

# Role of solar UVB irradiance and smoking in cancer as inferred from cancer incidence rates by occupation in Nordic countries

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A large body of evidence indicates that solar ultraviolet-B (UVB) irradiance and vitamin D reduce the risk of incidence and death for many types of cancer. However, most of that evidence comes from midlatitude regions, where solar UVB doses are generally high in summer. Data on cancer standardized incidence ratios (SIRs) by sex and 54 occupation categories based on 1.4 million male and 1.36 million female cancer cases for 1961–2005 in the five Nordic countries provide the basis for an ecological study of the role of solar UVB in the risk of many types of cancer at high latitudes. Lip cancer SIRs less lung cancer SIRs for men was the best index of solar UVB dose, which was weakly inversely correlated with both melanoma and nonmelanoma skin cancer (NMSC) SIRs. Lung cancer SIRs were used as the index of the effects of smoking. For men, the UVB index was significantly inversely correlated with 14 types of internal cancer—bladder, breast, colon, gallbladder, kidney, laryngeal, liver, lung, oral, pancreatic, pharyngeal, prostate, rectal and small intestine cancer. For women, the same UVB index was inversely correlated with bladder, breast and colon cancer. These results generally agree with findings from other studies. These results provide more support for the UVB-vitamin D-cancer hypothesis and suggest that widespread fear of chronic solar ultraviolet (UV) irradiance may be misplaced.

The ultraviolet-B (UVB)-vitamin D-cancer hypothesis<sup>1</sup> has strong support from ecological studies,<sup>2</sup> observational studies,<sup>3,4</sup> and randomized controlled trials.<sup>5,6</sup> The mechanisms whereby vitamin D reduces the risk of cancer are reasonably well understood.<sup>7,8</sup> The findings generally satisfy Hill's criteria for causality in a biological system.<sup>9</sup> However, some studies find no evidence to support the hypothesis, such as observational studies with follow-up times longer than 3 y for breast cancer,<sup>10</sup> and some studies in Nordic countries.<sup>11</sup> Given such disagreements and the paucity of randomized controlled trials, the world's health systems are reluctant to accept the hypothesis.<sup>12</sup> Thus, additional evidence regarding the hypothesis is warranted before it can gain widespread acceptance.

An earlier paper used mortality rates for nonmelanoma skin cancer (NMSC) by province as the index of integrated solar UVB dose for residents in Spain.<sup>13</sup> Seventeen types of cancer inversely correlated with this index. Subsequently, a record-linkage study in sunny countries (Australia, Singapore and Spain) found that NMSC diagnosis was significantly inversely correlated with three types of cancer (liver, pancreatic, and prostate) and nonsignificantly correlated with six more (bladder, colon, gastric, ovarian, rectal and renal).<sup>14</sup> However, in less sunny countries (Canada and seven northern European countries), all solid tumors except those of the lip and skin were significantly directly correlated with NMSC diagnosis.<sup>14</sup> A recent paper from Sweden found an

increased risk of internal cancers for those diagnosed with basal cell carcinoma (BCC).<sup>15</sup> However, studies in The Netherlands found inverse correlations between NMSC and prostate<sup>16</sup> and colorectal<sup>17</sup> cancer.

Another index of integrated solar UVB irradiance that could be employed is diagnosis of lip cancer. Solar UVB irradiance is the most important risk factor for this cancer. Smoking is also a risk factor for lip cancer. An occupational study in Nordic countries pointed out that outdoor workers had much higher rates of lip cancer than indoor workers.<sup>18</sup> A study in Denmark found that lip cancer incidence rates had a statistically significant increase with respect to outdoor work while basal cell carcinoma had a statistically significant decreased incidence rate, squamous cell carcinoma (SCC) had practically no relation to outdoor work, and cutaneous malignant melanoma had an insignificant decrease with respect to outdoor work.<sup>19</sup>

To be useful in an ecological study, the population should be large and divided into various categories. A database satisfying these criteria was found: the follow-up of 15 million people in five Nordic countries in which 1,400,682 male and 1,357,616 female cancer cases were documented from 1961 to 2005.<sup>20</sup> The data by cancer types were also organized into 54 occupation categories, some of which were primarily outdoor occupations, whereas others were primarily indoor occupations.

## Results

The cross correlations for the independent factors used in this study, along with the correlations for melanoma and NMSC, are given in Table 1. There is a modest interaction between the UVB index and lung cancer for males, which could affect the multiple linear regression results. Therefore, results for the UVB index and lung cancer are often presented separately as well in the results for the other cancers.

