

Geographic Correlations Between Cancer Mortality Rates and Alcohol-Tobacco Consumption in the United States^{1,2}

Norman E. Breslow³ and James E. Enstrom⁴

SUMMARY—Average annual age-adjusted cancer mortality rates for 1950–67 were correlated with per-capita consumption of cigarettes, spirits, wine, and beer as estimated from tax receipts in 41 States of the United States in 1960. These correlations were made for cancers of 19 sites for white males and of 20 sites for white females. Multiple regression analyses were used to estimate the simultaneous effects on cancer mortality of State-to-State variation in the urban component of the population and in the consumption of spirits, beer, and cigarettes. Respiratory cancers were related to cigarette consumption, certain cancers of the upper alimentary tract to consumption of spirits, and cancers of the stomach, large bowel, kidney, bladder (for men), and breast (for women) to consumption of beer. The strongest single association was between rectal cancer and beer consumption, a result found also with similar data for 24 other countries. The hazards of attempting to draw sound scientific inferences from such data are acknowledged.—*J Natl Cancer Inst* 53: 631–639 1974.

AS PART of the continuing inquiry into the etiologic role of alcohol and tobacco in human cancer, the geographic correlations were recently studied between consumption of alcohol or tobacco and cancer mortality in the United States (1–3) and elsewhere (4). The work reported here re-examines and extends these studies systematically to more cancer sites. The goal was not only to confirm known relationships, e.g., between respiratory cancer and cigarette consumption, but also to suggest hypotheses for possible investigation by case-control and cohort studies. Toward this end, most major cancer sites in the digestive, respiratory, and genitourinary systems were considered, with leukemia and cancer of the thyroid included as “control” sites as suggested by Fraumeni (2).

MATERIALS AND METHODS

U.S. cancer data.—Average annual cancer mortality rates during 1950–67, age-adjusted to the 1960 U.S. population, have been published (5) for each 3-digit cancer site—140–205 according to the Sixth and Seventh Revisions of the International Classification of Diseases (ICD) (6, 7). Apart from rewording of ICD categories 162 and 163, no major shifts between 3-digit categories occurred with the change to the Seventh Revision in 1958. The rates were tabulated separately by State for the 4 categories: white male, nonwhite male, white female, and nonwhite female. They were also calculated for the combinations of sites—buccal cavity and pharynx (ICD 140–148), digestive organs (ICD 150–155, 157–159), and respiratory organs (ICD 160–164)—by addition of the age-adjusted rates for the component sites (5).

U.S. consumption data.—Apparent per-capita consumption of distilled spirits, wine, and beer was compiled (2, 3) for each State from tax figures (8–10) for 1960. The consumption data represent official deliveries of tax-paid beverages and account neither for transport across State lines nor for home production. Estimates of per-capita consumption of cigarettes for 1960 were similarly compiled (2, 11) from tax figures (12). The urban percentage of the population of each State in 1960 was derived (1, 2) from census data (13) and is henceforth referred to as “% urban.” Inclusion of this variable in the regression and correlation analyses (see below) represented an attempt to determine alcohol-tobacco effects that were not simply a consequence of the greater consumption of alcohol and tobacco products by urban populations (table 1). These 5 variables (% urban, spirits, wine, beer, and cigarettes) were considered as “exposure” or independent variables in the statistical analyses.

Correlation analysis.—Statistical analysis was based on the 41 States considered in (1). Estimates of cigarette sales were not available in Colorado, Georgia, Hawaii, New Hampshire, North Carolina, Oregon, and Virginia. Mississippi had no legal alcohol sales in 1960. Nevada and the District of Columbia were excluded because of heavy sales to nonresidents. Unfortunately the published cancer mortality figures combined Maryland with the District of Columbia (5); however, since the 1960 population of Maryland was more than 4 times that of the District of Columbia, little bias should have been introduced.

In a preliminary analysis, simple correlation coefficients (r) were calculated between each of the site-, sex-, and race-specific cancer mortality rates and each of the 5 exposure variables (see table 2). Only results for whites are shown, since it was believed that consumption figures were most representative of these groups (see “Discussion”); corresponding relationships for nonwhites were generally weaker and less consistent. Coefficients of 0.40 and above were statistically significant at $P < 0.01$, whereas those of 0.50 and above were significant at $P < 0.001$. Less significant results were not considered, due to the many coefficients examined. In view of the descriptive nature of this study, the magnitude of these coefficients should be emphasized more than their statistical significance.

¹ Received February 14, 1974; accepted May 29, 1974.

² Work supported in part by contract HSM 42-73-116 with the U.S. National Institute for Alcohol Abuse and Alcoholism.

³ International Agency for Research on Cancer, 150, cours Albert Thomas, 69008 Lyons, France.

