Air Pollution in Relation to U.S. Cancer Mortality Rates: An Ecological Study; Likely Role of Carbonaceous Aerosols and Polycyclic Aromatic Hydrocarbons

WILLIAM B. GRANT

Sunlight, Nutrition and Health Research Center (SUNARC), San Francisco, CA, U.S.A.

Abstract. *Background: There are large geographical variations of cancer mortality rates in the United States. In a series of ecological studies in the U.S., a number of risk-modifying factors including alcohol, diet, ethnic background, poverty, smoking, solar ultraviolet-B (UVB), and urban/rural residence have been linked to many types of cancer. Air pollution also plays a role in cancer risk. Materials and Methods: Cancer mortality rates averaged by state for two periods, 1950-1969 and 1970-1994, were used in multiple-linear regression analyses with respect to many of the risk-modifying factors mentioned with the addition of an air pollution index in the form of a map of acid deposition in 1985. This index is correlated with emissions from coal-fired power plants. In addition, lung cancer mortality rates for five-year periods from 1970-74 to 1990-94 were used in multiple linear regression analyses including air pollution and cigarette smoking. Results: The air pollution index correlated with respiratory, digestive tract, urogenital, female, blood and skin cancer. Air pollution was estimated to account for 5% of male cancer deaths and 3% of female cancer deaths between 1970-1994. Solar UVB was inversely correlated with all these types of cancer except the respiratory, skin and cervical cancer. Cigarette smoking was directly linked to lung cancer but not to other types of cancer in this study. Conclusion: Combustion of coal, diesel fuel and wood is the likely source of air pollution that affects cancer risk on a large scale, through production of black carbon aerosols with adsorbed polycyclic aromatic hydrocarbons.*

Correspondence to: William B. Grant, Ph.D., Sunlight, Nutrition and Health Research Center (SUNARC), P.O. Box 641603, San Francisco, CA 94164-1603, U.S.A. Tel: +1 4154091980, e-mail: wbgrant@infionline.net

There are large-scale variations in cancer mortality rates in the United States: For the period 1970–1994, rates for white males were higher in the eastern United States than in the western United States, whereas for white females, rates were highest in the northeast and west. In 1950–1969, rates for white males were highest in the northeast, Louisiana and California, whereas for white females, they were highest only in the northeast. Previous ecological studies first investigated the correlations with solar ultraviolet-B (UVB) doses (1-6). More recently, additional factors have also been included: alcohol consumption, ethnic background, poverty level, lung cancer (an index for smoking), and urban *versus* rural residence (7, 8). Although these investigations have yielded results in general agreement with the literature for many of the factors and have added several types of cancer to the list of those for which solar UVB and vitamin D appear to be protective, there is always the possibility that, as new indices become apparent, they can be added to the analysis to develop better models to explain the geographic variation of U.S. cancer mortality rates.

Another important factor for cancer is air pollution, primarily from fossil fuel combustion. Particulates were identified as the pollutant most highly correlated with mortality rates from air pollution in the U.S. (9). An article in 2002 reported that each 10 μg/m^3 elevation in fine particulate air pollution was associated with approximately a 4%, 6% and 8% increased risk of all-cause, cardiopulmonary and lung cancer mortality, respectively (10). A more recent study found that a 10 μg/m^3 increase in the yearly average PM2.5 (air pollutants particles with a diameter of 2.5 micrometers or less) is associated with 10.9% (95% confidence interval=9.0%-12.8%) and 20.8% (95% confidence interval=14.8%-27.1%) increases in all-cause mortality for the American Cancer Society and Harvard Six Cities study counties, respectively (11). Air pollution levels are generally higher in the eastern United States than in the west (12) because of such factors as the prevailing westerly winds that bring air from over the Pacific Ocean to the west and a higher population and industrial density in the east, which thus uses more fossil fuels.

Many of the studies on the effects of air pollution and cancer identify aerosols and polycyclic aromatic hydrocarbons (PAHs) such as benzo(a)pyrene as the components seemingly most associated with cancer risk (13). Aerosols associated with transportation, coal combustion and wood burning have higher benzo[a]pyrene concentrations (14-16). In contrast, oil combustion is not a major source of PAHs (17). PAHs are adsorbed onto many types of solid aerosols, including black carbon and road dust, and when they reach the lungs, PAHs can be activated, having cytotoxic effects (18) and possibly generating DNA adducts (19, 20).

More recently, adenocarcinoma of the lung (ADL) time trends and geographic patterns seemed to be strongly correlated with atmospheric emissions of nitrogen oxides (NOx) (21). ADL rates started to rise rapidly in the 1970s, about 10-20 years after an equally fast rise in NOx levels, and ADL rates were about twice as high in regions with high NOx emissions than in regions with low NOx emissions. ADL accounted for about 35% of lung cancer cases in 1973-1994 on the basis of Surveillance, Epidemiology and End Results (SEER) (22) data. During that period, rates for squamous cell lung carcinoma and small cell lung cancer peaked in the late 1970s or early 1980s.

Thus, there is good evidence that ambient air pollution increases the risk of lung cancer. This report presents an ecological study of cancer mortality rates in the U.S. with respect to a suitable index for air pollution, as well as several other cancer risk-modifying factors.

Materials and Methods

The data and methods used in this study are similar to those used in a previous study (7). Details of why each index was chosen are given therein.

Age-adjusted, gender-specific and race-specific cancer mortality rates were obtained from the National Cancer Institute's Atlas of Cancer Mortality in the United States (23). This study used state-averaged data for whites for the periods 1950-1969 and 1970-1994, age adjusted to the age distribution of the total U.S. population in 1970.

DNA-weighted UVB data for July 1992 derived from Total Ozone Mapping Spectrometer measurements (24) were determined for each state. This index is highly asymmetric, with highest doses in the southwest and lowest doses in the northeast. This asymmetry is due to two factors: higher surface elevation in the west and the thinner stratospheric ozone layer west of the Rocky Mountains.

