

# An ecological study of cancer mortality rates in California, 1950–64, with respect to solar UVB and smoking indices

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**Purpose:** This paper addresses whether nonmelanoma skin cancer (NMSC) mortality rates can serve as a useful index of population ultraviolet-B (UVB) irradiance and vitamin D production in a manner that affects the risk of internal cancers

**Methods:** This analysis uses the ecological study approach with cancer mortality rate data from 19 state economic areas in California. This paper uses age-adjusted data for those aged 40 y or older. Two additional indices for solar UVB doses were also used: latitude and surface UVB doses for July 1992 from the total ozone mapping spectrometer. Lung cancer mortality rates served as the index of the health effects of smoking

**Results:** Significant inverse correlations with NMSC mortality rate in multiple linear regression analyses were found during the period 1950–64 for eight types of cancer for males: bladder, brain, colon, gastric, prostate, and rectal cancer; multiple myeloma; and non-Hodgkin lymphoma. No similar results emerged for females with respect to all three UVB indices. Their NMSC mortality rates averaged 60% lower than those for males. Lung cancer mortality rates were directly correlated with three types of cancer for males: laryngeal, oral, and renal. No significant correlations with NMSC mortality rates appeared for later periods

**Conclusions:** NMSC mortality rates were found inversely correlated with internal cancers for males in the period 1950–64. After that period, no further such correlations were found. The reasons may hypothetically include reduced NMSC mortality rates, high immigration rates, movement from rural to urban locations and reduced solar UVB irradiance.

## Introduction

Debate regarding the validity of the ultraviolet-B (UVB)-vitamin D-cancer hypothesis continues. The brothers Cedric Garland and Frank Garland proposed this hypothesis in 1980 after seeing the map of US colon cancer mortality rates and recognizing that rates were lowest in the sunny Southwest and highest in the cloudy Northeast.<sup>1</sup> Many ecological studies have since concurred with their finding, raising to 20 the number of cancers for which UVB doses are associated with reduced incidence and/or mortality rate.<sup>2–6</sup> However, results of observational studies based on serum 25-hydroxyvitamin D [25(OH)D] concentration are mixed: reasonable evidence exists for breast and colorectal cancer,<sup>7,8</sup> mixed results for pancreatic<sup>9,10</sup> and ovarian<sup>11,12</sup> cancer, but practically no evidence exists for other types of cancer.<sup>11</sup> Studies of UV irradiance for non-Hodgkin lymphoma<sup>13</sup> support the hypothesis. The only randomized controlled trial (RCT) that used a sufficient vitamin D dose (1,100 IU/d) to produce a significant effect yielded good results.<sup>14</sup> In addition, an RCT that used 400 IU/d vitamin D<sub>3</sub> found a significantly reduced risk of total and colorectal cancer and non-significantly reduced risk for participants who had not used vitamins before enrolling

in the study, and a non-significant reduced risk of breast cancer.<sup>15</sup> Nonetheless, by the end of 2010, panels formed to review the evidence concluded that it was inadequate for policy recommendations.<sup>16,17</sup>

Subsequently, Grant<sup>18</sup> suggested that the reason for the discrepancy between observational studies with long follow-up times after serum draw was that the single measurement loses predictive power after a few years.<sup>19</sup> Most case-control studies, which consider serum 25(OH)D concentration or oral vitamin D intake at the time of diagnosis, have found significant inverse correlations with cancer incidence rates.<sup>18</sup>

Although most ecological studies of UVB and cancer rates use geographical variations in the UVB index and cancer outcome, some ecological studies use an alternative approach, examining the link between nonmelanoma skin cancer (NMSC) and cancer risk. The first such study was reported in 1937, in which men in the US Navy with “skin irritation,” that is, NMSC, had reduced risk of internal cancers.<sup>20</sup> Tanning was popular then.<sup>21</sup> Not until the 1940s did the relationship between UV and skin cancer become generally known.<sup>22</sup>