Table 2 gives the regression results for men, whereas Table 3 gives those for women. Results are generally given for the multiple linear regression with lip less lung cancer and lung cancer unless the regression result for one type of cancer was very weak. Results

**Table 1.** Cross-correlation results for lip and lung cancer, melanoma and NMSC

Cancer	N	Lip cancer less lung cancer (males) ( $\beta$ , p)	Lung cancer (males) ( $\beta$ , p)	Adjusted R <sup>2</sup> , F, p
<b>Males</b>				
Lung	45	-0.40, 0.006		0.14, 8.3, 0.006
Melanoma	45	-0.69*	-0.85*	0.72, 56*
	45	-0.35, 0.02		0.10, 5.9, 0.02
	45		-0.57*	0.31, 21*
NMSC	45	-0.43, 0.002	-0.67*	0.38, 14*
	45		-0.50*	0.23, 14*
<b>Females</b>				
			Lung cancer (females)	
Lung	39	-0.27, 0.10		0.05, 2.8, 0.10
Melanoma	37	-0.26, 0.009	-0.53, 0.001	0.24, 6.7, 0.003
	37		-0.47, 0.003	0.20, 9.8, 0.003
NMSC	38	-0.26, 0.10	-0.50, 0.002	0.21, 6.0, 0.006
	38		-0.44, 0.006	0.17, 8.6, 0.006

\*p < 0.001.

**Table 2.** Regression results for males

Cancer	N	Lip cancer less lung cancer ( $\beta$ , p)	Lung cancer ( $\beta$ , p)	Adjusted R <sup>2</sup> , F, p
All	45	-0.44*	0.97*	0.82, 104*
	45	-0.70*		0.48, 42*
	45		0.82*	0.66, 85*
All less lung	45	-0.67*	0.69*	0.58, 32*
	45	-0.76*		0.57, 59*
	45		0.45, 0.002	0.19, 11, 8
Bladder	45	-0.60*	0.78*	0.58, 32*
	45	-0.73*		0.52, 48*
	45		0.54*	0.27, 18*
Brain	45	-0.45, 0.001	-0.32, 0.02	0.38, 15*
	45	-0.20, 0.20		0.02, 1.7, 0.2
	45		-0.48, 0.001	0.21, 13, 0.001

**Table 2.** Regression results for males (continued)

Cancer	N	Lip cancer less lung cancer ( $\beta$ , p)	Lung cancer ( $\beta$ , p)	Adjusted R <sup>2</sup> , F, p
Breast	39	-0.41, 0.01	0.31, 0.06	0.15, 4.3, 0.02
	39	-0.44, 0.005		0.17, 8.8, 0.005
Colon	45	-0.66*	0.35, 0.009	0.37, 14*
	45	-0.61*		0.36, 26*
Esophageal	45	-0.05, 0.60	0.83*	0.64, 40*
	45	-0.37, 0.01		0.12, 6.8, 0.01
	45		0.81*	0.65, 82*
Gallbladder	42	-0.41, 0.003	0.68*	0.42, 16*
	42	-0.57*		0.31, 20*
	42		0.55*	0.28, 17*
Kidney	45	-0.57*	0.74*	0.55, 28*
	45	-0.70*		0.48, 42*
	45		0.54*	0.28, 17*
Laryngeal	45	-0.26, 0.01	0.85*	0.61, 36*
	45	-0.53*		0.26, 16*
	45		0.76*	0.56, 57*
Liver	45	-0.43, 0.001	0.73*	0.47, 20*
	45	-0.60*		0.34, 24*
	45		0.58*	0.32, 22*
NHL	45	-0.28, 0.07	-0.23, 0.14	0.13, 4.4, 0.02
	45		-0.33, 0.03	0.09, 5.1, 0.03
Oral	43	-0.34, 0.01	0.65*	0.36, 13*
	43	-0.51, 0.001		0.24, 14, 0.001
	43		0.53*	0.27, 16*
Pancreatic	45	-0.39, 0.001	0.81*	0.57, 30*
	45	-0.61*		0.35, 25*
	45		0.68*	0.44, 36*
Pharynx	44	-0.29, 0.04	0.59*	0.29, 9.6*
	44	-0.46, 0.002		0.19, 11, 0.002
	44		0.49, 0.001	0.23, 14, 0.001
Prostate	45	-0.58*	-0.20, 0.11	0.44, 18*
	45	-0.34, 0.02		0.09, 5.5, 0.02
	45		-0.41, 0.006	0.15, 8.4, 0.006
Rectal	45	-0.46, 0.001	0.66*	0.41, 16*
	45	-0.60*		0.34, 24*
	45		0.50*	0.23, 14*
Small intestine	43	-0.64*	0.16, 0.23	0.33, 11*
	43	-0.53*		0.27, 16*
Stomach	45	-0.52*	0.58*	0.81, 94*
	45		0.76*	0.57, 60*
Testis	44	-0.51*	-0.33, 0.008	0.47, 20*
	44	-0.24, 0.12		0.04, 2.6, 0.12
	44		-0.51*	0.24, 14*

\*p < 0.001.