Data on smoking prevalence by state were obtained from Shopland *et al*. (25). The respective minimum, maximum and mean values were 18.9%, 39.5% and 32.6% (standard deviation, 4.2%) for males and 10.6%, 34.9% and 26.0% (standard deviation, 3.9%) for females. The 95% confidence intervals of the data in (25) were reported as between 3% and 9%. Lung cancer mortality rates were used as the index of the health effects of smoking. Lung cancer death rates are a good index of tobacco smoke exposure for approximating non-lung cancer death rates in black men (26). This index yielded correlations with cancer mortality rates in previous ecological studies that are in good agreement with the literature (7, 8, 27).

For the period 1950-1969, data on alcohol consumption (gallons of ethanol per capita of the drinking-age population) for 1960-1962 were obtained from the Center of Alcohol Studies, Rutgers University (28). Additional data starting with 1970 were available from the National Institutes of Alcohol Abuse and Alcoholism (29). The 1970 data were used for the period 1970-1994. Alcohol consumption rates vary slowly, and the relative consumption rates stay somewhat constant.

Hispanic heritage is a known risk factor for several types of cancer (30). The category "white Americans" includes people of Hispanic heritage. This analysis included the proportion of white Americans in each state considered Hispanic. The values used here were for 1980, the earliest year for which comprehensive data were available (31).

The fraction of each state's population living in urban areas from 1940 to 1970 was obtained from the U.S. Census Bureau (32). Data for 1960 were used for the period 1950-1969, whereas data for 1970 were used for the period 1970-1994.

The index used for poverty in this study was the fraction of inhabitants living below the poverty level in 1969 (33).

The National Atmospheric Deposition Program has made a series of maps of acid precipitation. The maps represent kriged data based on measurements at about 100 field laboratories around the country. Maps are available for hydrogen, nitrate, sulfate and various minerals. The index chosen for air pollution was hydrogen ion concentration as pH from measurements made at the field laboratories (34). In the web site where the National Atmospheric Deposition Program pH maps are archived, the oldest available one is for 1994. A map from 1985 was kindly provided by Roger Claybrooke (University of Illinois). It is the oldest map that has data from a large number of stations. As can be seen at the web site, pH is lowest (4.2) in regions around Ohio and Pennsylvania, a region with large emissions from coal-fired power plants, and highest (5.2-5.8) in the western half of the country. That this map is representative of carbon emissions from fossil fuel combustion, especially from coal-fired power plants, is strongly supported by a modeling study of carbonaceous aerosols (35) based on an inventory of fossil fuel emission data for 1984 (36). Data from these maps were digitized for each state on the basis of an estimate of the pH value at the center of population for each state.

The data were used in multiple linear regression analyses with the SPSS version 13.0 (Chicago, IL, USA). The square roots of the mortality rates were used in the analysis to reduce the effect of extreme values. However, the regression results using the actual values rather than the square roots were not noticeably different. Most factors were initially used in the analysis for each cancer, but only factors that were statistically significant in at least one analysis for the particular cancer were retained in the final result.

The correlations between the various factors used in this study are presented in Table I. Many of the factors are highly correlated with other factors. In the analysis, highly correlated factors were examined individually to help ensure that the results were not due to interactions between the independent factors.

Results

The regression results are given in Tables II and III. Twelve cancers, as well as all excluding lung cancer, were directly correlated with the index of air pollution in this study: respiratory (oral, nasopharyngeal, laryngeal and lung),

Table I. *Correlations between the factors used in this study for 1970-1994.*

Factor	Hispanic (r, p)	Lung cancer, M (r, p)	Lung cancer, F (r, p)	pH (r, p)	Poverty (r, p)	Urban (r, p)	UVB (r, p)
Alcohol	0.13, 0.37	–0.17, 0.24	0.35, 0.015	–0.17, 0.25	–0.40, 0.005	0.42, 0.003	–0.13, 0.37
Hispanic		–0.30, 0.03	0.07, 0.64	0.22, 0.13	0.03, 0.85	0.39, 0.005	0.57, *
Lung cancer, M			0.67, *	–0.60, *	0.41, 0.004	–0.22, 0.12	–0.006, 0.97
Lung cancer, F				–0.40, 0.005	–0.06, 0.67	0.17, 0.25	0.06, 0.68
pH					0.04, 0.80	–0.10, 0.50	0.37, 0.01
Poverty						–0.44, 0.001	0.47, 0.001
Urban							0.14, 0.33

*$p<0.001$.

Table II. *1970-1994 cancer regressions.*

Cancer	Gender	pH 1985 (β, p)	Lung cancer (β, p)	UVB or latitude[2a] (β, p)	Alcohol 1970 (β, p)	Poverty 1969 (β, p)	Urban 1970 (β, p)	Hispanic 1980 (β, p)	Adjusted R^2, F, p
All less lung	M	–0.56,*		–0.35,*	0.30,*				0.73, 44,*
	F	–0.38,*	0.16, 0.02	–0.57,*	0.13, 0.04	–0.22, 0.009		0.23, 0.004	0.87, 51,*
Nasopharyngeal	M	–0.23, 0.10	0.52,*				0.44,*		0.55, 20,*
	F	–0.39, 0.003	0.37, 0.004				0.20, 0.06		0.48, 15,*
Oral	M	–0.53,*	0.23, 0.03		0.46,*				0.73, 43,*
		–0.68,*			0.39,*				0.70, 57,*
	F	–0.16, 0.13	0.39, 0.001		0.48,*				0.58, 23,*
Esophageal	M	–0.45,*		–0.32,*	0.39,*	–0.25,*			0.87, 82,*
	F	–0.19, 0.02	0.34,*	–0.31, 0.001	0.53,*			0.17, 0.05	0.79, 37,*
Colon	M	–0.41,*		–0.59,*			0.36,*		0.78, 57,*
	F	–0.49,*		–0.39,*		–0.30, 0.001			0.72, 42,*
Rectal	M	–0.32,*		–0.68,*		–0.28, 0.001		0.28, 0.002	0.81, 50,*
	F	–0.40,*		–0.51,*		–0.35, 0.001		0.23, 0.03	0.72, 32,*
Laryngeal	M	–0.65,*	0.25, 0.01		0.26, 0.001				0.77, 55,*
	F	–0.45,*	0.32, 0.001		0.42,*				0.73, 45,*
Lung [omit Nevada (NV)]	M	–0.71,*			–0.27, 0.008	0.36, 0.001			0.63, 28,*
(with NV)		–0.62,*				0.43,*			0.53, 28,*
(with NV)	F	–0.35, 0.01			0.29, 0.03				0.21, 7.2, 0.002
(omit NV)		–0.50,*							0.23, 15,*
Other skin	M	–0.30, 0.01	0.30, 0.03	–0.37, 0.001		0.38, 0.002			0.69, 27,*
	F	–0.37, 0.004			–0.33, 0.001	0.38, 0.009			0.37, 10,*
Breast	F	–0.25,*		–0.42,*	0.27,*	–0.27, 0.001	0.24, 0.002		0.87, 65,*
Cervical	F	–0.41,*	0.38,*				–0.49,*		0.54, 20,*
Endometrial	F			–0.54,*		–0.38, 0.002	0.19, 0.06		0.71, 39,*
Bladder	M	–0.19, 0.07	–0.39, 0.001	–0.21, 0.02	0.27, 0.001	–0.57,*			0.77, 34,*
	F	–0.45,*	0.35,*	–0.17, 0.03	0.26, 0.001	–0.21, 0.009			0.82, 46,*
Hodgkin's lymphoma	M			–0.80,*		0.33, 0.04	0.35, 0.01		0.40, 12,*
	F	–0.40,*		–0.54,*			0.23, 0.01		0.62, 27,*