More recently, I proposed that a diagnosis of NMSC could serve as an index of chronic UVB irradiance and, thus, either a

personal or group index of vitamin D production.<sup>23</sup> Because smoking also appears to be a risk factor for NMSC,<sup>24</sup> that study corrected the data for smoking by considering the incidence of lung cancer for each cohort. Using 15-y mortality rate data, a later study applied this approach to the 48 continental provinces of Spain. That study found 15 cancers inversely correlated with NMSC in linear regression analyses.<sup>25</sup>

However, the use of diagnosis of NMSC is not always useful as an index of risk for cancer. A recent review of risk of subsequent cancer following a diagnosis of basal cell carcinoma (BCC), squamous cell carcinoma (SCC) or NMSC found a summary random-effects relative risks of 1.12 (95% CI, 1.07–1.17) for 12 largely European registry-based studies and 1.49 (1.12–1.98) for three United States cohort studies.<sup>26</sup> For individual cancers, statistically significant direct correlations were found only for several cancers for which UV irradiance can be a risk factor: lip cancer,<sup>27</sup> melanoma and non-Hodgkin lymphoma;<sup>28</sup> and some related to smoking: lung, mouth and pharynx, and salivary gland cancer. Significant direct correlations were found for only two types of cancer not linked to smoking or UV irradiance: leukemia and myeloma.

A study not considered by Wheless<sup>26</sup> was one that used cancer records with respect to BCC and SCC in a set of three sunny countries (Australia, Singapore, and Spain) and eight less sunny countries (Canada, Denmark, Finland, Iceland, Norway, Scotland, Slovenia and Sweden).<sup>29</sup> In comparing results for sunny vs. less sunny countries, ten types of cancer were found to have significantly reduced standardized incidence ratios for sunny countries for BCC and/or SCC: bladder, breast, colorectal, kidney, liver, lung, pancreas, pharynx, prostate and stomach

cancer. It is generally colder in the less sunny countries, so people likely expose less body surface area when in the sun compared with the case for the sunny countries.<sup>30</sup> Thus, comparing results for sunny vs. less sunny countries incorporates various factors that contribute to NMSC and other types of cancer including solar UV irradiance, vitamin D production, dietary factors<sup>31</sup> and smoking.<sup>24</sup>

Against this backdrop, I noticed that NMSC and melanoma mortality rates were lower along the US West Coast than inland in California, Oregon, and Washington, whereas mortality rates for many of the internal cancers were often elevated along the coast compared with inland.<sup>32</sup> The prevailing westerly winds and resulting increased fog and low-level clouds along the coast are the most likely explanation for the disparity. Several studies of dental caries rates among adolescents in Oregon in the 1950s used this difference to find an effect of vitamin D.<sup>33</sup> Several other studies have examined clouds for their effect on solar UVB doses reaching the earth's surface.<sup>34–37</sup>

This study uses data from California to examine the link between NMSC and internal cancers. The rationale for this study was that cancer mortality rates along the western coast of the United States are often lower than those in adjacent areas to the east, providing the opportunity to conduct another ecological study of the effect of solar UVB doses on cancer mortality rates. The aims of this study include determining whether NMSC mortality rates are a useful index of solar UVB irradiance by small regions [state economic areas (SAEs)] within the state of California, whether there has been a change in the coastal-inland cancer differences with time, and whether beneficial effects can be found for both males and females.

**Table 1.** Regression results for cancer mortality rate data for 1950–64 with respect to UVB/vitamin D and smoking indices

Cancer	Sex	U.S. rate, 1950–69**	NMSC, M (β, p)	Lung Cancer, M (β, p)	Latitude (β, p)	Regression (Adj. R <sup>2</sup> , p)
All	M	184.46	-0.69, *		0.47, 0.009	0.56, 0.001
All less lung	M	145.21	-0.70, 0.001		0.58, 0.001	0.68, *
Bladder	M	7.38	-0.54, 0.02			0.26, 0.02
Brain	M	4.37	-0.62, 0.004			0.35, 0.004
Colon	M	17.79	-0.64, 0.002		0.47, 0.01	0.50, 0.002
Esophageal	M	4.34			0.51, 0.02	0.31, 0.02
Gastric	M	16.34	-0.45, 0.003		0.79, *	0.70, *
Laryngeal	M	2.67		0.73, *		0.51, *
Lung	M	39.25	-0.38, 0.11			0.09, 0.11
Melanoma	M	1.57	0.46, 0.03		-0.57, 0.008	0.38, 0.008
Multiple myeloma	M	1.84	-0.66, 0.002			0.41, 0.002
NHL	M	5.05	-0.54, 0.02			0.25, 0.02
Oral	M	4.80		0.57, 0.01		0.28, 0.01
Prostate	M	20.15	-0.62, 0.005			0.34, 0.005
Rectal	M	8.18	-0.48, 0.009	0.42, 0.02	0.48, 0.007	0.60, 0.001
Renal	M	3.99	-0.35, 0.06	0.59, 0.003		0.57, *
Skin cancer	M	1.70			0.13, 0.58	0.13, 0.58