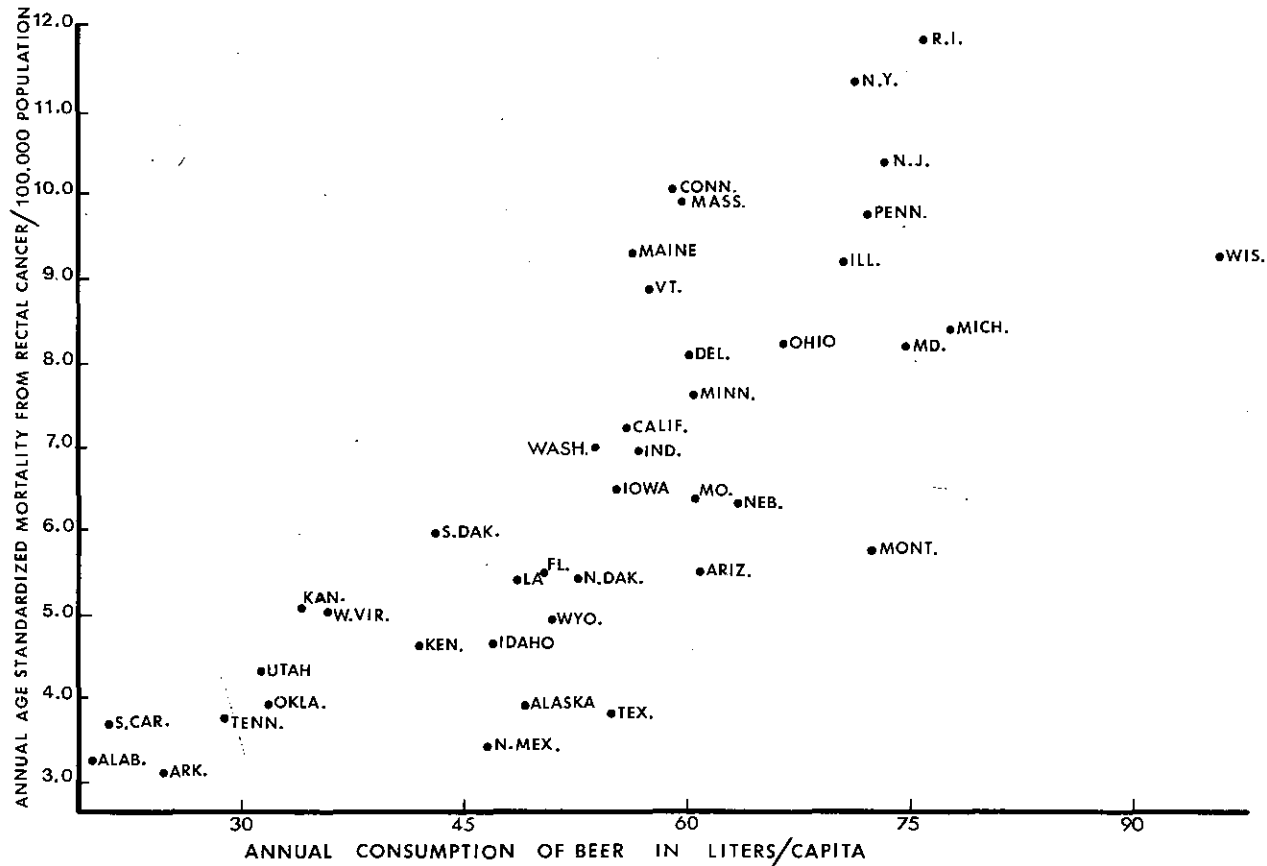
⁴ School of Public Health, University of California, Los Angeles, Calif. 90024.

TABLE 1.—Correlations among exposure variables for 41 States of the United States (below diagonal line) and 24 other countries (above diagonal line)

Variable	% Urban	Spirits	Wine	Beer	Cigarettes
% Urban	1.00	NA*	NA	NA	NA
Spirits	0.38	1.00	-0.02†	-0.15†	NA
Wine	.67	0.67	1.00	.31	NA
Beer	.50	.48	.44	1.00	NA
Cigarettes	.43	.79	.58	.56	1.00

*NA=not applicable.

†Japan excluded from the calculation of spirits correlations due to inadequate data (21).



TEXT-FIGURE 1.—Scattergram showing relationship between apparent 1960 per-capita beer consumption and average annual age-adjusted mortality rates, 1950-67, for rectal cancer among males in 41 States of the United States.

A scattergram illustrates one of the most striking associations (text-fig. 1).

Multiple regression analyses.—Since all 5 exposure variables were positively correlated (table 1), an examination of their individual effects in a multivariate framework was essential to interpretation. Thus a multiple regression analysis (14) was made of the site-specific rates for white males and females on the 4 exposure variables: % urban, spirits, beer, and cigarettes. Wine was not included in this analysis because of the generally low levels of its consumption in the United States (see table 5) and the fact that preliminary analyses indicated that wine was related only marginally, if at all, to cancer at a few sites. *F*

statistics with 3 and 36 degrees of freedom (15) were used to determine the statistical significance of the combined effects of spirits, beer, and cigarettes on cancer mortality after adjustment for % urban. Comparison of estimated regression coefficients with their standard errors indicated the alcohol/tobacco variables with the greatest individual effects for each sex and site. The square of the multiple correlation (*R*²) showed the percentage of State-to-State variation in mortality which is "explained" by linear regression on the 4 variables entering the equation.

The isolation of individual effects of correlated exposure variables with the multiple regression approach is an uncertain process (16). Estimates of

regression coefficients and evaluation of statistical significance for individual variables may depend heavily on the other variables included in the equation. Because of the high correlations among exposure variables and the small number of population units (States), interaction effects were not estimated. Thus it may eventually prove worthwhile to contrast the findings reported here with those obtained with other, more refined, statistical methods.

International rates and correlations.—For comparison with U.S. results, estimated incidence rates for cancer at selected sites in 24 of 25 countries considered in (17) were also correlated with apparent consumption of distilled spirits, wine, and beer. The figures for cancer, given by Doll (18), represent average annual incidence rates for males (except for "female" sites) ages 35–64 years, standardized to the "world" population (19), for 1960–62. For 11 countries, actual incidence rates (19) were used, whereas for the other countries, mortality rates (20) had been multiplied by a site-specific scale factor to estimate incidence. According to (18), the error in these estimated rates is in most instances likely to be less than 20%, though more extreme variations cannot be ruled out. Overall rates for the United States, the United Kingdom, and Canada were obtained by the combination of figures for individual races or regions.