[a]Latitude^2 for other skin cancer; UVB for all other cancer; *$p<0.001$.

digestive tract (esophageal, colon, rectal), bladder, female organs (cervical, endometrial and breast), and blood cancer (Hodgkin's lymphoma). Most of these types of cancer were correlated with lung cancer in the period 1970-1994; endometrial cancer and Hodgkin's lymphoma were not correlated in this study nor a previous one (7); colon and rectal cancer were not correlated with lung cancer for the period 1970-1994 in this study but were in the previous study (7). For the period 1970-1994, the adjusted R^2 values were 0.03 to 0.20 higher than in the previous work for males, except for Hodgkin's lymphoma for males, probably due to the low mortality rate and paucity of data. The corresponding

Table III. *1950-1969 cancer regressions*.

Cancer	Gender	pH 1985 (β, p)	Lung cancer (β, p)	UVB or latitude[2a] (β, p)	Alcohol 1960 (β, p)	Poverty 1969 (β, p)	Urban 1960 (β, p)	Hispanic 1980 (β, p)	Adjusted R^2, F, p
All less lung	M		0.27,*	–0.61,*	0.15, 0.06		0.36,*		0.84, 62,*
		–0.20, 0.009		–0.58,*			0.54,*		0.80, 63,*
	F	–0.29,*		–0.74,*	0.14, 0.04		0.23, 0.003	0.20, 0.007	0.88, 71,*
Oral	M	–0.47,*	0.28,*				0.34,*		0.82, 72,*
	F	–0.27, 0.03				–0.61,*			0.39, 15,*
Esophageal	M	–0.40,*		–0.33,*	0.30,*		0.34,*		0.85, 71,*
	F	–0.46,*	0.39, 0.001						0.53, 28,*
Colon	M	–0.20, 0.001		–0.62,*			0.56,*		0.87, 109,*
	F	–0.36,*		–0.50,*		–0.24, 0.01	0.24, 0.006		0.84, 63,*
Rectal	M		0.20, 0.008	–0.56,*		–0.31, 0.001	0.28, 0.003		0.85, 68,*
	F	–0.30,*		–0.42,*	0.29, 0.001	–0.34, 0.001			0.77, 41,*
Laryngeal	M	–0.40,*	0.48,*		0.31,*				0.90, 143,*
	F	–0.42, 0.002	0.40, 0.003			0.35, 0.008			0.44, 11,*
Lung	M	–0.54,*				0.22, 0.05	0.49,*		0.57, 22,*
	F	–0.50,*					0.27, 0.03	0.30, 0.02	0.44, 14,*
Other skin	M			–0.66,*	–0.21, 0.007	0.25, 0.01		–0.20, 0.005	0.81, 53,*
	F			–0.41, 0.002		0.51,*		–0.28, 0.004	0.68, 32,*
Breast	F			–0.65,*	0.23, 0.002		0.46,*		0.88, 115,*
Cervical	F	–0.63,*	0.27, 0.05	0.33, 0.006			–0.54,*		0.54, 15,*
Endometrial	F	–0.47,*		–0.35,*	–0.34, 0.008	–0.29, 0.004			0.52, 14,*
Bladder	M		0.42,*	–0.27,*	0.31,*	–0.35,*			0.83, 58,*
			0.28, 0.001	–0.43,*	0.34,*		0.28, 0.005		0.79, 47,*
	F	–0.65,*			0.47,*				0.74, 68,*
Hodgkin's lymphoma	M			–0.56,*					0.30, 21,*
	F			–0.67,*			0.25, 0.02		0.49, 23,*

[a]Latitude[2] for other skin cancer; UVB for all other cancer; *$p<0.001$.

values for females are –0.02 to 0.17. For the period 1950-1969, the differences ranged from –0.01 to 0.02 for males and from –0.05 to 0.26 for females. Thus, it appears as if this air pollution index had little effect on male cancer in the earlier period.

Solar UVB was inversely correlated with the digestive and elimination organs, two of the female organs (breast and endometrial cancer), and Hodgkin's lymphoma in the second period, in agreement with the previous study (7). However, UVB was no longer significantly inversely correlated with laryngeal cancer as reported in (7).

Alcohol was correlated with several of the respiratory organ cancers (oral, nasopharyngeal and laryngeal), two of the digestive/elimination organ cancers (esophageal and bladder), and one female organ cancer (breast). The alcohol index is more appropriate for males than females because males drink more than females. Results were similar to those for the first period.

Urban residence was directly correlated with all excluding lung, one respiratory cancer (nasopharyngeal), two female organ cancers (breast and endometrial), and Hodgkin's lymphoma, and it was inversely correlated with cervical cancer in both periods.

Table IV. *Estimate of effect of air pollution on mortality rates*.

