

## An Ecological Study of Cancer Mortality Rates Including Indices for Dietary Iron and Zinc

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**Abstract.** *Background: Dietary iron and zinc affect the risk of cancer, with dietary iron generally correlated with increased risk and dietary zinc with reduced risk. However, zinc supplements have been found correlated with increased risk of cancer. Patients and Methods: An ecological study was conducted using state-averaged cancer mortality rate data for white Americans for 1970-94 with indices for alcohol consumption, smoking, Hispanic heritage, and urban residence plus dietary factors for four large U.S. regions. Results: The dietary zinc index was inversely correlated with 12 types of cancer, whereas the dietary iron index was directly correlated with 10 types of cancer which correlated with both iron directly and zinc inversely were bladder, breast, colon, esophageal, gastric, rectal cancer, and Hodgkin's lymphoma; those inversely with zinc only were laryngeal, nasopharyngeal, oral, skin and vulvar cancer. Solar UVB was inversely correlated with 10 of the 15 types of cancer for which the iron and/or zinc indices had significant correlations, the smoking and urban indices with nine, and the alcohol index with eight. Conclusion: Although there are mechanisms that explain why zinc should reduce the risk of cancer, whereas iron should increase the risk, these indices may represent the dietary sources of these nutrients, e.g. whole grains for zinc and red meat for iron, and other components of these dietary factors.*

There are large geographic variations in cancer mortality rates in the United States. *The Atlas of Cancer Mortality Rate in the United States, 1950-94* (1), gives the distributions for two periods, 1950-69 and 1970-94, averaged at the county level, state economic area, and state level.

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Perhaps the most important inference made from these geographical patterns was the development of the ultraviolet-B (UVB)/vitamin D<sub>3</sub>/cancer hypothesis by Cedric and Frank Garland (2). They based their hypothesis, that vitamin D is a protective factor against colon cancer and that photoproduction of vitamin D by casual solar UVB irradiance provides sufficient vitamin D in some locations to have a profound effect, on the pattern for colon cancer mortality rates in the United States, low in the South-west, high in the North-east (3). They later extended the hypothesis to breast cancer (4) and ovarian cancer (5). Prostate cancer was added in 1990 (6). The inverse correlation of non-Hodgkin's lymphoma (NHL) mortality rates with solar UVB was found in 1996 (7), although the connection with vitamin D was not recognized. After the updated *Atlas* appeared in 1999, another nine types of cancer were added to the list of UVB/vitamin D<sub>3</sub>-sensitive cancers (8). Subsequent observational studies also reported inverse correlations between cancer mortality rates and indices for sunlight (9) and cancer incidence rates and an index for vitamin D from sunlight and oral intake (10). Later, after adding indices for other risk-modifying factors in the ecological study (smoking, alcohol consumption, urban/rural residence, poverty level, and Hispanic heritage), three more types of cancer were added (11). Another ecological study based on more recent cancer incidence and mortality rate added seven more types of cancer (12). Thus, these various ecologic studies identified 23 types of cancer for which UVB doses were inversely correlated with incidence and/or mortality rates and determined that photoproduction of vitamin D<sub>3</sub> was the likely physiological effect of UVB irradiance. The mechanisms whereby vitamin D<sub>3</sub> reduces the risk of cancer are well known (13-15).

In international comparisons, differences in dietary factors make an important contribution to observed differences in cancer incidence and mortality rates (16, 17). One can also develop models that include both dietary factors and solar UVB irradiance (18-21). As yet, there has not been an effort to do the same in the United States in an ecologic study. However, the dietary data from the National Health and Nutritional Examination Survey III for 1988-94 (NHANES-

III) (22) appear to make this possible, even though the data are average values for each of the four major U.S. regions. These data include the major macronutrients as well as some important micronutrients.

Among the micronutrients, the trace metals are of most interest. Dietary iron and zinc are known to affect the risk of cancer. Iron increases the risk, probably through increased production of free radicals and oxidative stress (23, 24). Zinc is a key constituent or cofactor for more than 300 mammalian proteins or enzymes, including those involved in DNA repair (25). Zinc is involved with metallothionein synthesis, which is thought to inhibit free-radical production (26) and also plays an important role in transcription factor function, antioxidant defense, and DNA repair (25, 27). Thus, dietary zinc deficiencies can contribute to DNA breaks and oxidative modifications to DNA that can increase the risk for cancer (25).