Estimates of the apparent consumption of alcohol in liters per capita of the population in each country were compiled (21) from various sources for 1960. Data on consumption of spirits were inadequate for Japan in 1960, which explains Japan's omission from certain portions of tables 1, 4, and 5.

RESULTS

The 41 States of the United States

Simple correlations.—Table 2 shows the simple correlation coefficients between site- and sex-specific cancer mortality rates and the 5 exposure variables, % urban, spirits, wine, beer, and cigarettes. Most sites, except for those of the cervix, prostate, buccal cavity (females), and larynx (females), had a positive relationship to one or more of the exposure variables. Leukemia was negatively related to most exposures in both sexes. The most striking results were the high correlations (over 0.70) between apparent consumption of beer drinking and the development of cancers of the lower bowel, breast (female), kidney (male), and bladder (male). Text-figure 1 illustrates the relation between beer and the development of rectal cancer among males ($r=0.78$). For respiratory cancers, the strongest correlations were with cigarettes ($r=0.60$ and 0.62 for males and females, respectively). Cancers of the esophagus and nasopharynx were most strongly related to spirits.

Multiple regression analyses.—Results of the multiple regression analyses are summarized in table 3. Consider, for example, the line corresponding to cancer of the esophagus in males. The multiple correlation coefficient R indicated that $(0.82)^2 \times 100\% = 67\%$ of the State-to-State variation in mortality from esophageal cancer among males was "explained" by linear regression on the 4 dependent

variables—% urban, spirits, beer, and cigarettes. After adjustment for % urban, the 3 alcohol/tobacco variables considered together had highly significant effects on cancer mortality as indicated by the F statistic value of 11.40 ($P<0.001$). The statistical significance of their individual effects, as indicated by comparisons of the regression coefficients with their standard errors (SE), with the t -test (15), was less pronounced. Spirits and beer showed effects significant at $P<0.05$. Cigarettes, which had a significant simple correlation with esophageal cancer in males (table 2), were not implicated by this approach when account was taken of the apparently stronger effects of spirits and beer. Because of the high correlation (0.79) between spirits and cigarettes, inclusion of the latter variable in the equation substantially reduced the statistical significance of the former. When only % urban, spirits, and beer were included, the regression coefficient for spirits was 1.145 ± 0.303 ($P<0.001$). For esophageal cancer in females, spirits was the only alcohol/tobacco variable with a significant effect after adjustment for % urban.

Other sites for which spirits were positively related to cancer mortality by the regression analysis were nasopharynx (females), small intestines (males), and pancreas (females). Beer drinking was associated with cancers of many lower digestive sites, including stomach, small intestine (female), colon, and rectum, and also with liver (female), kidney, and bladder (male). Cigarettes were associated with lung cancers, the similar results for all respiratory organs reflecting the overwhelming contribution made by lung cancers to this group. Cigarettes were also related to cancers of the colon and cervix among females. However, this latter result appeared only after we took into account the negative relations with spirits: Neither variable was significant by itself after adjustment for % urban, but only when considered in the same equation with the other. A similar phenomenon accounted for the apparent positive association between the consumption of beer and the development of thyroid cancer among females, though in this instance the negative relation with spirits was initially significant. The negative relationship between urban factors and leukemia was noted in (2).

Study of 24 Countries

The correlations for a restricted range of sites, based on more heterogeneous data for 24 countries (table 4), were significant ($r>0.52$, $P<0.01$) only for the association of cancers of the colon, rectum, and lung with beer consumption and for the association of esophageal cancer with wine consumption. However, the beer-rectum relationship was just as striking as it had been for the 41 States of the United States (text-fig. 2, table 4). The patterns and volume of consumption of the various alcoholic beverages differed markedly between the 24 countries and the 41 States, with the average 1960 U.S. consumption of spirits about 40% greater than the average consumption for the 24 countries and with wine consumption about one-seventh (table 5). The ranges of beer consumption were more similar. While no comparable figures for

TABLE 2.—Simple correlations between exposure variables and site-specific, age-adjusted cancer mortality rates for whites, by sex, for 41 States of the United States*