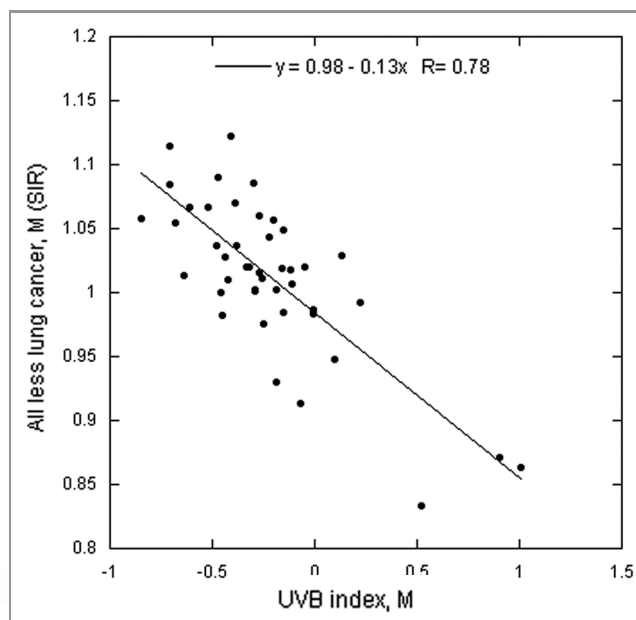
**Table 3.** Regression results for females

Cancer	N	Lip cancer less lung cancer for males ( $\beta$ , p)	Lung cancer for females ( $\beta$ , p)	Adjusted R <sup>2</sup> , F, p
All	39	-0.63*	0.22, 0.08	0.49, 19*
	39	-0.68*		0.45, 33*
	42		0.38, 0.01	0.12, 6.6, 0.01
All less lung	39	-0.69*	-0.40, 0.002	0.47, 18*
	39	-0.59*		0.33, 19*
	42		-0.24, 0.13	0.03, 23, 0.13
Bladder	37	-0.51, 0.001	0.20, 0.18	0.31, 9.1, 0.001
	37	-0.56*		0.29, 16*
Breast	39	-0.69*	-0.43, 0.003	0.38, 12*
	39	-0.49*		0.22, 12*
	42		-0.25, 0.12	0.04, 2.6, 0.12
Cervix	39	0.01, 0.90	0.77*	0.57, 26*
	39		0.75*	0.55, 50*
Colon	39	-0.41, 0.02	-0.08, 0.62	0.11, 33, 0.05
	39	-0.39, 0.02		0.13, 6.5, 0.02
Corpus uteri	39	-0.39, 0.01	-0.44, 0.005	0.22, 6.2, 0.005
	39	-0.27, 0.09		0.05, 3.0, 0.09
	39		-0.38, 0.01	0.12, 6.6, 0.01
Esophageal	29	-0.03, 0.89	0.52, 0.01	0.23, 5.1, 0.01
	29		0.53, 0.003	0.25, 11, 0.003
Kidney	36	0.22, 0.16	0.53, 0.01	0.23, 6.3, 0.005
	38		0.50, 0.001	0.23, 12, 0.001
Liver	32	-0.23, 0.14	0.50, 0.003	0.33, 8.8, 0.004
	32		0.57, 0.001	0.31, 15, 0.001
Pancreatic	37	-0.28, 0.08	0.36, 0.03	0.21, 5.8, 0.007
	37	-0.37, 0.03		0.11, 5.4, 0.03
	39		0.50, 0.001	0.23, 12, 0.001
Rectal	39	-0.31, 0.06	0.11, 0.52	0.08, 2.6, 0.09
	39	-0.34, 0.03		0.09, 4.9, 0.03
Stomach	38	0.26, 0.07	0.64*	0.36, 11*
	41		0.46, 0.003	0.19, 10, 0.003

\*p < 0.001.

are also given for each type of cancer for which statistically significant (or nearly so) results were obtained. For men, the same occupations were used for lung cancer alone as for the UVB index, whereas for women, the separate regression for lung cancer used all occupations with useful lung cancer SIRs.

For men, the smoking index was directly correlated with bladder, esophageal, gallbladder, kidney, laryngeal, liver, oral, pancreatic, pharyngeal, rectal and stomach cancer, and inversely correlated with prostate and testicular cancer, all less lung cancer, melanoma and NMSC. For women, the smoking index was directly correlated with cervical, esophageal, kidney, liver, pancreatic and stomach cancer and inversely correlated with corpus uteri cancer, melanoma and NMSC.



