Decarli A, et al. A case-control study of cancers of the gastric cardia in Italy. *Br J Cancer* 1992; 65: 263-6.
20. Pottern LM, Morris LE, Blot WJ, Ziegler RG, Fraumeni JF Jr. Esophageal cancer among black men in Washington, DC. I. Alcohol, tobacco, and other risk factors. *JNCI* 1981; 67: 777-83.
21. Wynder EL, Bross IJ. A study of etiological factors in cancer of the esophagus. *Cancer* 1961; 14: 389-413.

22. Mettlin C, Graham S, Priore R, Marshall J, Swanson M. Diet and cancer of the esophagus. *Nutr Cancer* 1981; 2: 143-7.
23. Tuyns AJ, Pequignot G, Abbatucci JS. Oesophageal cancer and alcohol consumption; importance of type of beverage. *Int J Cancer* 1979; 23: 443-7.
24. Victora CG, Muñoz N, Day NE, Barcelos LB, Peccin DA, Braga NM. Hot beverages and oesophageal cancer in southern Brazil: a case-control study. *Int J Cancer* 1987; 39: 710-6.
25. Wu-Williams AH, Yu MC, Mack TM. Life-style, workplace, and stomach cancer by subsite in young men of Los Angeles County. *Cancer Res* 1990; 50: 2569-76.
26. Garro AJ, Lieber CS. Alcohol and cancer. *Annu Rev Pharmacol Toxicol* 1990; 30: 219-49.
27. MacDonald WC, MacDonald JB. Adenocarcinoma of the esophagus and/or gastric cardia. *Cancer* 1987; 60: 1094-8.
28. Bartelsman JFWM, Hameeteman W, Tytgat GN. Barrett's oesophagus. *Eur J Cancer Prev* 1992; 1: 323-5.
29. Collins BJ, Abbott M, Thomas RJS, Morstyn G, St John DJB. Clinical profile in Barrett's esophagus: who should be screened for cancer? *Hepato-Gastroenterol* 1991; 38: 341-433.
30. Hansson L-E, Engstrand L, Nyrén O, et al. *Helicobacter pylori* infection: independent risk indicator of gastric adenocarcinoma. *Gastroenterology* 1993; 105: 1098-103.
31. Nomura A. Stomach. In: Schottenfeld D, Fraumeni JF Jr, eds. *Cancer Epidemiology and Prevention*. Philadelphia, PA (US): W.B. Saunders, 1982: 624-37.
32. Powell J, McConkey CC. The rising trend in oesophageal adenocarcinoma and gastric cardia. *Eur J Cancer Prev* 1992; 1: 265-9.
33. Fiore MC, Novotney TE, Pierce JP, Hatziandreu EJ, Patel KM, Davis RM. Trends in cigarette smoking in the United States: the changing influence of gender and race. *JAMA* 1989; 261: 49-55.
34. Hilton ME. The demographic distribution of drinking patterns in 1984. In: Clark WB, Hilton ME, eds. *Alcohol in America*. Albany, NY (US): State University of New York, 1991: 73-86.