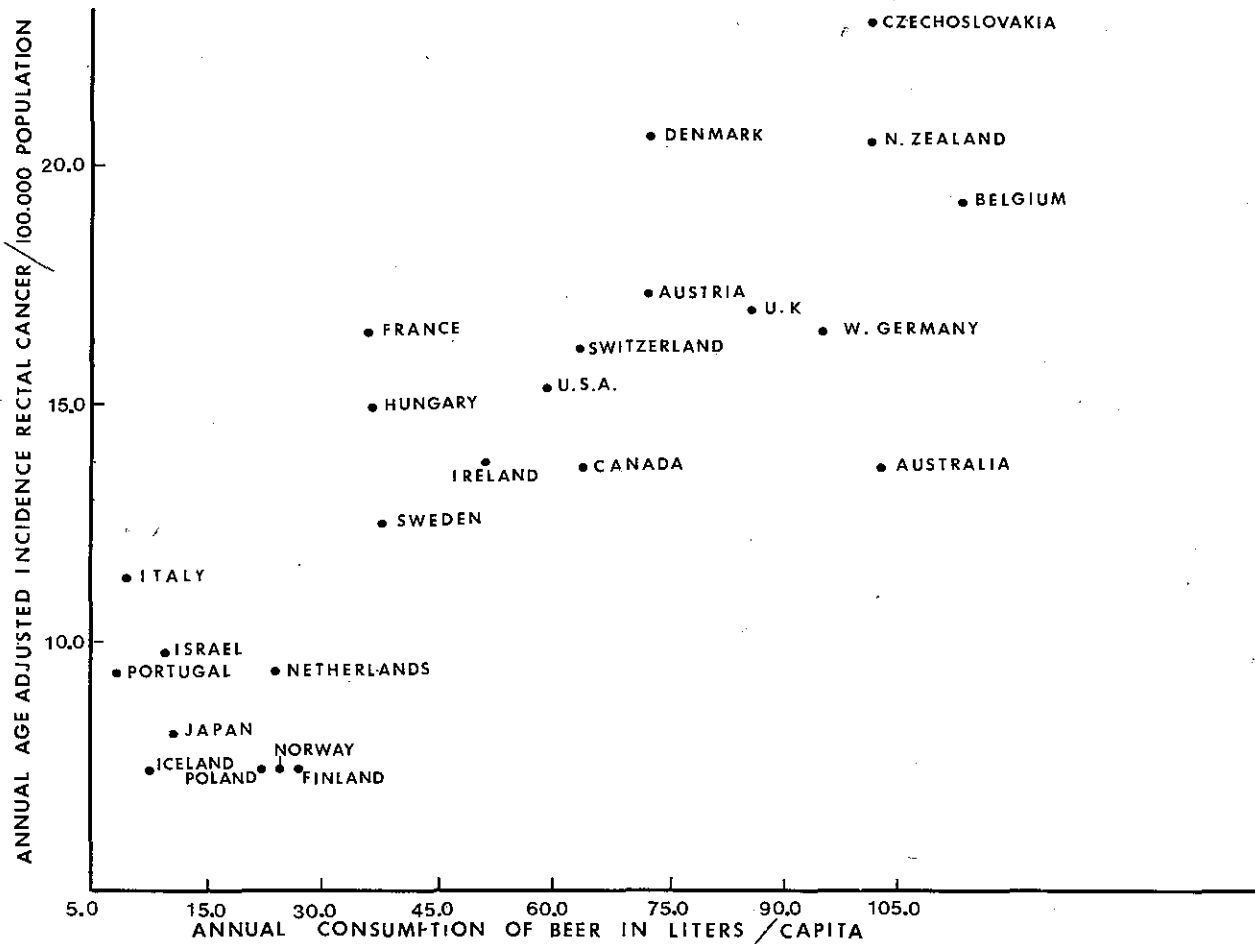
Site	ICD Nos. (Sixth and Seventh Revisions)	Exposure variables and sex											
		% Urban		Spirits		Wine		Beer		Cigarettes			
		M	F	M	F	M	F	M	F	M	F		
Mouth (floor)	143	0.69	0.28	0.44	-0.01	0.59	0.34	0.45	0.11	0.47	-0.03		
Nasopharynx	146	.08	-.05	.46	.51	.32	.29	.00	.15	.26	.46		
Buccal cavity and pharynx	140-148	.59	.01	.51	-.13	.53	.04	.37	-.41	.55	.13		
Esophagus	150	.61	-.03	.68	.59	.60	.29	.67	.07	.64	.45		
Stomach	151	.28	.24	.29	.23	.32	.30	.62	.57	.21	.15		
Small intestine	152	-.08	.05	.46	.43	.06	.20	.18	.52	.34	.52		
Colon	153	.56	.40	.60	.54	.45	.37	.73	.69	.68	.71		
Rectum	154	.57	.45	.54	.53	.52	.53	.61	.71	.53	.62		
Liver	155	.56	.25	.16	-.22	.37	.02	.36	.41	.18	-.09		
Pancreas	157	.10	-.12	.42	.61	.42	.26	.14	.18	.18	.38		
Digestive organs	150-155, 157-159	.55	.39	.61	.56	.54	.46	.79	.76	.60	.63		
Larynx	161	.60	.04	.48	.20	.62	.34	.45	-.13	.57	.26		
Lung	162-163	.45	.30	.53	.58	.58	.59	.24	.16	.59	.63		
Respiratory organs	160-164	.47	.30	.53	.56	.59	.58	.26	.13	.60	.62		
Breast	170	---	.53	---	.60	---	.51	---	.78	---	.61		
Cervix	171	---	-.26	---	-.32	---	-.19	---	-.31	---	-.02		
Prostatic	177	-.13	---	.25	---	.23	---	.15	---	.21	---		
Kidney	180	.33	-.13	.49	.02	.32	.10	.75	.42	.48	.04		
Bladder	181	.61	.41	.59	.46	.64	.50	.73	.47	.62	.56		
Thyroid	194	.43	.41	.30	-.20	.27	.08	.32	.42	.25	.12		
Leukemia	204	-.41	-.36	-.48	-.51	-.49	-.45	-.05	-.06	-.40	-.41		

*Coefficients of 0.40 and above are statistically significant at $P < 0.01$; coefficients of 0.30 are significant at $P < 0.001$.