**Figure 1.** Scatter plot of all cancer less lung cancer SIR for males vs. the UVB index.

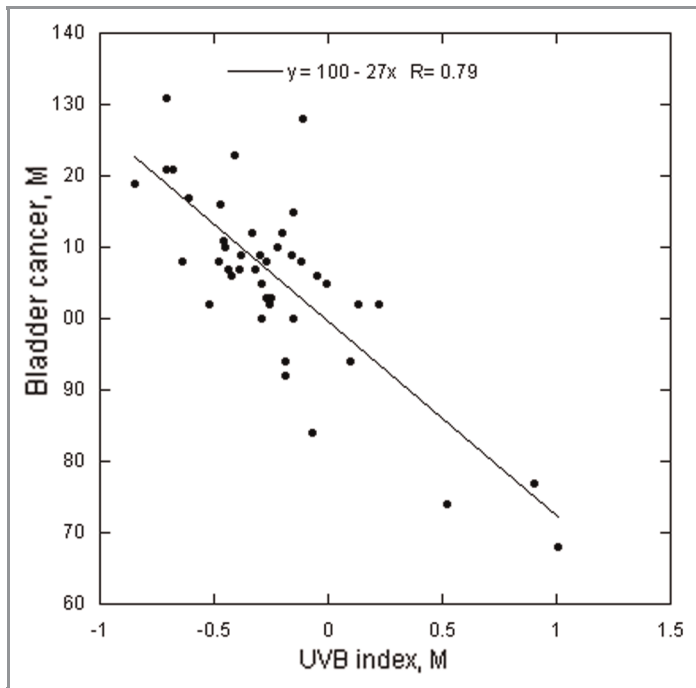
For men, the UVB index by itself was significantly inversely correlated with 15 types of cancer—bladder, breast, colon, gallbladder, kidney, laryngeal, liver, lung, oral, pancreatic, pharyngeal, prostate, rectal, small intestine cancer and melanoma—and all malignant neoplasms less lung cancer. In a multiple linear regression with lung cancer, the UVB index is inversely correlated with testicular cancer. However, since the UVB index is not inversely correlated with testicular cancer in a linear regression analysis, it is unlikely that the UVB index is inversely correlated with testicular cancer.

For women, the same UVB index by itself and in multiple linear regression with lung cancer was inversely correlated with bladder, breast, colon and rectal cancer, as well as all malignant neoplasms less lung cancer. In a multiple linear regression with lung cancer, the UVB index is inversely correlated with corpus uteri (endometrial) cancer. While the UVB index was significantly inversely correlated by itself with pancreatic and rectal cancer, the significance disappeared in multiple linear regressions with lung cancer.

Figures 1–6 are scatterplots of SIRs for all cancers less lung cancer, bladder cancer, kidney cancer, and pancreatic cancer for males, all cancers less lung cancer and breast cancer for females, respectively, vs. the UVB index, with linear regression fits to the data.

## Discussion

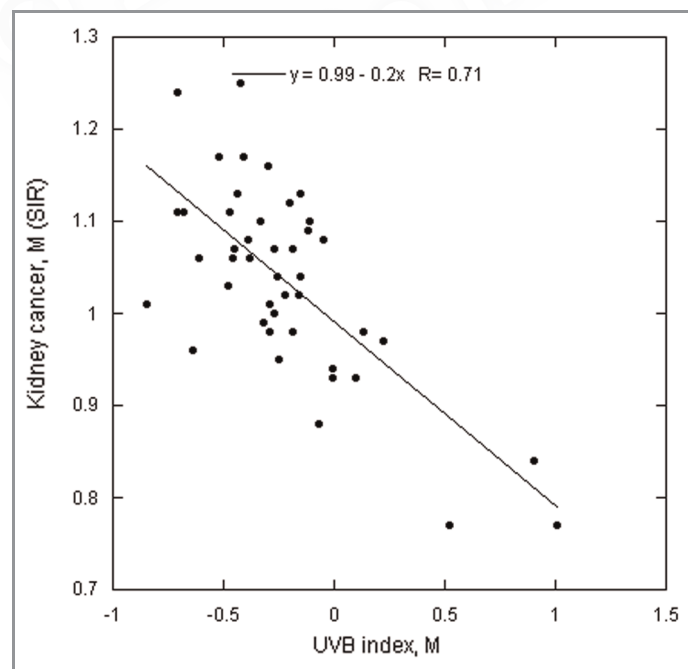
The findings for most cancers agree well with the results of other ecological studies for cancer incidence and/or mortality rates for men. The findings for women are in good agreement for breast, colon, and corpus uteri cancer. Smoking is considered an important risk factor for all of the cancers for which that was found to



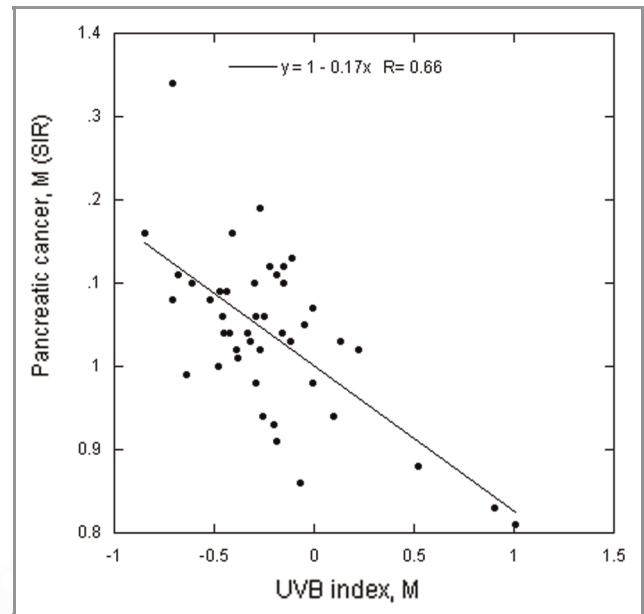
**Figure 2.** Same as Figure 1 for bladder cancer for males.

