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Short Communication

The effect of solar UVB doses and vitamin D production, skin cancer action spectra, and smoking in explaining links between skin cancers and solid tumours

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ABSTRACT

The report of differences between skin cancer rates and solid tumours in sunny versus less sunny countries [Tuohimaa P, Pukkala E, Scelo G, et al. Does solar exposure, as indicated by the non-melanoma skin cancers, protect from solid cancers: Vitamin D as a possible explanation. *Eur J Cancer* 2007; 43: 1701–12] raised some important questions regarding the roles of solar ultraviolet (UV) irradiance and cancer risk. The findings can likely be explained based on the effects of UVB dose on cancer risk, the action spectra of different skin cancers, the amount of skin exposed, and the differential effects of smoking on cancer risk. Solar UVB has been found inversely correlated with about 20 types of cancer in ecological and cohort studies in sunny countries. Vitamin D and calcium were recently found to greatly reduce cancer incidence in a prospective double-blind study. Epidemiological studies suggest that the action spectra for skin cancers vary, with solar UVB most important for squamous cell carcinoma, UVA most important for melanoma, and both important for basal cell carcinoma. These differences may explain the different standardised incidence ratios for solid tumours with respect to the different skin cancers in sunny countries. Smoking has been reported as a risk factor for non-melanoma skin cancers, but has been found inversely correlated with melanoma, which may explain some of the differences in standardised incidence ratios for solid tumours linked to smoking with respect to type of skin cancer. In Nordic countries, less skin is generally exposed, resulting in reduced vitamin D production, and in head and neck regions the most frequent sites of squamous cell carcinoma.

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The discordant correlations found between different skin cancers and second primary cancers and between sunny countries versus less-sunny countries by Tuohimaa et al.¹ is quite interesting. However, the discussion of the findings provided more questions than answers. In order to more fully understand the findings, several aspects of cancer risk have to be evaluated: the role of solar UVB doses and vita-

min D photoproduction in reducing the risk of cancer; the ultraviolet (UV) action spectra for basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and melanoma; and the effects of other factors on cancer risk, especially that of smoking. This short communication attempts to provide such information so that the results of Tuohimaa et al.¹ can be better understood.

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The incidence and mortality rates for over 20 types of cancer have been found inversely correlated with both solar UVB and vitamin D.²⁻⁶ While most of these findings are based on ecological or cohort studies, a recent prospective double-blind placebo calcium and vitamin D intervention study found a 77% reduction in cancer incidence for post-menopausal women after the first year of the 4-year study, including a benefit for lung cancer.⁷

The dose-response relations for vitamin D and cancer risk reduction have been estimated with the findings that it takes 1500 International Units (IU) of vitamin D3 per day for a 29% cancer risk reduction for male cancer mortality rates in the United States³ and 50% reduction in colorectal cancer incidence,⁸ but 4000 IU for a 50% reduction in breast cancer incidence.⁹ In the less-sunny countries, vitamin D production from solar UVB is lower due to both shorter vitamin D-production seasons and lower peak UVB doses.¹⁰ Thus, those living in sunny countries are much more likely to produce sufficient amounts of vitamin D to have significant impacts on cancer rates than those living in less-sunny countries.