Period	Gender	Cancer	Fraction (β^2)	Variance*	Attributable mortality rate* (fraction X variance)
1970-1994	M	All less lung	0.18	38	6.8
		Lung	0.10	36	3.6
	F	All less lung	0.14	31	4.3
		Lung	0	10	0
		Total			14.7
1950-1969	M	All less lung	0.04	60	2.4
		Lung	(0.22)	28	(6.2)
	F	All less lung	0.08	44	3.5
		Lung	(0.18)	2.8	(0.5)
		Total			5.9

*Deaths/100,000/year, with respect to pH 1985 in a linear regression using the regression results in Tables II and III.

Hispanic heritage was directly correlated with all cancer excluding lung (females in both periods), rectal in the second period, and all less lung (females) and lung (females) in the first period.

Table V. *Regression results for lung cancer for various periods.*

Gender	Years	Smoking (β, p)	pH (β, p)	Alcohol (β, p)	Hispanic	Adjusted R^2, F, p
M	1950-1969	0.19, 0.14	−0.47, 0.001	0.36, 0.002		0.50, 17,*
	1970-1974	0.41,*	−0.46,*	−0.07, 0.83		0.55, 21,*
	1975-1979	0.53,*	−0.39, 0.001	−0.15, 0.11		0.63, 28,*
	1980-1984	0.56,*	−0.35, 0.001	−0.26, 0.004		0.67, 33,*
	1985-1989	0.64,*	−0.24, 0.002	−0.31,*		0.69, 36,*
	1990-1994	0.66,*	−0.20, 0.04	−0.33,*		0.69, 37,*
	1970-1994	0.61,*	−0.31, 0.003	−0.24, 0.006		0.68, 35,*
F	1950-1969	0.23, 0.05	−0.42,*	0.28, 0.02	0.39, 0.001	0.52, 14,*
	1970-1974	0.34, 0.005	−0.30, 0.009	0.28, 0.02	0.39, 0.001	0.52, 14,*
	1980-1984	0.42, 0.001	−0.23, 0.06	0.28, 0.02	0.12, 0.32	0.44, 10,*
	1990-1994	0.57,*	−0.19, 0.14	0.04, 0.72	0.002, 0.98	0.40, 9.0,*
	1970-1994	0.50,*	−0.16, 0.21	0.17, 0.19	0.15, 0.21	0.38, 8.2,*

*p<0.001.

The regression results in Tables II and III can be used to estimate the probable mortality rate due to this air pollution index. For this calculation, the square of the highest partial regression coefficient, β, for pH in the multiple regression analysis is used to determine the fraction of the variance attributable to air pollution. The variance is determined by graphing the regression results *versus* the original data and determining the linear fit to the data. The results are given in Table IV. In the period 1970-1994, the air pollution index was thought to account for 3.6 deaths/100,000/year from lung cancer and 11.1 deaths/100,000/year from other types of cancer. For the period 1950-1969, up to 5.9 deaths/100,000/year were from cancer other than lung cancer. Without good information on smoking rates by state for the first period, it is impossible to provide a useful estimate of the contribution of air pollution to lung cancer rates. Moreover, a significant fraction of lung cancer rates in that period were due to exposure to asbestos such as at shipyards (37). Thus, the non-lung cancer mortality rates may have increased by 90% . However, the number of cancer deaths per year increased by a factor of 1.58 between the two periods (23), so that the total effect of air pollution was magnified by that factor as well. The effect of air pollution in the second period corresponds to 5% of male cancer deaths and 3% of female cancer deaths.

Because these results were for 25- and 30-year periods, any variations with time at smaller time scales are obscured. To examine any trends, two sets of data for 5-year intervals were studied: all excluding lung and lung cancer. The situation is complicated because whereas male lung cancer mortality rates increased from 60.79 deaths/100,000/year in the period 1970-1974 to 73.05 between 1985-1990 and then declined, female mortality rates increased from 12.80 deaths/100,000/year in the period 1970-1974 to 33.43 deaths/100,000/year between 1990-1994. These differences generally relate to increased smoking by females after their doing so became socially acceptable. The

Table VI. *Reports of cancer significantly correlated with ambient pollution or occupational exposure, smoking, and PAHs.*

Cancer (Reference)	Smoking (Reference)	Ambient pollution (Reference)	Occupational exposure to PAHs (Reference)	PAHs
Bladder	40	41	42, 43	13
Breast	44	45	46	47
Cervical	40		48	49
Colon	50	51	52	53
Endometrial	54		55	
Esophageal	40		56	57
Gastric	40		58	
Laryngeal	40	59	42, 60, 61	62
Liver	40		42	21
Lung	40	10, 11, 63, 64	42, 58, 60	13
Nasopharyngeal	40			
Oral	40	45	60	
Ovarian			43	
Pancreatic	40		58	
Pharyngeal	40	45	60	
Rectal	50		42	65
Renal	40		42, 43, 58	
Skin	66		42	67, 68
Small bowel	50		67	
Urothelial				69

Bold type indicates cancer linked to air pollution in this study.

regression results are given in Table V. For males, the effect of pH diminished with time, whereas the correlation with poverty level in 1969 increased with time. The effect of Hispanic heritage increased with time. For females, the effect of pH was relatively unchanged for the three periods; the effect of alcohol in 1970 was not apparent in the third period.

Discussion

The results of this study are generally similar to those in the previous multifactorial study (7). In the present work, factors that were not statistically significant were generally removed from the analysis. Thus, a few factors previously considered significant for some types of cancer were no longer found to be significant. Some of these would not have been considered significant if the Bonferroni criterion ($p<0.05/n$, where n is the number of factors) were invoked. More importantly, UVB did not significantly correlate with any of the types of respiratory cancer in this study but did for laryngeal cancer in the previous study.

These results indicate that air pollution is an important contributor to many types of cancer in the U.S., going well beyond lung cancer. The likely mechanism linking ambient air pollution to risk of cancer in this study is deposition of black carbon aerosols with adsorbed PAHs in the respiratory system (38, 39). PAHs have been correlated with nearly all the types of cancer linked to air pollution in this study but not with some linked to smoking and not to air pollution (Table VI). For example, a PubMed search found no reports of ambient air pollution as a risk factor for endometrial, gastric, ovarian, pancreatic or renal cancer, in agreement with this work.