\*p < 0.001; \*\*deaths/100,000/yr.

## Results

**Table 1** shows the results for 1950–64 with respect to latitude, lung cancer, and NMSC. Significant inverse correlations with NMSC mortality rate in multiple linear regression analyses appeared for 1950–64 for eight types of cancer for males: bladder, brain, colon, gastric, prostate, and rectal cancer; multiple myeloma; and non-Hodgkin lymphoma. No similar results occurred for females. Significant direct correlations emerged with respect to latitude for four types of cancer: colon, esophageal, gastric and rectal cancer. Lung cancer mortality rates were directly correlated with three types of cancer: laryngeal, oral, and renal and marginally with rectal cancer on the basis of Bernoulli's principle ( $p$  must be less than  $0.05/n$ , where  $n$  is the number of variables). Melanoma was inversely correlated with latitude, and marginally insignificantly with NMSC. The data for NMSC and lung cancer for females were too sparse to use in the analyses, with NMSC averaging 60% lower for females than males and lung cancer averaging 80–85% lower than for males.

**Table 2** shows the results for the July UVB doses and lung cancer. The number of cancers with significant inverse correlations with respect to the UVB index dropped to six, whereas four had significant direct correlations with lung cancer and one had a marginally insignificant correlation.

**Table 2.** Regression results for cancer mortality rates in California by SEA for 1950–64 with respect to solar UVB doses from TOMS

Cancer	Sex	UVB ( $\beta$ , $p$ )	Lung cancer ( $\beta$ , $p$ )	Adj. $R^2$ , $p$
All	M	-0.44, 0.06		0.15, 0.06
All less lung	M	-0.53, 0.02		0.24, 0.02
		-0.57, 0.003	0.53, 0.005	0.52, 0.001
	F	-0.35, 0.14		0.07, 0.14
Bladder	M	-0.32, 0.19		0.05, 0.19
Breast	F	-0.30, 0.21		0.04, 0.21
Colon	M	-0.58, 0.009		0.30, 0.009
		-0.62, 0.002	0.44, 0.02	0.48, 0.002
	F	-0.28, 0.25		0.02, 0.25
Esophageal	M	-0.82, *		0.66, *
		-0.84, *	0.28, 0.04	0.73, *
Gastric	M	-0.52, 0.02		0.23, 0.02
Laryngeal	M	-0.40, 0.09		0.11, 0.09
		-0.46, 0.002	0.77, *	0.71, *
Melanoma	M	0.42, 0.08		0.13, 0.08
NHL	M	-0.41, 0.09		0.11, 0.09
Oral	M	-0.44, 0.06		0.15, 0.06
		-0.49, 0.01	0.60, 0.002	0.50, 0.001
Ovarian	F	-0.40, 0.09		0.11, 0.09
Rectal	M	-0.68, 0.001		0.43, 0.001
		-0.72, *	0.58, *	0.77, *
Skin cancer	M	0.30, 0.21		0.02, 0.21

\* $p < 0.001$ .

## Discussion

The cancers found inversely correlated with NMSC and/or directly correlated with latitude in this study have all been identified as having similar relations in other ecological studies.<sup>2,3,25</sup> The results of this study can be compared with those from other studies that used NMSC prevalence or mortality rates as an index of vitamin D production (**Table 3**).