be so in this study.<sup>21,22</sup> Smoking has been found inversely correlated with melanoma<sup>23</sup> and corpus uteri (endometrial) cancer.<sup>24</sup> Thus, these findings help build confidence in the results for the UVB index in this study.

One measure of vitamin D's effect on cancer risk is survival with respect to serum 25-hydroxyvitamin D [25(OH)D] concen-

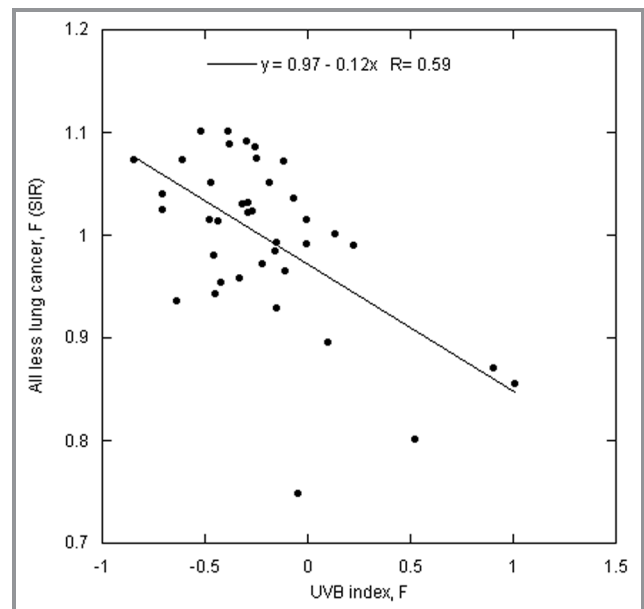


**Figure 3.** Same as Figure 1 for kidney cancer for males.

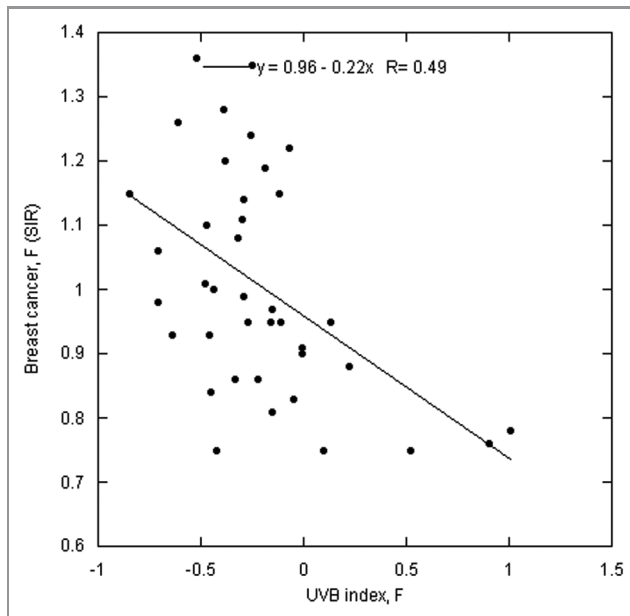


**Figure 4.** Same as Figure 1 for pancreatic cancer for males.

tration at time of diagnosis. Higher concentrations were associated with higher survival rates for breast, colon, lung cancer, and Hodgkin lymphoma in Norway.<sup>25</sup> Survival with respect to season of incidence is another measure. Another study in Norway found 20–25% reduced 36-mo mortality rates for breast, colon, and prostate cancer and Hodgkin's lymphoma for summer compared with winter diagnosis, but no effect for bladder, lung and ovarian cancer.<sup>26</sup> The findings from these two studies are in very good agreement with the findings in this study for breast, colon, lung and ovarian cancer.



**Figure 5.** Scatter plot of all cancer less lung cancer SIR for females vs. the UVB index.



**Figure 6.** Same as Figure 5 for breast cancer for females.

A study of women in Sweden found significant inverse correlations with respect to some indices of ultraviolet (UV) irradiance for breast cancer, lung, and overall cancer but not for brain or colorectal cancer.<sup>27</sup> However, the study found non-significant inverse correlations for all measures of sunbathing vacations for ovarian cancer. A similar study in Norway found no benefit of higher vitamin D concentration or sun exposure.<sup>11</sup> From my analysis in the present study, it might be concluded that most of those studied had indoor occupations.