TABLE 3.—Summary of regression analyses of site-specific cancer mortality (deaths/100,000 population/yr) on 4 exposure variables by sex, for 41 States

Site	ICD Nos. (Sixth and Seventh Revisions)	Sex	Multiple R	F test for alcohol/ tobacco effects	% Urban	Regression coefficients \pm SE for 4 exposure variables			
						Spirits (gallons/capita/yr)	Beer (gallons/capita/yr)	Cigarettes (per 100/capita/yr)	
Mouth (floor)-----	143	M	0.72	1.08	0.005 \pm 0.001*	0.038 \pm 0.063	0.001 \pm 0.005	0.004 \pm 0.007	
Nasopharynx-----	146	F	.33	0.34	0.001 \pm 0.000	-0.000 \pm 0.018	0.000 \pm 0.001	-0.002 \pm 0.002	
Buccal cavity and pharynx-----	140-8	M	.54	4.73†	0.000 \pm 0.001	0.166 \pm 0.053†	-0.006 \pm 0.004	-0.004 \pm 0.006	
Isophagus-----	150	F	.60	6.38†	-0.041 \pm 0.000	0.042 \pm 0.021	-0.001 \pm 0.002	0.003 \pm 0.002	
Stomach-----	151	M	.48	3.52†	0.041 \pm 0.013†	0.490 \pm 0.626	-0.027 \pm 0.048	0.092 \pm 0.071	
Small intestine-----	152	M	.82	11.40*	0.005 \pm 0.003	1.107 \pm 0.438†	-0.039 \pm 0.013†	0.009 \pm 0.019	
Colon-----	153	F	.67	9.61*	-0.006 \pm 0.004	0.602 \pm 0.182†	0.091 \pm 0.034†	0.006 \pm 0.050	
Rectum-----	154	M	.67	8.12*	0.002 \pm 0.026	1.794 \pm 1.287	-0.018 \pm 0.014	0.012 \pm 0.021	
Liver-----	155	F	.62	6.33†	-0.001 \pm 0.015	0.804 \pm 0.742	0.459 \pm 0.100*	0.286 \pm 0.146	
Pancreas-----	157	M	.55	5.32†	0.003 \pm 0.002	0.180 \pm 0.076†	0.239 \pm 0.057*	-0.156 \pm 0.084	
Digestive organs-----	150-155 157-159	F	.66	9.20*	-0.002 \pm 0.001†	0.009 \pm 0.046	0.003 \pm 0.006	0.000 \pm 0.009	
Larynx-----	161	M	.80	15.54*	0.041 \pm 0.025	0.794 \pm 1.264	0.345 \pm 0.098†	0.009 \pm 0.005	
Lung-----	162-3	F	.82	14.03*	-0.003 \pm 0.023	0.771 \pm 1.123	0.291 \pm 0.066*	0.238 \pm 0.143	
Respiratory organs-----	160-4	M	.76	10.85*	0.031 \pm 0.018	0.429 \pm 0.854	0.301 \pm 0.087*	0.403 \pm 0.127*	
Breast-----	170	F	.65	7.56*	0.005 \pm 0.010	-0.016 \pm 0.211	0.136 \pm 0.038*	0.080 \pm 0.056	
Cervix-----	171	M	.49	3.84†	0.015 \pm 0.004†	0.880 \pm 0.378†	0.016 \pm 0.016	-0.014 \pm 0.024	
Prostate-----	177	F	.73	12.95†	0.009 \pm 0.008	1.354 \pm 0.435†	0.114 \pm 0.029*	-0.026 \pm 0.043	
Kidney-----	180	M	.84	17.20*	-0.024 \pm 0.008†	1.819 \pm 0.396*	0.003 \pm 0.034	-0.080 \pm 0.049	
Bladder-----	181	F	.80	16.94*	0.100 \pm 0.065	6.038 \pm 3.175	1.221 \pm 0.031	-0.037 \pm 0.045	
Thyroid-----	194	M	.70	3.00†	-0.020 \pm 0.044	1.638 \pm 2.142	0.792 \pm 0.166*	-0.061 \pm 0.360	
Leukemia-----	204	F	.42	2.51	0.000 \pm 0.001	0.024 \pm 0.320	0.004 \pm 0.025	0.293 \pm 0.243	
		F	.67	5.54†	0.142 \pm 0.067†	2.612 \pm 3.290	-0.006 \pm 0.003†	0.063 \pm 0.036	
		M	.70	9.29*	0.008 \pm 0.008	0.521 \pm 0.411	-0.408 \pm 0.255	0.007 \pm 0.004	
		F	.67	3.28†	0.164 \pm 0.073†	2.510 \pm 3.562	-0.072 \pm 0.032†	0.804 \pm 0.373†	
		M	.70	9.18*	0.009 \pm 0.009	0.438 \pm 0.420	-0.400 \pm 0.276	0.126 \pm 0.047†	
		F	.83	15.85*	0.032 \pm 0.025	1.883 \pm 1.208	0.082 \pm 0.033†	0.872 \pm 0.404†	
		F	.62	6.11†	-0.019 \pm 0.018	-3.148 \pm 0.872*	-0.456 \pm 0.093*	0.137 \pm 0.137	
		M	.45	2.71	0.018 \pm 0.018	0.898 \pm 0.859	-0.136 \pm 0.067	0.025 \pm 0.048†	
		M	.77	14.69*	0.003 \pm 0.004	0.268 \pm 0.206	0.162 \pm 0.066†	0.370 \pm 0.099*	
		F	.60	6.39†	0.009 \pm 0.004	-0.114 \pm 0.174	0.083 \pm 0.016*	-0.071 \pm 0.097	
		M	.82	11.05*	0.026 \pm 0.011	0.622 \pm 0.522	0.058 \pm 0.014*	-0.009 \pm 0.023	
		F	.61	3.86†	0.004 \pm 0.004	0.012 \pm 0.201	0.144 \pm 0.040†	-0.008 \pm 0.020	
		M	.47	0.56	0.002 \pm 0.001	0.042 \pm 0.047	0.016 \pm 0.016	-0.034 \pm 0.059	
		F	.73	9.09*	0.004 \pm 0.001†	-0.123 \pm 0.062	0.002 \pm 0.004	-0.003 \pm 0.005	
		M	.63	4.95†	-0.012 \pm 0.005†	-0.474 \pm 0.226†	0.019 \pm 0.005*	-0.012 \pm 0.007	
		F	.62	4.93†	-0.006 \pm 0.003†	-0.320 \pm 0.138†	0.045 \pm 0.018†	-0.012 \pm 0.026	

*P<0.001.
†P<0.01.
‡P<0.05.