This study found evidence that during 1950–64, before any great concern about skin cancer, regions of California with lower solar UVB irradiances (as measured according to NMSC mortality rates) generally had higher internal cancer mortality rates for males. A simple division between inland and coastal regions suggests that for every additional 1.07 deaths/100,000 population/year from NMSC, a corresponding drop of 19.3 deaths/100,000/year occurred in all cancer less lung cancer and NMSC mortality rates.

NMSC rates for females were less than half those for males for all periods, and no significant correlations were apparent with solar UVB doses for July. Evidently females spent less time in the sun than did males or covered up more when in the sun. Interestingly, NMSC was inversely correlated with more types of cancer for females (ten) than for males (three) in the similar ecological study in Spain.<sup>25</sup>

The association of cancer mortality rates with lung cancer mortality rate for four types of cancer is consistent with the literature, which increases confidence in the findings. Smoking is a well-known risk factor for both laryngeal and oral cancer.<sup>38</sup> It is also associated with advanced renal cancer<sup>39</sup> and poorer survival after diagnosis of colorectal cancer.<sup>40</sup>

The inclusion of Hispanic Americans with European Americans in the category whites used in this study could affect the results. One study<sup>3</sup> included a factor for the fraction of state population with Hispanic heritage for 1980. Reliable data for Hispanic populations of the 19 SAEs for 1950–64 may be available from the Census Bureau but were not sought. However, data for Hispanic populations of the major cities in each SAE for 2000 were obtained from the Web (<http://santacruz.areaconnect.com/statistics.htm>). With that index, only one cancer had a significant correlation, melanoma. However, this finding could be coincidental in that Hispanics more often live in sunnier locations.

**Post 1964.** There are several possible reasons why NMSC was not inversely correlated with other cancers after 1960–64. For one, immigration from within the US and California and from other countries could also affect cancer rates. California's population increased from 6.9 million in 1940 to 10.6 million in 1950, 15.7 million in 1960, and 20.0 million in 1970 (US Census Bureau). Although no further details were sought, the rapid increases during this period could affect the death rate through changes in the number of residents who lived in a particular UV environment as well as the age distribution used to calculate rates from numbers of deaths.

Another reason may be that California's population changed from one with 25–30% rural population in the 1930s to 1950 according to one measure used by the Census Bureau, then

**Table 3.** Regression results, 1950–64, comparing with other related studies, either an ecological study using solar UVB doses or studies in which cancer risk with respect to NMSC was reported

Cancer	This Study M	[3] M, F	[23] M, F	[25] M	[25] F	[29] M, F	Other (M, F)
All less lung	–O, lat	UV, lun				–O	
Bladder	–O	UV, lun				–O *	
Brain	–O	—		Lun, lat	–O, lat		
Breast, F		UV			–O, lun		
Cervical			–O				
Colon	–O, lat	UV, lun	–O	–O, lun		–O *	–O [54]
Endometrial	—	UV, lun					
Esophageal	Lat	UV, lun	–O	–O, lun			
Gallbladder			–O *		–O	–O	
Gastric	–O, lat	UV	–O	Lat	Lat	–O	
Hodgkin's	—	UV			–O, lun		
Laryngeal	Lun	UV, lun					
Leukemia							
Lung	—	—		Lat	–O		
Melanoma	O, –lat	—			–O		
Multiple Myeloma	–O	—			–O		
NHL	–O	UV			–O, lun*		
Oral	Lun	UV, lun					
Ovarian		UV			–O, lun	–O *	
Pancreatic	—	UV, lun		Lat	Lun*, lat	O	
Pleural				–O, lun	–O		
Prostate	–O	—				–O	–O [55]
Rectal	–O, lat	UV, lun	–O	Lat		–O *	–O [54]
Renal	Lun	UV				–O *	
Skin cancer				Lat	–Lat		
Thyroid				Lun, lat	Lat		

\*insignificant; —, no data; F, female; lat, latitude; lun, lung cancer; M, male; O, NMSC.

dropped by another measure from 19% in 1959 to 14% in 1960, 9% in 1970 and 1980, and 7% in 1990 (US. Census Bureau).