Silver and Rohan (28) reviewed the observational study findings on zinc from diet, from supplements, and in sera or tissues for breast, gastric, lung, and prostate cancer. They identified four significant risk reduction findings of 17 studies – two for breast cancer and one each for lung and prostate cancer – but no significant risk findings. Steel workers had a significantly increased risk of lung cancer (29), but whether zinc was the reason is not clear. For some reason, they overlooked several similar studies. As shown in Table I, a higher dietary intake of zinc has been found inversely correlated with many types of cancer in observational studies. Table II presents several findings from the literature regarding the relation between iron and cancer risk.

## Patients and Methods

This study is an extension of three previous ecologic studies of cancer mortality rates in the United States from cancer mortality rate data for white Americans for 1950-69 and 1970-94, age adjusted to the U.S. population for 1970 (1). The first paper used solar UVB doses for July 1992(53) for 466 of the 508 state economic areas in the United States for white and black Americans (8). Two later papers used data averaged by state for all states and the District of Columbia, except for Alaska, and included several potential cancer risk-modifying factors. One was for white Americans (11), whereas another was for black Americans (54). Lung cancer mortality rates were used as the index of the effects of smoking on cancer risk (55). Other factors used in that study were alcohol consumption rates for 1970 (56), the fraction of the population with Hispanic heritage for 1980 (for white Americans) (57), the fraction of the population living below the poverty level in 1969 (58), and the fraction of the population living in urban regions (59). The present study determined that the poverty index did not have a significant correlation with cancer except for bladder cancer (inverse), so it was omitted from further analysis.

The dietary data are from the NHANES-III survey for 1988-94 (22), as reported in Hajjar and Kotchen (60), and are averaged for each of the four major U.S. regions [(NHANES-III divided the United States into four regions: North-east (Maine, North

Hampshire, Vermont, Connecticut, Massachusetts, Rhode Island, New Jersey, New York and Pennsylvania), Mid-west (Ohio, Indiana, Michigan, Illinois, Wisconsin, Missouri, Iowa, Minnesota, Kansas, South Dakota, North Dakota and Nebraska), South (Delaware, Maryland, District of Columbia, West Virginia, Virginia, Kentucky, Tennessee, North Carolina, South Carolina, Georgia, Florida, Alabama, Mississippi, Louisiana, Oklahoma, Arkansas and Texas) and West (Wyoming, Montana, Idaho, Nevada, Utah, Colorado, New Mexico, Arizona, California, Oregon and Washington)]. Even though they are averages over large regions and for the last 7 years of 1970-94 in the *Atlas*, they are considered useful since there are broad variations in cancer mortality rates and since U.S. dietary patterns were not changing rapidly during that period.

Mean values and standard error of the mean or standard deviation for the independent factors used in this study are presented in Table III. The variations in dietary factors are rather small on the basis of comparisons of the highest and lowest amounts [carbohydrates (2%), fiber (25%), iron (8%), and zinc (7%)]. Such low differences are thought to attenuate the effects, but that if the effects are robust, they would be identified in the ecologic study nonetheless.

The data were used in multiple linear regression analyses using SPSS 13.0 (SPSS, Chicago, IL, USA). The square roots of the mortality data were used to reduce the effect of extreme values. Various combinations of the independent factors were used for each cancer and sex, eliminating those that did not have an independent significant correlation with the mortality rates in either single or multiple linear regression analyses. The Bonferroni criterion for significance at the 95% confidence level,  $p < 0.05/n$ , where  $n$  is the number of factors in the model, was used and factors not satisfying this criterion were omitted unless one sex had a significant correlation with that factor.

## Results

Only types of cancer for which iron and/or zinc was significantly correlated are included in this report since the results for the nondietary factors were reported elsewhere (11), and the results for carbohydrates and fiber were significant for only a few types of cancer. The regression results are presented in Table IV. More than half of the adjusted  $R^2$  values are greater than 0.70, indicating that the models effectively explain the variance of cancer mortality rates in the continental United States. The factors are arranged in descending order according to the number of cancers with which they are correlated. Zinc, solar UVB, iron, lung cancer, urban residence, and alcohol consumption were each correlated with eight or more types of cancer; Hispanic heritage, carbohydrates, and fiber were each correlated with two types of cancer. Some of the factors, such as fiber and zinc, and carbohydrates and iron, are highly correlated with each other, so the two interacting factors were considered independently for colon, gastric, ovarian, and pancreatic cancer.

There is very good agreement for most factors between males and females. UVB had a higher normalized correlation coefficient,  $\beta$ , for males than for females, which is consistent

Table I. Representative studies of cancer risk with respect to zinc.