The air pollution index directly correlated with endometrial cancer mortality rates in the first period but not the second one. From the cancer atlas maps (23), it appears that rates in several states in the South – Alabama, Louisiana and Georgia – decreased more rapidly than in most other states. Smoking has been found to be inversely correlated with risk of endometrial cancer in postmenopausal women but not premenopausal women (54). Lung cancer rates for males but not females increased dramatically in the South in the second period. This study cannot determine whether there is any difference between the effects of cigarette smoke and air pollution on the risk of endometrial cancer.

Poverty increased the risk of lung cancer, had no effect on other respiratory system cancers, but decreased the risk of the digestive tract, elimination and female organs types of cancer. In earlier decades, smoking was more common among those of higher socioeconomic status (SES), changing to where now those of lower SES are more likely to smoke. This change is reflected in lung cancer mortality rate trends: rates were higher for the highest SES for males until about 1980 and remained highest for females through 1998 (70). Because smoking is a significant risk factor for many types of cancer, those below the poverty level would have had lower rates for smoking-related cancer, as was generally found to be the case (Tables II and III).

California. The San Francisco Bay Area has several counties with cancer mortality rates among the highest in the country between 1950–1969: including all, other oral cavity and pharynx, esophagus, stomach, rectum, lung, female breast,

ovary cancer and non-Hodgkin's lymphoma (23). Bladder and kidney cancer and multiple myeloma mortality rates were elevated compared with the rest of California. Kidney, lung and stomach cancer were linked to residential exposure to petroleum and chemical air emissions in that region (71).

Southern California is a region infamous for its smog during the period 1950-1990 or so. However, by 1985, air pollution in Los Angeles as measured by pH was intermediate (4.8) between the northeast (4.2) and the northwest (5.3) regions, whereas within 100 miles of Los Angeles, pH was 5.1 (National Atmospheric Deposition Program, 2008). Rates were elevated in Los Angeles County for the period 1950-1969 for the following types of cancer: all, other oral cavity and pharynx, stomach, rectum, lung, female breast, ovary, bladder, brain and non-Hodgkin's lymphoma. These types of cancer generally overlap those identified as correlated with the air pollution index in this study.

Louisiana. Mortality rates for several types of cancer are higher in southeast Louisiana than in surrounding regions. Effects are most noticeable for several respiratory organ cancers: larynx, lung, nasopharynx, and other oral and pharynx, as well as cancer of several other organs, including bladder, kidney, pancreas and other or unspecified cancer (23). Most of these are cancer of the respiratory organ, which would implicate industrial emissions to the atmosphere. Several other organs are also involved. Some excessive cancer mortality rates in the region are linked to hydrocarbon emissions from local industries, followed by chlorination in the water purification process to make the water safe for drinking (72-74). However, the effects attributed to drinking water are limited to a small region in and around Baton Rouge and New Orleans.

Vitamin D. Solar UVB through vitamin D production remains one of most important factors affecting cancer rates. Although UV irradiance entails the risk of developing skin cancer and immune suppression, increasing vitamin D oral intake and photoproduction appears to be the most cost-effective way to reduce the burden of cancer in the U.S. (75, 76) and Europe (77). A recent randomized controlled trial found a 77% reduction in all-cancer incidence rates for those women taking 1,100 IU of vitamin D and 1,500 mg of calcium per day (78), with about 35% reduction attributed to vitamin D intake.

Summary and Conclusion

This work extends the analysis of the geographical variation in cancer mortality rates in the United States, confirming the effect of several factors considered in previous studies and including air pollution.

This study appears to be the first to link ambient air pollution from fossil fuel combustion in the United States to the risk of digestive tract and elimination organs and female reproductive

organs. Although the results seem reasonable based on the journal literature for occupational exposures, because this is an ecological study, the findings should be investigated further using other approaches. One way to do this is to measure PAHs in urine and PAH–DNA adducts in lymphocytes, as has been previously performed in Thailand (79, 80).

Acknowledgements

References

1 Garland CF and Garland FC: Do sunlight and vitamin D reduce the likelihood of colon cancer? Int J Epidemiol *9*: 227-231, 1980.

2 Garland FC, Garland CF, Gorham ED and Young JF: Geographic variation in breast cancer mortality in the United States: a hypothesis involving exposure to solar radiation. Prev Med *19*: 614-622, 1990.

3 Hanchette CL and Schwartz GG: Geographic patterns of prostate cancer mortality. Evidence for a protective effect of ultraviolet radiation. Cancer *70*: 2861-2869, 1992.

4 Lefkowitz ES and Garland CF: Sunlight, vitamin D and ovarian cancer mortality rates in US women. Int J Epidemiol *23*: 1133-1136, 1994.

5 Grant WB: An estimate of premature cancer mortality in the U.S. due to inadequate doses of solar ultraviolet-B radiation. Cancer *94*: 1867-1875, 2002.

6 Boscoe FP and Schymura MJ: Solar ultraviolet-B exposure and cancer incidence and mortality in the United States, 1993-2000. BMC Cancer *6*: 264, 2006.

7 Grant WB and Garland CF: The association of solar ultraviolet B (UVB) with reducing risk of cancer: multifactorial ecologic analysis of geographic variation in age-adjusted cancer mortality rates. Anticancer Res *26*: 2687-2699, 2006.

8 Grant WB: Lower vitamin-D production from solar ultraviolet-B irradiance may explain some differences in cancer survival rates. J Natl Med Assoc *98*: 357-364, 2006.

9 Samet JM, Dominici F, Curriero FC, Coursac I and Zeger SL: Fine particulate air pollution and mortality in 20 U.S. cities, 1987-1994. N Engl J Med *343*: 1742-1749, 2000.

10 Pope CA 3rd, Burnett RT, Thun MJ, Calle EE, Krewski D, Ito K and Thurston GD: Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. JAMA *287*: 1132-1141, 2002.

11 Eftim SE, Samet JM, Janes H, McDermott A and Dominici F: Fine particulate matter and mortality: A comparison of the Six Cities and American Cancer Society cohorts with a Medicare cohort. Epidemiology *19*: 209-216, 2008.

12 Dominici F, McDermott A, Zeger SL and Samet JM: National maps of the effects of particulate matter on mortality: exploring geographical variation. Environ Health Perspect *111*: 39-44, 2003.