TEXT-FIGURE 2.—Scattergram showing relationship between apparent 1960 per-capita beer consumption and estimated average annual age-adjusted incidence rates, 1960-62 (approx.), for rectal cancer among males in 24 countries.

TABLE 4.—Simple correlations between per-capita consumption of alcoholic beverages and estimated site-specific, age-adjusted incidence rates for 24 countries shown in text-figure 2

Coefficients of 0.52 and higher for wine and beer and 0.53 and higher for spirits are statistically significant ($P < 0.01$).

Site	ICD Nos. (Sixth and Seventh Revisions)	Sex	Spirits*	Wine	Beer
Esophagus.....	150	M	0.17	0.53	-0.28
Stomach.....	151	M	.12	-.07	-.40
Colon.....	153	M	-.16	.05	.58
Rectum.....	154	M	-.16	.04	.83
Lung (primary).....	162-3	M	-.11	-.17	.55
Breast.....	170	F	-.16	-.31	.30
Prostate.....	177	M	.08	.13	.44
Leukemia.....	204	M	.51	.04	.06

*Japan omitted from the calculation of spirits correlations due to inadequate data (?).

% urban were available for the 24 countries (22), cigarette consumption was estimated for some of them (23). Consumption figures for the 3 types of alcoholic beverages did not correlate as well for the countries as they did for the 41 States of the United States (table 1), so that the relationships in table 4 should be relatively free from the effects of other alcoholic beverages.

DISCUSSION

Sources of Error

Sources of error in the basic data used are well recognized and discussed in the source documents (5, 17). For incidence rates these relate mainly to completeness of reporting and problems of diagnosis

TABLE 5.—Annual alcohol consumption in liters per capita for 1960

Beverage	24 countries			41 States of the United States		
	Mean	SD	Range	Mean	SD	Range
Spirits*-----	3.4	1.5	1.2- 6.0	4.7	1.7	2.3- 9.2
Wine-----	20.0	35.5	0.1-126.9	2.7	1.6	0.6- 7.9
Beer-----	50.6	35.3	3.0-112.0	54.1	16.9	19.7-96.9

*Japan omitted from the calculation of spirits consumption due to inadequate data (27).

and coding; for exposure data, to the discrepancies between tax-paid deliveries and actual consumption.

Many additional problems complicate the interpretation of correlation studies; it is therefore not surprising that results are often inconsistent (24, 25). Difficulties arise particularly from the use of populations as sampling units, the long latent interval for most human cancers, and the presence of multiple etiologic agents.

Population versus individuals as sampling units.—In a correlation study, population incidence or mortality rates are related to per-capita (average) levels of exposure. Since the true interest is in individual risk as determined by individual exposure, such a study is fully justified only in that ideal situation in which each individual within a population has the same exposure. With the heterogeneity of exposure observed in real situations, 2 problems emerge. 1) The relationship based on average exposures need not reflect the individual dose-response relationship; populations with identical per-capita exposures may differ markedly in the distribution of exposure levels and consequently, depending on the shape of the individual dose-response relationship, in overall incidence. 2) Ignoring the within-population variation in exposures results in a loss of the detailed information needed to sort out the effects of different environmental agents.

Correspondence between consumption and incidence populations.—Official statistics on consumption usually concern populations delineated by national or regional boundaries. Incidence data from cancer registries often are limited to smaller populations. A greater degree of correspondence can be achieved with official or semiofficial mortality statistics, though with these the problem is that the ratio of mortality to incidence need not be constant over the populations of interest.

Mortality or incidence data may be given for population subgroups, e.g., by sex and race, for which no corresponding breakdown on consumption is available. Errors arise from the fact that per-capita rates of consumption for each of the sex/race categories may not be in a constant proportion in the population groups considered. For the U.S. population, alcohol and tobacco consumption figures might be thought to be most representative of the white (especially male) subgroups used here. Some authors (1, 2) prefer to base their calculations on overall mortality figures, with or without adjustment for race and sex in addition to age. The figures adjusted for age alone would seem to make sense if it were thought that the race and sex differences in mortality were due mostly to

differences in the environmental exposures under study. None of these solutions is entirely satisfactory.

Exposures to other etiologic agents.—For most cancers, many environmental and other factors are known or suspected to be etiologically significant. In addition to tobacco and alcohol, the confounding effects of diet and such specific urban hazards as air pollution should be especially mentioned. Adjustment for such variables in correlation studies is hampered by problems in obtaining comparable data, by the high degree of confounding (table 1), and by the few units available for analysis. Moreover, the multiple regression approach used here represents only the most rudimentary type of adjustment.

Cancers in some regions may be caused by agents having no relation to any of the quantities measured. No appreciable quantities of alcohol and tobacco, for example, are used in the Caspian littoral, an area with a high incidence of esophageal cancer, which is as yet unexplained (26). Inclusion of this region in a correlation study of countries for which alcohol and tobacco were the major etiologic factors could severely distort the results.