Cancer	Source	Odds ratio, high vs. low (95% CI)	p trend	$\chi^2$ trend	Reference
Breast	Toenails	1.09 (0.70-1.70)*	0.35		30
Breast	Diet	0.35 (0.15-0.78)	<0.01		31
Colon	Diet (non-alcohol drinkers)	0.63 (0.24-1.64)	0.38		32
Colon	Diet (alcohol drinkers)	0.22 (0.07-0.67)	<0.01		32
Colon	Diet	0.90 (0.65-1.25)	0.71		33
Esophageal	Diet	0.28 (0.11-0.70)*	0.01		34
Esophageal or gastric	Diet	0.13 (0.03-0.63)*	<0.01		32
Laryngeal	Diet	1.5 (1.0-2.2)*		3.93	36
Lung	Diet	0.46 (0.31-0.68)*	<0.0001		37
Lung	Diet	0.11	0.12		35
Lung	Diet	0.57 (0.42-0.75)*	0.0004		38
Melanoma	Diet + supplements	0.46 (0.24-0.91)	0.01		39
Melanoma	Diet	No effect			40
NHL	Diet	0.58 (0.36-91)*	0.02		41
NHL	Total	0.68 (0.45-1.02)*	0.17		41
Oral and pharyngeal	Diet	0.79 (0.45-1.41)	0.45	0.55	42
Ovarian	Supplements	2.19 (1.41, 3.40)			43
Pancreatic	Tissues	No effect			44
Prostate	Suppl.	1.43 (0.95 to 2.15)	0.10		45
Prostate-advanced	Suppl.	2.91 (1.23 to 6.90)	0.002		45
Prostate	Diet	1.56 (1.07-2.27)	0.94	4.06	46
Renal	Medulla tissue	Lower in cases than controls (103.5 vs. 162.2)			47

\*Multivariable adjusted.

Table II. Representative studies of cancer risk with respect to iron.

Cancer	Population	Source	Odds ratio, high vs. low (95% CI)	p trend	Reference
Breast	Females	Toenail	0.89 (0.56-1.40)	0.36	30
Breast	Females	Diet	No significant association		31
Colon		Diet	2.43 (1.2-5.1)		48
Colon	Non-drinkers	Heme	1.55 (0.71-3.37)	0.31	32
Colon	Drinkers	Heme	3.23 (1.40-7.47)	<0.001	32
Colon	Females, all	Heme	1.31 (0.98-1.75)	0.03	33
Colon	Females who consume alcohol	Heme	2.29 (1.25-4.21)	0.007	33
Colon		Diet	0.3 (0.1-1.6)	0.09	49
Colon		Serum	0.2 (0.1-0.9)	0.02	49
Colon	Males and females	Total intake	1.30 (0.34-2.01)	0.43	50
Colon	Males	Heme intake	1.29	0.10	50
Colon	Females	Heme intake	1.20	0.56	50
Esophageal			0.72 (0.30-1.73)	0.25	34
Esophageal or gastric			2.83 (0.84-9.59)	0.06	32
Laryngeal			1.0 (0.6-1.5)	0.04	36
Liver	All	Iron overload	10.6 (1.5-76.8)		51
Lung			1.95 (1.33-2.86)	0.00002	37
Lung	Postmenopausal females	Heme	3.77	0.05	35
Melanoma			Effect		40
Oral and pharyngeal			0.82 (continuous)		42
Ovarian			No effect		52
Rectal		Serum	1.7 (0.5-6.1)	0.35	49
Rectal	Males and females	Total intake	1.44 (0.85-2.45)	0.08	50

\*Multivariable adjusted.

Table III. Values for the factors used in this study by major regions of the United States\*.

Factor	Northeast (mean, $\sigma$ )	Midwest (mean, $\sigma$ )	South (mean, $\sigma$ )	West (mean, $\sigma$ )	Max/ Min
Alcohol (gal/person/year)	37, 9	28, 6	28, 15	35, 12	1.32
Carbohydrates (g/day)	257, 3	254, 2	249, 2	259, 2	1.04
Fiber (g/day)	16.0, 0.2	16.0, 0.2	16.0, 0.2	20.0, 0.2	1.25
Hispanic heritage (%)	3.1, 3.1	1.6, 1.4	2.9, 5.0	10.0, 10.6	6.25
Iron (mg/day)	15.2, 0.2	14.5, 0.2	14.1, 0.1	15.1, 0.2	1.08
Lung cancer, males (deaths/100,000/year)	69.4, 4.2	63.6, 10.0	78.9, 7.8	57.3, 11.5	1.38
Lung cancer, females (deaths/100,000/year)	24.0, 1.3	20.1, 3.3	24.3, 2.6	23.4, 7.1	1.21
Urban residence (%)	67, 25	65, 12	62, 16	72, 12	1.16
UVB dose (kJ/m <sup>2</sup> )	4.5, 0.3	4.8, 0.7	6.6, 1.1	7.3, 1.7	1.62
Zinc (mg/day)	11.1, 0.2	11.3, 0.2	11.3, 0.2	11.9, 0.2	1.07