13 Bosetti C, Boffetta P and La Vecchia C: Occupational exposures to polycyclic aromatic hydrocarbons, and respiratory and urinary tract cancers: a quantitative review to 2005. Ann Oncol *18*: 431-446, 2007.

14 Boström CE, Gerde P, Hanberg A, Jernström B, Johansson C, Kyrklund T, Rannug A, Törnqvist M, Victorin K and Westerholm R: Cancer risk assessment, indicators, and guidelines for polycyclic aromatic hydrocarbons in the ambient air. Environ Health Perspect *110(Suppl 3)*: 451-488, 2002.

15 Lodovici M, Venturini M, Marini E, Grechi D and Dolara P: Polycyclic aromatic hydrocarbons air levels in Florence, Italy, and their correlation with other air pollutants. Chemosphere *50*: 377-382, 2003.

16 Christensen ER and Arora S: Source apportionment of PAHs in sediments using factor analysis by time records: application to Lake Michigan, USA. Water Res *41*: 168-176, 2007.

17 Louchouarn P, Chillrud SN, Houel S, Yan B, Chaky D, Rumpel C, Largeau C, Bardoux G, Walsh D and Bopp RF: Elemental and molecular evidence of soot- and char-derived black carbon inputs to New York City's atmosphere during the 20th century. Environ Sci Technol *41*: 82-87, 2007.

18 Billet S, Garçon G, Dagher Z, Verdin A, Ledoux F, Cazier F, Courcot D, Aboukais A and Shirali P: Ambient particulate matter (PM2.5): physicochemical characterization and metabolic activation of the organic fraction in human lung epithelial cells (A549). Environ Res *105*: 212-223, 2007.

19 Lewtas J, Walsh D, Williams R and Dobiás L: Air pollution exposure-DNA adduct dosimetry in humans and rodents: evidence for non-linearity at high doses. Mutat Res *378*: 51-63, 1997.

20 Binkova B, Chvatalova I, Lnenickova Z, Milcova A, Tulupova E, Farmer PB and Sram RJ: PAH-DNA adducts in environmentally exposed population in relation to metabolic and DNA repair gene polymorphisms. Mutat Res *620*: 49-61, 2007.

21 Chen SY, Wang LY, Lunn RM, Tsai WY, Lee PH, Lee CS, Ahsan H, Zhang YJ, Chen CJ and Santella RM: Polycyclic aromatic hydrocarbon-DNA adducts in liver tissues of hepatocellular carcinoma patients and controls. Int J Cancer *99*: 14-21, 2002.

22 Surveillance, Epidemiology and End Results. http://seer.cancer.gov/ (accessed June 24, 2008)

23 Devesa SS, Grauman DJ, Blot WJ, Pennello GA, Hoover RN and Fraumeni JF Jr: Atlas of Cancer Mortality in the United States, 1950-1994. NIH Publication No. 99-4564, 1999. http://cancer.gov/atlasplus/new.html (accessed June 20, 2008)

24 Leffell DJ and Brash DE: Sunlight and skin cancer. Sci Am. 275: 52-53, 56-59, 1996. http://toms.gsfc.nasa.gov/ery_uv/dna_exp.gif (accessed June 20, 2008).

25 Shopland DR, Niemcryk SJ and Marconi KM: Geographic and gender variations in total tobacco use. Am J Public Health *82*: 103-106, 1992.

26 Leistikow B: Lung cancer rates as an index of tobacco smoke exposures: validation against black male approximate non-lung cancer death rates, 1969-2000. Prev Med *38*: 511-515, 2004.

27 Grant WB: An ecologic study of cancer mortality rates in Spain with respect to indices of solar UVB irradiance and smoking. Int J Cancer *120*: 1123-1128, 2007.

28 Hyman MM, Zimmermann MA, Gurioli C and Helrich A: Drinkers, Drinking, and Alcohol-Related Mortality and Hospitalizations; A Statistical Compendium. Center of Alcohol Studies, Rutgers University, New Burnswick, NJ, 1980.

29 Lakins NS, Williams GD, Li HY and Smothers BA: Surveillance Report #66: Apparent Per Capita Alcohol Consumption: National, State, and Regional Trends, 1977-2002. Washington, DC: NIAAA, 2004. http://pubs.niaaa.nih.gov/publications/surveillance66/CONS_02.pdf (accessed October 26, 2005).

30 O'Brien K, Cokkinides V, Jemal A, Cardinez CJ, Murray T, Samuels A, Ward E and Thun MJ: Cancer statistics for Hispanics, 2003. CA Cancer J Clin *53*: 208-226, 2003.

31 Gibson C and Jung K: Historical Census Statistics on Population Totals By Race, 1790 to 1990, and By Hispanic Origin, 1970 to 1990, For The United States, Regions, Divisions, and States. Population Division. U.S. Census Bureau. Washington, DC 20233. Working Paper Series No. 56. 2002. http://www.census.gov/population/www/documentation/twps0056.html (accessed June 24, 2008).

32 U.S. Census Bureau: Urban and Rural Populations: 1900 to 1990. Source: 1990 Census of Population and Housing, "1990 Population and Housing Unit Counts: United States", (CPH-2); and 1980 PC80-1-1, 1990. http://www.census.gov/population/censusdata/urpop0090.txt (accessed June 24, 2008)

33 U.S. Census Bureau (1995) Census Historical Poverty Tables. CPH-L-162. Persons by Poverty Status in 1969, 1979, and 1989, by State. http://www.census.gov/hhes/poverty/census/cphl162.html, accessed October 26, 2005).

34 National Atmospheric Deposition Program (2008) Isopleth Maps. http://nadp.sws.uiuc.edu/isopleths/annualmaps.asp (accessed June 24, 2008).

35 Park RJ, Jacob DJ, Chin M and Martin RV: Sources of carbonaceous aerosols over the United States and implications for natural visibility. J Geophys. Res *108*: 4355, 2003.

36 Cooke, WF, Liousse C, Cachier H and Feichter J: Construction of a 1 x 1 fossil fuel emission data set for carbonaceous aerosol and implementation and radiation impact in the ECHAM-4 model. J Geophys Res *104*: 22, 137-162, 1999.