Although the present study found no correlation between lip cancer and ovarian cancer, evidence from other studies indicates that UVB, vitamin D status, or both can reduce the risk.<sup>13,27-30</sup>

The non-significant inverse correlation finding for non-Hodgkin lymphoma (NHL) may be due to competing effects of UV on risk: reduced risk from production of vitamin D, but increased risk from immunosuppression for B-cell lymphoma<sup>31</sup> and T-cell lymphoma.<sup>32</sup> However, in regions with a high ratio of UVB to UVA, UV irradiance is associated with reduced risk of B-cell but not T-cell NHL.<sup>33</sup> This topic has been discussed in more detail in a paper in press.<sup>34</sup>

The results for prostate cancer are consistent with those of several other studies with respect to solar UVB irradiance.<sup>16,35</sup> However, prediagnostic serum 25(OH)D concentration has virtually no relation to prostate cancer incidence.<sup>3,4</sup> The disparity in findings between those for UV irradiance and prediagnostic serum 25(OH)D concentrations suggests that early-life UVB and vitamin D may be protective. John and colleagues<sup>36</sup> found a protective effect of early-life UV exposure. Alternatively, serum 25(OH)D concentrations in observational studies to date may have been too low.

It is interesting to compare the results of this study with those of the Vitamin D Pooling (VDPP) Project of Rarer Cancers. That study found no correlation between prediagnostic serum

25(OH)D concentration and incidence of endometrial, esophageal, kidney, ovarian, stomach cancer and NHL and a direct correlation with pancreatic cancer incidence.<sup>37</sup> This study found inverse correlations with the UVB index for endometrial, kidney, and pancreatic cancer but not the other four types of cancer. Evidently the VDPP study was underpowered to find any beneficial effects of vitamin D. Part of the problem was that the mean follow-up time after enrollment and serum draw was 6.63 y. As discussed previously, serum 25(OH)D concentrations change with time, and follow-up times of that magnitude can wash out any correlations.<sup>10</sup> See, also, a study of NHL in Finland, where the correlation with 25(OH)D changed from inverse for follow-up time less than seven years to direct for longer follow-up times.<sup>38</sup> In addition, so few cases were included that the 95% confidence intervals (CIs) were about 50%. This problem was addressed in a recent ecological study in which it was shown that as the number of cases increases, the 95% CI shrinks.<sup>39</sup>

This study offers further evidence that diagnosis of NMSC in Nordic countries is associated with increased risk of internal cancers.<sup>14,15</sup> In this study, both melanoma and NMSC are inversely correlated with the UVB index, although the link is not statistically significant for NMSC for females. Basal cell carcinoma (BCC) is the most common form of NMSC, and it apparently shares some characteristics of melanoma. A paper from Germany reported that “occupational ultraviolet (UV) exposure appeared to be a risk factor (OR 2.4). In contrast, clinical actinic elastosis showed a protective effect (OR 0.1).”<sup>40</sup> Those with greater outdoor work experience may have been more likely to develop actinic elastosis, thereby reducing risk of NMSC.

As Table 1 shows, the UVB index is inversely correlated with both NMSC and melanoma. One reason could be that both NMSC and melanoma may be more influenced by long-wave UVA rather than UVB. The ratio of UVA to UVB increases with latitude in Europe.<sup>41</sup> Data on age-adjusted (world) incidence rates for BCC, SCC, and melanoma for 2000 are available from reference 42. Mean values for the five Nordic countries and three southern European countries (Greece, Italy and Spain) are given in Table 4. Rates for both BCC and melanoma are higher in the north than in the south, with little difference for SCC. Another reason could be that melanoma is inversely correlated with smoking.<sup>43</sup> However, the relationship of smoking with BCC is not clear.<sup>44</sup>

**Table 4.** Age-adjusted (world) incidence rates for BCC, SCC and melanoma for 2000 for Nordic and Southern European countries and their ratios<sup>42</sup>

Region	Sex	BCC*	SCC*	Melanoma*
Nordic	M	62.5	10.3	12.4
	F	54.5	4.2	14.3
Southern	M	50.0	12.4	7.4
	F	29.3	4.0	6.6
N/S	M	1.25	0.83	1.68
N/S	F	1.86	1.1	2.17

\*cases/100,000/year, N/S, Northern/Southern.

One reason melanoma is inversely correlated with lung cancer is that smoking increases skin elastosis, which retards the growth of melanoma. A study in Sweden reported that melanoma on the regularly sun-exposed parts of the body have higher incidence rates at older ages, whereas parts of the body not regularly exposed have a peak incidence rate in middle age.<sup>45</sup> Flach and colleagues<sup>46</sup> recently reported that melanoma tumors acquire fibroblasts from surrounding tissue. Elastosis may impair melanoma's ability to acquire fibroblasts.