\*The values shown were the mean values used in this study and the standard error,  $\sigma$ , of the mean for carbohydrates, fiber, iron and zinc; the values for the other factors were state means and standard deviations,  $\sigma$ ; Max/Min, maximum value divided by minimum value.

with males spending more time in the sun. UVB was inversely correlated with Hodgkin's lymphoma for females but not males. Alcohol consumption generally had higher correlations for males than females. Iron generally had a higher correlation for males than females, whereas the results for zinc were more evenly matched. Zinc was inversely correlated with oral cancer for males but not females, with the reverse found for bladder cancer.

## Discussion

These results reconfirm that solar UVB is inversely correlated with several cancers in the United States. Of the 14 types of cancer identified in Grant (8) and Grant and Garland (11), only cervical, laryngeal, and pancreatic cancer should be removed from the list on the basis of these results. However, there is good evidence that vitamin D<sub>3</sub> reduces the risk of pancreatic cancer (10, 61). Thus, this study's using an expanded set of factors provides more support for the UVB/vitamin D<sub>3</sub>/cancer theory. The study also supports the finding that the economic burden from too little solar UVB irradiance and vitamin D<sub>3</sub> is much higher than that for excess solar UV irradiance (62).

The results for the index of smoking are in excellent agreement with the literature (63, 64), including nonmelanoma skin cancer (65), except perhaps for colon cancer, whose results are mixed (66-68). However, since diet also affects the risk for lung cancer, with animal products increasing the risk and vegetable products decreasing the risk

(38, 69, 70), using lung cancer mortality rates as the index of the effects of smoking may also include some effects of diet. The results for alcohol consumption are in good agreement, especially for the upper gastrointestinal tract (71, 72), breast cancer (73), and ovarian cancer (74). Only limited correlations of alcohol consumption with bladder cancer have been reported (75). Urban residence has long been considered a risk factor for cancer (76). Many factors possibly contribute to increased risk compared to rural residence. The effect of Hispanic heritage on cancer risk is most obvious for gastric cancer, which is consistent with the literature (77). As for other dietary factors, simple carbohydrates are probably a risk factor for colon cancer (78) and pancreatic cancer (79), whereas fiber is probably a risk reduction factor for colon cancer (80). Thus, the results for factors that have well-known correlations with cancer rates are in very good to excellent agreement with the literature.

The results for dietary zinc and iron are in excellent agreement with the expectations based on proposed mechanisms (23-27) and in good agreement with the observational literature. For zinc, agreement is found here for reduced risk in comparison with the literature for breast (31), colon (32), and esophageal (32, 34) cancer. For iron, the agreement is found for colon cancer (32, 33, 49). The associations of both metals with lung cancer shown in Tables I and II were not confirmed in this study, probably because there are no useful data on cigarette smoking rates to use in such a study.

However, the correlations with zinc and iron in this study may indicate general dietary factors rather than zinc and iron in particular. The important dietary sources for zinc include meats, offal, shellfish, nuts, whole grains, beans, peas, lentils, and fortified breakfast cereals, whereas those for iron include meats and seafood (81). Consumption of whole grains has been found inversely correlated with cancer in several studies (82-84), and several mechanisms have been identified (85). Fewer observational studies have been reported regarding beans and legumes other than soybeans, but these foods appear to be protective (86, 87). The same seems to be the case for nuts (88, 89).

Red meat consumption has often been found correlated with the risk of many types of cancer (69, 90-97). However, some of the observed risk depends on the method of preparation, with cooking at high temperature and formation of heterocyclic amines or processed meats with more nitrites being associated with somewhat higher risk.

An Italian study (90) found no convincing relation with red meat intake for cancers of the oral cavity, pharynx and esophagus, liver, gallbladder, larynx, kidney, thyroid, prostate; Hodgkin's disease; non-Hodgkin's lymphomas; and multiple myeloma. The results of my study are in very good agreement with the Italian study. The only two types of

Table IV. Regression results for cancers for which iron and/or zinc were found to modify cancer risk using NHANES-III dietary data, 1988-94 (60) with mortality rate data for 1970-94 (1).