37 Jemal A, Grauman D and Devesa S: Recent geographic patterns of lung cancer and mesothelioma mortality rates in 49 shipyard counties in the United States, 1970-94. Am J Ind Med *37*: 512-521, 2000.

38 Vineis P and Husgafvel-Pursiainen K: Air pollution and cancer: biomarker studies in human populations. Carcinogenesis *26*: 1846-1855, 2005.

39 Lewtas J: Air pollution combustion emissions: characterization of causative agents and mechanisms associated with cancer, reproductive, and cardiovascular effects. Mutat Res *636*: 95-133, 2007.

40 Sasco AJ, Secretan MB and Straif K: Tobacco smoking and cancer: a brief review of recent epidemiological evidence. Lung Cancer *45(Suppl 2)*: S3-S9, 2004.

41 Castaño-Vinyals G, Cantor KP, Malats N, Tardon A, Garcia-Closas R, Serra C, Carrato A, Rothman N, Vermeulen R, Silverman D, Dosemeci M and Kogevinas M: Air pollution and risk of urinary bladder cancer in a case-control study in Spain. Occup Environ Med *65*: 56-60, 2008.

42 Soll-Johanning H, Bach E, Olsen JH and Tüchsen F: Cancer incidence in urban bus drivers and tramway employees: a retrospective cohort study. Occup Environ Med *55*: 594-598, 1998.

43 Guo J, Kauppinen T, Kyyrönen P, Heikkilä P, Lindbohm ML and Pukkala E: Risk of esophageal, ovarian, testicular, kidney and bladder cancers and leukemia among Finnish workers exposed to diesel or gasoline engine exhaust. Int J Cancer *111*: 286-292, 2004.

44 Nagata C, Mizoue T, Tanaka K, Tsuji I, Wakai K, Inoue M, Tsugane S, and Research Group for the Development and Evaluation of Cancer Prevention Strategies in Japan: Tobacco smoking and breast cancer risk: an evaluation based on a systematic review of epidemiological evidence among the Japanese population. Jpn J Clin Oncol *36*: 387-394, 2006.

45 Amaral A, Rodrigues V, Oliveira J, Pinto C, Carneiro V, Sanbento R, Cunha R and Rodrigues A: Chronic exposure to volcanic environments and cancer incidence in the Azores, Portugal. Sci Total Environ *367*: 123-128, 2006.

46 Lewis-Michl EL, Melius JM, Kallenbach LR, Ju CL, Talbot TO, Orr MF and Lauridsen PE: Breast cancer risk and residence near industry or traffic in Nassau and Suffolk Counties, Long Island, New York. Arch Environ Health *51*: 255-265, 1996.

47 Crew KD, Gammon MD, Terry MB, Zhang FF, Zablotska LB, Agrawal M, Shen J, Long CM, Eng SM, Sagiv SK, Teitelbaum SL, Neugut AI and Santella RM: Polymorphisms in nucleotide excision repair genes, polycyclic aromatic hydrocarbon-DNA adducts, and breast cancer risk. Cancer Epidemiol Biomarkers Prev 2007 *16*: 2033-2041, 2007.

48 Wu MT, Lee LH, Ho CK, Liu CL, Wu TN, Wu SC, Lin LY, Cheng BH and Yang CY: Environmental exposure to cooking oil fumes and cervical intraepithelial neoplasm. Environ Res *94*: 25-32, 2004.

49 Mancini R, Romano G, Sgambato A, Flamini G, Giovagnoli MR, Boninsegna A, Carraro C, Vecchione A and Cittadini A: Polycyclic aromatic hydrocarbon-DNA adducts in cervical smears of smokers and nonsmokers. Gynecol Oncol *75*: 68-71, 1999.

50 Lüchtenborg M, White KK, Wilkens L, Kolonel LN and Le Marchand L: Smoking and colorectal cancer: different effects by type of cigarettes? Cancer Epidemiol Biomarkers Prev *16*: 1341-1347, 2007.

51 Gorham ED, Garland CF and Garland FC: Acid haze air pollution and breast and colon cancer mortality in 20 Canadian cities. Can J Public Health *80*: 96-100, 1989.

52 Goldberg MS, Parent ME, Siemiatycki J, Désy M, Nadon L, Richardson L, Lakhani R, Latreille B and Valois MF: A case-control study of the relationship between the risk of colon cancer in men and exposures to occupational agents. Am J Ind Med *39*: 531-546, 2001.

53 Helleberg H, Xu H, Ehrenberg L, Hemminki K, Rannug U and Törnqvist M: Studies of dose distribution, premutagenic events and mutation frequencies for benzo[a]pyrene aiming at low dose cancer risk estimation. Mutagenesis *16*: 333-337, 2001.

54 Al-Zoughool M, Dossus L, Kaaks R, Clavel-Chapelon F, Tjønneland A, Olsen A, Overvad K, Boutron-Ruault MC, Gauthier E, Linseisen J, Chang-Claude J, Boeing H, Schulz M, Trichopoulou A, Chryssa T, Trichopoulos D, Berrino F, Palli D, Mattiello A, Tumino R, Sacerdote C, Bueno-de-Mesquita HB, Boshuizen HC, Peeters PH, Gram IT, Braaten T, Lund E, Chirlaque MD, Ardanaz E, Agudo A, Larrañaga N, Quirós JR, Berglund G, Manjer J, Lundin E, Hallmans G, Khaw KT, Bingham S, Allen N, Key T, Jenab M, Cust AE, Rinaldi S and Riboli E: Risk of endometrial cancer in relationship to cigarette smoking: results from the EPIC study. Int J Cancer *121*: 2741-2747, 2007.

55 Weiderpass E, Pukkala E, Vasama-Neuvonen K, Kauppinen T, Vainio H, Paakkulainen H, Boffetta P and Partanen T: Occupational exposures and cancers of the endometrium and cervix uteri in Finland. Am J Ind Med *39*: 572-580, 2001.

56 Jansson C, Johansson AL, Bergdahl IA, Dickman PW, Plato N, Adami J, Boffetta P and Lagergren J: Occupational exposures and risk of esophageal and gastric cardia cancers among male Swedish construction workers. Cancer Causes Control *16*: 755-764, 2005.