Also, NMSC mortality rates dropped. NMSC rates for males in California decreased from 2.6 deaths/100,000/year in 1950–54 to 1.8 deaths/100,000/year in 1965–69, dipped to 1.3 deaths/100,000/year in 1970–74, then increased slowly to 2.0 deaths/100,000/yr in 1985–89 and 1.8 deaths/100,000/yr in 2000–04. Kaposi sarcoma was added to NMSC after 1980, which could have affected NMSC trends slightly.<sup>32,41</sup> The fact that NMSC mortality rates were lower after 1964 is a further reason why they were not a useful index for UVB irradiance in ecological studies after the period 1960–64.

The NMSC mortality rates may have changed for a number of reasons including increased population living in urban rather than rural locations, fewer people working outdoors, concern about solar UV as a risk factor for NMSC, and better awareness of and medical treatment for NMSC. Sunscreen use in the United States seems to have increased in the 1970s with public awareness campaigns on the risk of skin cancer and melanoma

from solar UV irradiance.<sup>42</sup> Sunscreen use reduces the risk of SCC,<sup>43</sup> the primary type of skin cancer involved in NMSC mortality rates. Concerns regarding increased risk of skin cancer from loss of stratospheric ozone from chlorofluorocarbons was discussed at least by 1976,<sup>44</sup> and campaigns to inform the public and recommend sun avoidance and sunscreen use began in the 1980s.<sup>42</sup>

**Implications.** Several studies have estimated that if serum 25(OH)D concentrations were raised from population means of 20–25 ng/ml to 40–45 ng/ml, mortality rates might be reduced by 10–20% and life expectancy increased by two years.<sup>45</sup> Solar UVB is the primary source of vitamin D for most people in the US, Europe, and Austria. If people obtained vitamin D from solar UVB, the rate of NMSC incidence might increase. However, one study estimated that in the US, 400,000 premature deaths per year would be reduced under this scenario.<sup>46</sup> There are currently an estimated 8,790 melanoma and 3,190 NMSC deaths/year in the US.<sup>47</sup> Frequent moderate sun exposure to increase vitamin D concentrations should not increase these rates

significantly, as the rates were quite low in the 1950s when the sun was not demonized as it is today.

Interestingly, two studies in Denmark found reduced mortality rates for those diagnosed with BCC but increased mortality rates for those diagnosed with SCC.<sup>48,49</sup> The excess deaths for those diagnosed with SCC included cancers, obstructive pulmonary disease, cardiovascular disease, and infectious diseases, and smoking is an important risk factor for these diseases. There is good evidence that smoking is also a risk factor for SCC.<sup>24</sup> Thus, these studies provide further justification for reducing the concern about development of NMSC from solar UV irradiance.

Thus, this study provides evidence that when people live without fearing the sun, but, rather, take no particular efforts to avoid solar UV irradiance though sun avoidance, covering up, and/or wearing sunscreen, overall cancer mortality rates may be lower and both melanoma and NMSC mortality rates will also be low.

## Materials and Methods

Mortality rate data for this study are from the website for the *Atlas of Cancer Mortality in the United States*.<sup>32</sup> The particular data in

this study were mortality rate data for white Americans for SEAs of California for 1950–64 and 1965–74. This study used data for those older than 40 y. Data in this atlas come from the National Center for Health Statistics from information provided by counties where cancer was listed as the underlying cause of death. As with any large data set, it is subject to error. However, the errors associated with the data set were not assessed.

Using data for 5, 10 and 15 y, starting with 1950–54, I determined that using this factor as a reliable index of group UVB irradiance would require 15 y of NMSC mortality rate data to ensure adequate certainty. California has 19 SAEs, each consisting of one or more of the 58 counties. The category “white” includes those of Hispanic descent. This classification scheme could present a problem: Hispanics have darker skin pigmentation than European Americans, so their NMSC risks and vitamin D production rates would differ. An earlier ecological study<sup>2</sup> omitted California, Arizona, and New Mexico because of the high rates of cancers such as gastric cancer near the US-Mexico border.