Cancer	Gender	Zinc ( $\beta$ , $p$ )	UVB ( $\beta$ , $p$ )	Iron ( $\beta$ , $p$ )	Lung cancer ( $\beta$ , $p$ )	Urban ( $\beta$ , $p$ )	Alcohol (or Fiber) ( $\beta$ , $p$ )	Hispanic (or Carb.) ( $\beta$ , $p$ )	Adjusted $R^2$ , $F$ , $p$
All less lung	M	-0.42, *	-0.26, 0.005	0.46, *	0.44, *		0.40, *		0.80, 39, *
	F	-0.38, *	-0.42, *	0.34, *	0.33, *		0.26, *		0.83, 49, *
Gastrointestinal Esophageal	M		-0.66, *	0.19, 0.01	0.41, *	0.23, 0.001	0.45, *		0.84, 51, *
	F	-0.26, 0.001			0.37, *		0.64, *		0.74, 46, *
Gastric	M	-0.40, 0.001	-0.43, 0.002	0.51, *				0.47, *	0.65, 23, *
	F	-0.46, 0.001	-0.34, 0.02	0.45, *				0.54, *	0.57, 17, *
Colon	F		-0.33, 0.04	0.59, *			-0.52, 0.002 (Fiber)	0.53, *	0.56, 16, *
	M	-0.55, *	-0.42, *		0.28, *	0.45, *		0.39, * (Carb.)	0.85, 57, *
	M	-0.46, *	-0.46, *	0.31, *	0.24, 0.002	0.45, *			0.85, 54, *
	F		-0.28, 0.009		0.35, *		-0.84, * (Fiber)	0.68, * (Carb.)	0.75, 38, *
Rectal	F	-0.66, *	-0.33, 0.002		0.31, *			0.44, * (Carb.)	0.75, 37, *
	F		-0.34, 0.001	0.55, *	0.30, *		-0.65, * (Fiber)		0.75, 36, *
	F	-0.53, *	-0.38, *	0.36, *	0.28, 0.001				0.74, 34, *
	M	-0.27, 0.003	-0.65, *	0.41, *	0.21, 0.007		0.25, *	0.22, 0.007	0.85, 46, *
Female sites Breast	F	-0.38, *	-0.41, *	0.56, *	0.37, *				0.82, 56, *
	M		-0.41, 0.007						0.15, 8.2, 0.007
Ovarian	F	-0.29, *	-0.49, *	0.26, *		0.38, *	0.31, *		0.88, 69, *
	F		-0.70, *			0.28, *	0.25, 0.002	0.23, 0.002 (Carb.)	0.79, 47, *
Uterine corpus	F		-0.69, *	0.21, 0.005		0.29, *	0.24, 0.003		0.78, 44, *
	F		-0.74, *			0.32, *		0.28, 0.001 (Carb.)	0.71, 41, *
Vulvar	F		-0.73, *	0.27, 0.002		0.33, *			0.71, 39, *
	F	-0.41, 0.001	-0.40, 0.001				0.27, 0.009		0.57, 22, *
Urogenital Bladder	M		-0.46, *	0.51, *	0.55, *		0.37, *		0.76, 39, *
	F	-0.34, 0.002	-0.22, 0.03	0.26, 0.004	0.53, *		0.30, *		0.75, 30, *
Oral	M	-0.47, *			0.40, *	0.24, 0.003	0.51, *		0.77, 42, *
	F		0.40, 0.001		0.40, 0.002		0.41, 18, *		
Nasopharyngeal	M	-0.24, 0.04			0.54, *	0.48, *			0.52, 19, *
	F	-0.33, 0.003			0.62, *				0.48, 23, *
Laryngeal	M	-0.53, *			0.43, *		0.45, *		0.75, 49, *
	F	-0.27, 0.005			0.41, *		0.52, *		0.63, 27, *
Miscellaneous Hodgkin's	M	-0.76, *		0.46, *					0.54, 29, *
	F	-0.69, *	-0.27, 0.01	0.27, 0.007		0.24, 0.005			0.72, 31, *
NMSC	M	-0.45, *	0.72, *		0.43, *				0.71, 40, *
	F	-0.43, 0.006	0.50, 0.002		0.29, 0.03				0.26, 6.6, 0.001
Pancreatic	M			0.27, 0.05	0.70, *				0.35, 14, *
	F			0.39, 0.002	0.44, 0.001				0.31, 12, *
	F				0.47, *			0.36, 0.005 (Carb.)	0.29, 11, *