57 Kamangar F, Strickland PT, Pourshams A, Malekzadeh R, Boffetta P, Roth MJ, Abnet CC, Saadatian-Elahi M, Rakhshani N, Brennan P, Etemadi A and Dawsey SM: High exposure to polycyclic aromatic hydrocarbons may contribute to high risk of esophageal cancer in northeastern Iran. Anticancer Res *25*: 425-428, 2005.

58 Miller BA, Blair A and Reed EJ: Extended mortality follow-up among men and women in a U.S. furniture workers union. Am J Ind Med *25*: 537-549, 1994.

59 Pereira FA, de Assunção JV, Saldiva PH, Pereira LA, Mirra AP and Braga AL: Influence of air pollution on the incidence of respiratory tract neoplasm. J Air Waste Manag Assoc *55*: 83-87, 2005.

60 Pintos J, Franco EL, Kowalski LP, Oliveira BV and Curado MP: Use of wood stoves and risk of cancers of the upper aero-digestive tract: a case-control study. Int J Epidemiol *27*: 936-940, 1998.

61 Elci OC, Akpinar-Elci M, Blair A and Dosemeci M. Risk of laryngeal cancer by occupational chemical exposure in Turkey. J Occup Environ Med *45*: 1100-1106, 2003.

62 Becher H, Ramroth H, Ahrens W, Risch A, Schmezer P and Dietz A: Occupation, exposure to polycyclic aromatic hydrocarbons and laryngeal cancer risk. Int J Cancer *116*: 451-457, 2005.

63 Dockery DW, Pope CA 3rd, Xu X, Spengler JD, Ware JH, Fay ME, Ferris BG Jr and Speizer FE: An association between air pollution and mortality in six U.S. cities. N Engl J Med *329*: 1753-1759, 1993.

64 Naess Ø, Nafstad P, Aamodt G, Claussen B and Rosland P. Relation between concentration of air pollution and cause-specific mortality: four-year exposures to nitrogen dioxide and particulate matter pollutants in 470 neighborhoods in Oslo, Norway. Am J Epidemiol *165*: 435-443, 2007.

65 Gunter MJ, Probst-Hensch NM, Cortessis VK, Kulldorff M, Haile RW and Sinha R: Meat intake, cooking-related mutagens and risk of colorectal adenoma in a sigmoidoscopy-based case-control study. Carcinogenesis *26*: 637-642, 2005.

66 Boffetta P, Jourenkova N and Gustavsson P: Cancer risk from occupational and environmental exposure to polycyclic aromatic hydrocarbons. Cancer Causes Control *8*: 444-472, 1997.

67 Kaerlev L, Teglbjaerg PS, Sabroe S, Kolstad HA, Ahrens W, Eriksson M, González AL, Guénel P, Hardell L, Launoy G, Merler E, Merletti F, Suárez-Varela MM and Stang A: Occupation and small bowel adenocarcinoma: a European case-control study. Occup Environ Med *57*: 760-766, 2000.

68 Chen MR, Tsai PJ and Wang YF: Assessing inhalatory and dermal exposures and their resultant health-risks for workers exposed to polycyclic aromatic hydrocarbons (PAHs) contained in oil mists in a fastener manufacturing industry. Environ Int *34*: 971-975, 2008.

69 Pesch B, Haerting J, Ranft U, Klimpel A, Oelschlägel B and Schill W: Occupational risk factors for urothelial carcinoma: agent-specific results from a case-control study in Germany. MURC Study Group. Multicenter Urothelial and Renal Cancer. Int J Epidemiol *29*: 238-247, 2000.

70 Singh GK, Miller BA and Hankey BF: Changing area socioeconomic patterns in U.S. cancer mortality, 1950-1998: Part II – Lung and colorectal cancers. J Natl Cancer Inst *94*: 916-925, 2002.

71 Kaldor J, Harris JA, Glazer E, Glaser S, Neutra R, Mayberry R, Nelson V, Robinson L and Reed D: Statistical association between cancer incidence and major-cause mortality, and estimated residential exposure to air emissions from petroleum and chemical plants. Environ Health Perspect *54*: 319-332, 1984.

72 Gottlieb MS, Carr JK and Morris DT: Cancer and drinking water in Louisiana: colon and rectum. Int J Epidemiol *10*: 117-125, 1981.

73 Gottlieb MS and Carr JK: Case-control cancer mortality study and chlorination of drinking water in Louisiana. Environ Health Perspect *46*: 169-177, 1982.

74 Cantor KP, Lynch CF, Hildesheim ME, Dosemeci M, Lubin J, Alavanja M and Craun G: Drinking water source and chlorination byproducts. I. Risk of bladder cancer. Epidemiology *9*: 21-28, 1998.

75 Grant WB, Garland CF and Holick, MF: Comparisons of estimated economic burdens due to insufficient solar ultraviolet irradiance and vitamin D and excess solar UV irradiance for the United States. Photochem Photobiol *81*: 1276-1286, 2005.

76 Grant WB: Roles of solar ultraviolet radiation and vitamin D in human health and how to obtain vitamin D. Expert Rev Dermatol *2*: 563-577, 2007.

77 Grant WB, Garland CF and Gorham ED: An estimate of cancer mortality rate reductions in Europe and the U.S. with 1,000 I.U. of oral vitamin D per day. Rec Results Cancer Res *174*: 225-234, 2007.

78 Lappe JM, Travers-Gustafson D, Davies KM, Recker RR and Heaney RP: Vitamin D and calcium supplementation reduces cancer risk: results of a randomized trial. Am J Clin Nutr *85*: 1586-1591, 2007.

79 Ruchirawat M, Settachan D, Navasumrit P, Tuntawiroon J and Autrup H: Assessment of potential cancer risk in children exposed to urban air pollution in Bangkok, Thailand. Toxicol Lett *168*: 200-209, 2007.

80 Tuntawiroon J, Mahidol C, Navasumrit P, Autrup H and Ruchirawat M: Increased health risk in Bangkok children exposed to polycyclic aromatic hydrocarbons from traffic-related sources. Carcinogenesis *28*: 816-822, 2007.