This study used two additional indices for solar UVB doses: surface DNA-weighted UVB doses for July from the NASA Total

**Table 4.** Data used in this study for 1950–64

State economic area	Latitude* (**)	UVB (kJ/m <sup>2</sup> )	NMSC (**)	All less lung cancer (**)	Lung cancer (**)	Colorectal cancer (**)	Gastric cancer (**)	Melanoma (**)
<b>Coastal</b>								
Eureka	40.1	6.6	5.07	319.2	76.1	32.2	54.5	3.49
Santa Rosa	40.0	6.6	3.99	340.3	81.3	39.8	43.9	3.68
San Francisco	37.8	6.0	3.71	386.2	105.5	46.5	50.0	3.43
Santa Cruz	37.0	6.6	3.93	335.4	85.3	32.1	44.4	4.16
Santa Barbara	34.4	7.5	3.15	336.5	95.1	39.5	45.0	3.66
Oxnard	34.2	8.2	5.16	294.7	78.6	26.2	33.0	4.14
Los Angeles	34.0	8.3	3.57	346.1	100.6	40.1	43.9	3.83
San Diego	32.7	8.3	3.24	322.0	98.3	35.8	36.5	3.66
Mean values		6.4	3.98	335.1	90.1	36.5	43.8	3.76
<b>Inland</b>								
Chico	39.8	8.2	6.00	345.0	89.8	38.1	44.3	3.31
Woodland	38.6	8.0	5.11	315.2	88.0	33.6	42.2	4.07
Sacramento	38.6	8.0	5.22	367.2	111.0	36.5	50.1	3.66
Stockton	38.0	8.0	3.38	337.8	93.0	32.4	50.9	3.62
Modesto	37.6	8.2	5.28	301.7	87.4	29.5	39.6	3.33
San Jose	37.3	6.6	4.43	341.7	85.2	42.8	36.6	3.35
Madera	37.0	8.2	6.40	293.9	72.2	29.9	40.1	4.49
Fresno	36.8	8.2	4.14	345.7	88.3	35.9	47.8	3.48
San Bernadino	34.1	8.5	4.81	301.8	90.4	32.3	33.6	4.09
Bakersfield	33.7	8.6	3.42	312.6	91.7	28.4	32.5	4.03
El Centro	32.6	8.7	7.35	223.7	89.3	16.5	25.1	4.40
Mean values		8.1	5.05	316.9	89.7	32.4	40.3	3.80
Inland/coastal		1.26	1.27	0.95	1.00	0.89	0.92	1.01
Inland less coastal			1.07	-18.2	-0.4	-4.1	-3.5	0.04

\*<http://www.travelmath.com/city/Oxnard,+CA>; \*\*deaths/100,000/yr.



Ozone Mapping Spectrometer (TOMS)<sup>50</sup> and latitude.<sup>51</sup> The TOMS data were digitized for a previous paper.<sup>2</sup> A review of the data indicates that the values are correct. One problem with TOMS data are that they may not capture the effect of clouds and fog because the instrument has difficulty determining radiance from the lower kilometer or so of the atmosphere.<sup>52</sup> Another concern is that the TOMS data were for July 1992 and the cancer mortality data were for the period 1950–64.

Lung cancer was used as the index of smoking,<sup>53</sup> as has been done previously.<sup>3,25</sup>

Table 4 gives the independent variables in this study, along with mortality rate data for some of the cancers. When the SAEs are divided into coastal and inland categories, the simple mean ratio of the July UVB doses and NMSC mortality rates are 26% higher for the coastal SAEs than the inland ones. Rates of colon cancer, gastric cancer, and all less lung cancer rates are lower in the inland SAEs.

Multiple linear regression analyses were run using SPSS Graduate Pack 16.0. The preliminary analysis used latitude, lung cancer, and NMSC data. Any factor that was not statistically significant was omitted and the analysis was rerun. Little interaction occurred among the three variables. Nonetheless, some interference was present for two cancers, so linear regressions were run to see whether the factor had an independent correlation with the cancer; if not, it was eliminated from the final analysis.

The UVB doses from TOMS were run separately from the other two UVB indices but with the lung cancer index.

#### Disclosure of Potential Conflicts of Interest

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