F, F-statistic;  $\beta$ , standardized coefficient; Carb., carbohydrates; M, males; F, females; \* $p$ <0.001; NMSC, non-melanoma skin cancer.

cancer from this list for which iron was found correlated in the present study, esophageal cancer and Hodgkin's lymphoma, had weak correlations. Some of the reports on whole grains and meat as well as other studies have noted that the ratio of animal products to vegetable products is highly significant with respect to cancer risk (17, 91, 95-97).

Dietary zinc supplements are associated with increased risk of ovarian and prostate cancer (44, 46). These findings could be related to an optimal range for zinc, much as has

been observed for selenium with respect to prostate cancer (98). Iron has been found to have an optimal range, with both deficiency and excess damaging mitochondria and mitochondrial DNA in rats (99). Thus, obtaining zinc from dietary sources may provide adequate amounts of zinc as well as other macro- and micronutrients in the zinc-rich foods that reduce the risk. Extracting the probable beneficial nutrient from a dietary source inversely correlated with a particular cancer and administering it in the form of a

supplement does not necessarily lead to cancer risk reduction. In fact, the opposite was observed for  $\beta$ -carotene and lung cancer (100, 101). Consumption of tomatoes has been found to be inversely correlated with prostate cancer risk, but whether lycopene by itself reduces the risk of prostate cancer is not clear (102).

The model for all types of cancers except lung cancer uses five factors – alcohol consumption, dietary iron, lung cancer, solar UVB doses, and dietary zinc – seems to explain about 80% of the variance, with each factor accounting for roughly the same portion, about 16%, of the variance, although alcohol and lung cancer are more important for males than females. These factors vary by 7% -62% averaged over each of the four major regions of the United States (Table IV). The iron and zinc indices have larger effects on the model results compared with their regional variation than do alcohol, lung cancer and solar UVB. Certainly diet plays an important role in the etiology of cancer, as does smoking and, to a lesser extent, alcoholic beverage consumption. In 1995-99, smoking-attributed deaths accounted for 12% of cancer deaths other than lung cancer for males and 4.4% for females (103, 104). However, some types of cancer for which smoking may play a role, such as colon and rectal cancer, were not included in this estimate, so it is probably low (see also Liestikow (55)).

Previous work estimates that intake of 1,500 IU of vitamin D<sub>3</sub> per day, corresponding to 10 ng/mL of serum 25-hydroxyvitamin D<sub>3</sub> (calcidiol), would reduce male cancer mortality rates by 29%. The variation in serum calcidiol during the year for men in Oakland, California, was 6-7 ng/mL (105), whereas that for women in Boston was 10 ng/mL (106). Residents of Boston cannot make vitamin D<sub>3</sub> from solar UVB in winter (107). Average serum calcidiol levels for white women in Boston was 24 ng/mL in winter and 34 ng/mL in summer (106); for white men in Oakland, California, 24 ng/mL in winter, 32 ng/mL in summer (105); and elderly men in Southern California, 44 ng/mL averaged during the year (108). The annual average difference in serum calcidiol between regions of low and high solar UVB doses could be 5-10 ng/mL, corresponding to 15% -30% variations in cancer mortality rates.

Thus, the contribution of each factor to the variance is probably 10% -20%, in general agreement with the results presented here.

## Conclusion

In the ecological study of cancer mortality rates in the continental United States for 1970-94, several dietary factors were added to the list of factors used in a previous study, such as solar UVB, smoking and alcohol consumption. The previous factors generally retained their

associations, although that for poverty was found to be no longer significant. The inverse correlation with solar UVB doses for July was confirmed for 10 types of cancer in this study, providing more support for the UVB/vitamin D<sub>3</sub>/cancer theory since dietary factors were added to the analysis. The zinc index was inversely correlated with 12 types of cancer, whereas the iron index was directly correlated with 10. Since the dietary sources of zinc are primarily from vegetable products such as whole grains, legumes, and fortified breakfast cereals, whereas meat is the primary source of dietary iron, these two indices may represent broad dietary patterns rather than zinc and iron consumption patterns per se. However, there are known mechanisms associated with cancer risk modification that support a protective role for moderate zinc consumption and an adverse role for moderate iron consumption, so both trace metals probably contribute to the correlations observed for dietary components.

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