Latency.—No attempt has been made here to measure per-capita exposures during the 20- to 30-year period, which presumably covers the range of latent intervals for many cancers. This could be a serious drawback because tobacco and alcohol consumption has generally been increasing over the last decades and at a variable rate. For example (17), the percentage change in apparent per-capita total alcohol consumption between 1947 and 1970 ranged from -9% (W. Va.) to 200% (Vt.) for 38 of the 41 States considered in this study (Alaska, Kans., and Okla. omitted). Likewise, the percentage changes in apparent consumption for 18 countries over a 10- to 11-year period ranged from -14.4% (Israel) to +117.6% (Netherlands). However, the correlation between the 2 sets of figures was 0.97 for the countries and 0.79 for the States, which indicates that, especially for the countries, their relative positions have not changed that much. In any event, migration of large population units, as within the United States, makes problematic the comparison, on a geographic basis, of current incidence with past exposure.

Site-Specific Associations

Respiratory cancer and cigarette smoking.—Some confidence in the validity of the statistical methods of this study can perhaps be derived from the fact that they identified apparent cigarette consumption as the factor most closely related to respiratory cancers

(27), and that only this factor and % urban gave significant positive effects in the regression analyses. However, surprisingly, these results were not any more significant than those relating the consumption of alcohol with the development of cancer.

Esophageal cancer and spirits.—Consumption of spirits and (in males) beer was related in this study to the development of cancer of the esophagus, even after adjustment for % urban. This finding differs somewhat from that of a previous study (1) of the same States and exposures (omitting wine and beer). There, the partial correlation between development of cancer and consumption of spirits was calculated after adjustment for both % urban and cigarettes. Due to the high correlation between spirits and cigarette consumption, neither of these 2 variables was significantly related to esophageal cancer after adjustment for the other, though the 2 together were so related. The somewhat different cancer statistics used in the present paper identified spirits rather than cigarettes as the agent primarily responsible for this relationship. However, the uncertainties in this process, discussed above, need to be constantly borne in mind.

Evidence for an association between the development of esophageal cancer and the amount of alcohol consumed comes from both correlation and case-control studies (28–31). A study (31) involving 150 American males with esophageal cancer found the risk of developing esophageal cancer for a heavy whiskey drinker to be 25 times higher than that for a nondrinker, even when tobacco consumption was held constant. The risk for beer drinkers was 10 times higher. The present study seems to support these findings on a geographic basis.

Large-bowel cancer and beer drinking.—Although a relationship between large-bowel cancer and beer drinking has been suggested in some previous reports, the literature is not as consistent in this regard as for the previously discussed associations. Large-bowel cancer and beer drinking were associated (32) in 6 geographic areas of England and Wales. Some case-control studies (33, 34) gave negative results, another report (25) revealed 35 and 31% of males with rectal and colonic cancers, respectively, to be beer drinkers, compared with 19% of one control group. However, there were no such differences for women or on comparison with another male control group. A follow-up study of 1722 male Norwegian "alcoholics" revealed a slight excess of deaths due to rectal cancer in comparison with mortality figures for all Norway (35). A more recent follow-up study of 12,000 Norwegian men aged 45 years or more revealed a dose-response relationship for the risk of colorectal cancer and reported frequency of use of beer and spirits, with beer showing the steepest gradient (36). Only 45 colorectal cancers have appeared so far and more observation is needed to confirm these results.

One current hypothesis concerning large-bowel cancer is that dietary constituents, particularly fats or fibers, influence the types and amounts of bacteria and steroids in the gut and thus the concentration of possible carcinogens (24, 37). Therefore, it would be desirable to correct the associations found here for

dietary factors. Nevertheless, the associations (text-figs. 1, 2) seem sufficiently strong to suggest on their own that beer drinking also be considered in the etiology of large-bowel cancer in future investigations.

Other relationships.—These results confirmed 2 widely accepted relationships: those between cigarette smoking and respiratory cancers and those between alcohol consumption and esophageal cancer. They strongly suggested a relationship between beer drinking and colorectal cancer. A number of other relationships are also suggested by table 3: between beer drinking and cancers of the stomach, small intestine (female), liver (female), breast (female), kidney, and bladder (male); between consumption of spirits and cancers of the nasopharynx and small intestine (males) and pancreas (females); and between cigarette smoking and cancer of the colon (female). Although several of these sites already have been linked to alcohol or tobacco consumption, notably bladder cancer to cigarettes (2, 38), their possible significance will not be discussed in detail here. To do so would constitute an over-interpretation of the data and lend more credence to the methodology than is warranted. Indeed, the very lack of site specificity in the presumed effects of beer drinking argues against attaching too much etiologic significance to the findings already discussed: The results could simply indicate that certain categories of persons suffer increased mortality from a wide range of causes, as has been amply demonstrated for cigarette smokers (39). In studies of the etiology of human cancer, correlation results, however striking, must await confirmation and explanation by direct observation of individual human beings.