The fact that women have 3,008 cases of lip cancer compared with 14,477 cases for men is probably due to fewer women with outdoor occupations as well as use of lipstick, which reduces UV irradiance of the lips. For the seven occupations most closely associated with outdoor work, lip cancer constituted 2.1% of male cancers but only 0.32% of female cancers. One half (1,500) of the lip cancer cases for women were from the "economically inactive" category, compared with 6.7% for men.

It is interesting that in the Nordic countries, all-cancer rates are lowest in northern Finland and Sweden and highest in Iceland and southern Norway for the period 1998–2003.<sup>20,47</sup> Thus, looking at cancer rates by occupation appears to be a better method of determining the role of solar UVB irradiance and vitamin D status

**Table 5.** Regression results for males for cancers increased by UV irradiance

Cancer	N	Lip cancer ( $\beta$ , p)	Melanoma ( $\beta$ , p)	NMSC ( $\beta$ , p)	Adjusted R <sup>2</sup> , F, p
All less lung	47	-0.32, 0.03			0.09, 5.3, 0.03
Bladder	47	-0.31, 0.03			0.08, 4.9, 0.03
Colon	47	-0.50*			0.23, 15*
	51		0.35, 0.01		0.10, 6.8, 0.01
	51			0.41, 0.003	0.15, 9.7, 0.003
Kidney	47	-0.28, 0.06			0.06, 3.7, 0.06
Laryngeal	51		-0.22, 0.13		0.03, 2.4, 0.13
	51			-0.26, 0.06	0.05, 3.6, 0.06
Liver	51	-	-	-	
NHL	47	-0.34, 0.02			0.10, 5.8, 0.02
	52		0.21, 0.14		0.03, 2.3, 0.14
	51			0.31, 0.03	0.08, 5.1, 0.03
Oral	51	-	-	-	
Pancreatic	51		-0.18, 0.22		0.10, 1.6, 0.22
Prostate	47	-0.65*			0.40, 0.32*
	51		0.75*		0.55, 63*
	51			0.69*	0.47, 45*
Rectal	51			-0.18, 21	0.01, 1.6, 0.21
Small intestine	43	-0.58*			0.33, 21*
	46		0.40, 0.006		0.14, 8.3, 0.006
	46			0.44, 0.002	0.17, 10, 0.002
Testicular	45	-0.59*			0.34, 23*
	48		0.49, 0.001		0.23, 15*
	48			0.46, 0.001	0.19, 12, 0.001

NHL, Non-Hodgkin's lymphoma; \*p < 0.001.

in cancer risk than by geographical location in high-latitude countries. However, in midlatitude regions, geographical variations in cancer incidence and/or mortality rates work well.<sup>2</sup>

Some limitations may affect this study's findings. This ecological study used indices for only two factors, UVB irradiance (vitamin D status) and lung cancer (smoking). This study did not include many other cancer risk-modifying factors that could affect the relative SIRs for various types of cancer with respect to occupation. Several are discussed below. However, the first ecological study of many types of cancer in the US used only solar UVB doses for July, finding 15 types of cancer inversely correlated with that index.<sup>48</sup> A later study, which included the additional factors of alcohol consumption, ethnic background for whites, the poverty index, smoking, and urban/rural residence, found nearly the same results for those 15 types of cancer.<sup>28</sup>

One factor related to occupation that could affect the regression results is physical activity. Observational studies with respect to physical activity have found modest (10–25%) reductions in risk of many types of cancer.<sup>49</sup> However, the Freedman et al.<sup>29</sup> findings did not associate physical activity with reduced risk of prostate cancer. In consideration of the occupations included in Pukkala,<sup>20</sup> many of those in the high-UVB index category probably have high occupational activity levels, whereas many of those in the low-UVB index category probably have low occupational activity levels. However, some occupations in the low category may also have high levels of physical activity associated with them, such as shop workers and waiters.

A second factor is chemical exposures at work. There are numerous publications on this topic.<sup>50–54</sup> According to Parkin,<sup>54</sup> occupational exposures in the UK contributed about 4.9% of all male cancer cases and 2.4% of female cancer cases in 2010, with strongest impacts, in descending order, for mesothelioma, lung, nasopharynx, and bladder cancer. Other than for lung cancer, the rates are not high enough to affect the results of this study, and the results using lung cancer as the index of smoking agree well with the results in the literature.

A third factor is competition from other diseases. An inverse relation seems to exist with respect to occupation for cancer and cardiovascular disease. In Nordic countries, manual labor classes have higher ischemic heart disease mortality rates than nonmanual classes.<sup>55</sup> From mortality rate data for 2002 from the World Health Organization,<sup>56</sup> cancer disease mortality rates (deaths per 100,000 population per year) vary by 45% between Finland (202.8) and Denmark (294) (excluding Iceland, with its small population), whereas cardiovascular rates vary by 23% from Denmark (389.8) to Sweden (478.4). Thus, cardiovascular and other disease rates may affect the findings of this study.