REFERENCES

- (1) SCHOENBERG BS, BAILAR JC III, FRAUMENI JF JR.: Cancer mortality patterns of esophageal cancer in the United States, 1930–67. *J Natl Cancer Inst* 46:63–73, 1971
- (2) FRAUMENI JF JR: Cigarette smoking and cancers of the urinary tract: Geographic variations in the United States. *J Natl Cancer Inst* 41:1205–1211, 1968
- (3) ENSTROM JE: Cancer mortality and alcohol-tobacco consumption. Unpublished data to be submitted for publication
- (4) STOCKS P: Cancer mortality in relation to national consumption of cigarettes, solid fuel, tea, and coffee. *Br J Cancer* 24:215–225, 1970
- (5) BURBANK F: Patterns in cancer mortality in the United States: 1950–1967. *Natl Cancer Inst Monogr* 33:1–594, 1971
- (6) World Health Organization: Manual of the International Classification of Diseases, Injuries, and Causes of Death. Sixth Revision of the International List of Diseases and Causes of Death, adopted 1948, vol 1. Geneva, Switzerland, WHO, 1948
- (7) ———: Manual of the International Classification of Diseases, Injuries, and Causes of Death. Seventh Revision of the International List of Diseases and Causes of Death, adopted 1955, vol 1. Geneva, Switzerland, WHO, 1955
- (8) Wine Institute: Economic Research Report, No. ER-3, Sept. 26, 1968. San Francisco, Calif., Wine Institute, 1968
- (9) Distilled Spirits Institute: Annual Statistical Review: The Distilled Spirits Industry—1960. Washington, D.C., Distilled Spirits Institute, 1960, p 39
- (10) U.S. Brewers Association: Brewers Almanac 1966. New York, U.S. Brewers Association, 1966, p 56

- (11) FRIEDMAN GD: Cigarette smoking and geographic variation in coronary heart disease mortality in the United States. *J Chron Dis* 20:769-779, 1967
- (12) National Tobacco Tax Association: Comparative cigarette tax collections, per capita cigarette tax collections, per capita cigarette consumption by states for 1960. Chicago, Ill., National Tobacco Tax Association, 1961
- (13) U.S. Bureau of the Census: Census of Population: 1960, vol I, Characteristics of the Population, Part I, United States Summary. Washington, D.C., U.S. Govt Print Off, 1964
- (14) DIXON WJ, ed.: Biomedical Computer Programs. Berkeley, Los Angeles, London, Univ California Press, 1971, pp 233-259d
- (15) SNEDECOR GW, COCHRAN WG: Statistical Methods, 6th ed. Ames, Iowa, Iowa State Univ Press, 1967, pp 560-568
- (16) McDONALD GC, SCHWING RC: Instabilities of regression estimates relating air pollution to mortality. *Technometrics* 15:463-481, 1973
- (17) Rutgers Center of Alcohol Studies: Statistics on Consumption of Alcohol and on Alcoholism, 1972 ed. New Brunswick, N.J., Rutgers Center of Alcohol Studies, 1972
- (18) DOLL R: The geographical distribution of cancer. *Br J Cancer* 23:1-9, 1969
- (19) DOLL R, PAYNE P, WATERHOUSE J, eds.: International Union Against Cancer: Cancer Incidence in Five Continents. U.I.C.C. Technical Report. Berlin, Springer-Verlag, 1966
- (20) SEGI M, KURIHARA M: Cancer mortality for selected sites in 24 countries, No. 3 (1960-1961). Sendai, Japan, Department of Public Health, Tohoku Univ School of Medicine, 1964
- (21) Produktschap voor Gedistilleerde Dranken: Hoeveel alcoholhoudende dranken worden er in de wereld gedronken? 12e Uitgave. Produktschap voor Gedistilleerde Dranken, Schiedam-Nederland, 1973
- (22) United Nations: Demographic Yearbook 1971. New York, United Nations, 1972, p 139ff
- (23) BEESE DH, ed.: Tobacco Research Council: Tobacco Consumption in Various Countries, 2d ed. Research Paper 6. London, Tobacco Research Council, 1968
- (24) DRASAR B, IRVING D: Environmental factors and cancer of the colon and breast. *Br J Cancer* 27:167-172, 1973
- (25) WYNDER E, SHIGEMATSU F: Environmental factors of cancer of the colon and the rectum. *Cancer* 20:1520-1561, 1967
- (26) KMET J, MAHBOUBI E: Esophageal cancer in the Caspian littoral of Iran: Initial studies. *Science* 175:846-852, 1972
- (27) U.S. Public Health Service: Smoking and Health: Report of the Advisory Committee to the Surgeon General of the Public Health Service. U.S. PHS Publ No. 1103, 1963
- (28) SCHWARTZ D, LASSERRE O, FLAMANT R, et al: Alcohol et cancer—étude de pathologie géographique portant sur 19 pays. *Eur J Cancer* 2:367-372, 1966
- (29) TUYNS A: Personal communication
- (30) SCHWARTZ D, DENOIX P, ANGUERRA G: Recherche des localisations du cancer associés aux facteurs tabac et alcool chez l'homme. *Bull Assoc Fr Etude Cancer* 44:336-361, 1957
- (31) WYNDER E, BROSS I: A study of etiological factors in cancer of the esophagus. *Cancer* 14:389-413, 1961
- (32) STOCKS P: Cancer in North Wales and Liverpool Region. British Empire Cancer Campaign, 35th Annual Report (Suppl II), 1957, pp 51-113
- (33) HIGGINSON J: Etiological factors in gastrointestinal cancer in man. *J Natl Cancer Inst* 37:527-545, 1966
- (34) PERNU J: An epidemiological study on cancer of the digestive organs and respiratory system—a study based on 7078 cases. *Ann Med Intern Fenn* 49 (Suppl 33): 1-117, 1960
- (35) SUNDBY P: Alcoholism and Mortality. Oslo, Universitetsforlaget, 1967
- (36) BJELKE E: Personal communication
- (37) BURKITT D: Epidemiology of cancer of the colon and rectum. *Cancer* 28:3-13, 1971
- (38) WYNDER EL, ONDERDONK J, MANTEL N: An epidemiological investigation of cancer of the bladder. *Cancer* 16:1388-1407, 1963
- (39) KAHN HA: The Dörn study of smoking and mortality among U.S. veterans: Report on eight and one-half years of observation. *Natl Cancer Inst Monogr* 19:1-126, 1966