A fourth factor is mixture of people with different ethnic backgrounds or countries of origin. A search of the Internet indicates that 2–3% of the Finland population comes from outside the Nordic countries, whereas Denmark, Finland, Iceland, and Sweden may have 7–13% of the population from outside the Nordic countries. The only types of cancer for male outdoor workers for which Finland has different rates (higher) from those of the other four countries are the smoking-related cancers: bladder, esophageal, laryngeal, lung, and pharyngeal cancer.

Thus, no significant effect seems to come from different ethnic backgrounds or countries of origin.

## Summary and Conclusion

These results add support to the UVB-vitamin D-cancer hypothesis. Even in countries with relatively low annual and summertime solar UVB doses, significant inverse correlations exist between an index of solar UVB irradiance and 15 types of internal cancers as well as melanoma. The key to this finding was identification of people with different amounts of sun exposure based on occupation, then finding an optimal index of solar UV irradiance for each occupation.

This study also suggests that chronic solar UVB irradiance is more beneficial than harmful, as outlined in two recent papers.<sup>57,58</sup>

## Materials and Methods

This ecological study uses cancer standardized incidence ratios (SIRs) by sex and occupation from the tabulations in Pukkala and colleagues.<sup>20</sup> Several indices were evaluated for use as the UVB irradiance index. There are three types of cancer linked to UV irradiance: melanoma, NMSC (primarily SCC<sup>20</sup>), and lip cancer. A study in Denmark found that only lip cancer was consistently increased for outdoor work.<sup>19</sup> Nonetheless, in order to confirm that lip cancer is the best of these three cancers for the UVB index, regression coefficients were determined for these three cancers for some of the internal cancers with strongest indications of reduced risk with respect to UVB irradiance for males.<sup>2</sup> The results are given in Table 5. Lip cancer was significantly inversely correlated with all-cancer less lung cancer as well as bladder, colon, prostate, small intestine and testicular cancer. Both melanoma and NMSC were significantly directly correlated with colon, prostate, small intestine and testicular cancer but not significantly correlated with the other types of cancer.

Since lip cancer is caused both by UV irradiance and smoking, an index formed by lip cancer less lung cancer SIRs for males was developed and determined to be the best indicator of UVB irradiance from outdoor occupation. This index will be hereafter called the UVB index. Lung cancer SIRs were used as the index of the health effects of smoking, as done in previous ecological studies.<sup>13,21</sup>

Some entries have few cases and, therefore, large 95% CIs. To determine which values to exclude, I conducted regression analyses using lip cancer for males and lung cancer for males as the independent variables and all malignant neoplasms and melanoma

for males as the dependent variables, as well as lip cancer for males and lung cancer for females as the independent variables and breast cancer for females as the dependent variable. Lip cancer cases for females were too few to be useful ( $n = 3008$ ). However, the identification of the relative amount of outdoor work for the various occupations from the 14,477 lip cancer cases for males makes the same ranking useful for females. The analyses proceeded from omitting only those occupations with no cases to other occupations using the ratio of the highest 95% CI to the mean SIR ordered from highest to lowest ratio. I ran 18 combinations with lip cancer and the other cancers. This exercise found that after omitting the six occupations with the highest ratios of 95% CI to the SIR value (laboratory assistants, dentists, nurses, tobacco-workers, domestic assistants and launderers), little change occurred after removing another 12 occupations, so was adopted. The ratio of high 95% CI to SIR for the seventh occupation, assistant nurses, was 1.83, so this value served as the cutoff value for all other data. That value was obtained with approximately ten cases.

Using simple algebra involving number of cases and SIRs, I calculated the SIRs for all malignant neoplasms less lung cancer from the SIRs for all malignant neoplasms and lung cancer.

I ran the regressions by using SPSS 16.0 Grad Pack (IBM-SPSS) and made the graphs by using KaleidaGraph 4.0 (Synergy Software).

Nine occupations were omitted for males: six because there were insufficient numbers of men with lip cancer to generate upper 95% CIs within 83% of the mean SIR: laboratory assistants, nurses, tobacco-workers, domestic assistants, waiters, and launderers. In addition, dentists, fishermen, and beverage workers were omitted since their SIRs for lip cancer or other cancers appeared to be outliers. There were only 13 dentists and 16 beverage workers with lip cancer. The lip cancer SIR for fishermen was 2.27, which was the highest for any occupation, while their lung cancer SIR was 1.16. It could be that fishermen have a high risk for lip cancer due to getting bounce UV radiation from the water's surface. For females, six occupations were omitted since there were three or fewer cases of lung cancer: bricklayers, chimney sweeps, military personnel, miners and quarry workers, plumbers, and seaman. These are traditionally male occupations. In addition, chimney sweeps were omitted for females.

## Disclosure of Potential Conflicts of Interest

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