Each of the three types of skin cancer discussed in Tuohimaa et al.,¹ BCC, non-BCC (SCC), and melanoma, appear to have different action spectra. The action spectrum for SCC is primarily the UVB region, based on studies of watermen in Maryland (38° N)¹¹ and use of sunscreen that primarily blocks erythemal UV.¹² To compare the action spectra of SCC with those of BCC and melanoma, use can be made of the fact that the latitudinal variation of solar UVB is much stronger than that of UVA.¹³ Thus, as the action spectrum moves from the UVB spectral region to the UVA region, incidence rates should show a slower change with latitude. There are two studies that compare skin cancer incidence rates with respect to latitude. One study, in the United States in the period 1977-80 for BCC and SCC and 1973-87 for melanoma, found ratios between high and low UV indices of 5.3, 2.8, and 1.4 for SCC, BCC, and melanoma, respectively.¹⁴ A second study, based on those of northern European ancestry living in different countries in the period 1983-87, found ratios of the regression value of the UV indices at 10° and 70° of 2800, 230, and 8 for SCC, BCC, and melanoma, respectively for males.¹⁵ In addition, in the United States between the periods 1950-69 and 1970-94, NMSC mortality rates, for which about 80% is due to SCC, decreased by 31% for males and 47% for females while mortality rates for melanoma increased by 89% for males and 42% for females.¹⁶ These changes are consistent with adoption of widespread use of sunscreen that blocked UVB well but not UVA in the early 1980s.¹⁷ Different molecular mechanisms have also been identified for the three types of skin cancers.¹⁸

From this brief analysis, the three main types of skin cancer can be ranked according to sensitivity to solar UVB irradiance: strong for SCC, intermediate for BCC, and weak for melanoma. The standardised incidence ratios for all solid tumours except skin and lip for sunny countries in Tables 5-7 of Reference 1 are: 0.79 (95% confidence interval, 0.68-0.91), 0.86 (0.80-0.92) and 1.03 (0.99-1.08) for SCC, BCC, and melanoma, respectively, in good agreement with this analysis of action spectra for the various skin cancers.

Since many factors modify the risk of cancer, the UVB/vitamin D effect is strong in the sunny countries. The

UVB/vitamin D effect is particularly strong in the United States,³⁻⁵ and Spain.⁶ However, the UVB effect is weak in less sunny countries, and non-UVB effects dominate. In England, for example, occupational exposure to sunlight results in a modest reduction in risk for many types of cancer,¹⁹ but casual sunlight exposure does not, based on a comparison of cancer incidence data and mean hours of bright sunshine²⁰ [Grant, unpublished]. There is no correlation between solar UVB and place of residence in cancer mortality rates in Germany,²¹ although there is a significant correlation between lung cancer mortality rates, a useful index for the health effects of smoking,^{4,6} with several other, smoking-linked cancers.

However, there is still some effect attributed to UVB and vitamin D in less sunny countries. Cancer survival rates are higher in Norway for discovery of cancer in autumn²²⁻²⁴ and for lung cancer and female breast cancer in England for discovery in summer.²⁵ One linkage study in a less sunny country, The Netherlands, found an inverse correlation between NMSC and subsequent prostate cancer.²⁶ However, most of the other linkage studies between NMSC and subsequent prostate cancer incidence tabulated in Reference 26 did not find a statistically significant correlation. A meta-analysis of second primary cancers after diagnosis of skin cancer also found reduced risk for several types of cancer as long as the effects of smoking by the populations studied was considered.²⁷

Smoking is an important risk factor for many types of cancer. Smoking has been reported to be a risk factor for SCC^{28,29} and, in some studies, BCC.³⁰ However, smoking has been found inversely correlated with melanoma in several observational studies, although no explanation has been proposed.^{6,31,32} Inspection of Tables 5-7 in Reference 1 finds that for cancers linked to smoking such as bladder, liver, lung, oesophageal, pancreatic, and other female genital (e.g. cervical), cancer standardised incidence ratios are generally less than unity for melanoma but elevated for both BCC and SCC skin cancers, especially in the less sunny countries, in agreement with the hypothesis of different effects of smoking on the different types of skin cancer.

It is noted that vitamin D reduces the risk of lung cancer mortality.^{24,25} Lung cancer mortality rates are generally decreasing for males in Europe but increasing for females.³³ The changes for both males and females are more likely due to changes in smoking prevalence than changes in solar UVB irradiance. Since smoking increases the risk of SCC^{28,29} and likely BCC,³⁰ reduced lung cancer mortality rates would imply some reduced impact on rates of these cancers, which is not observed. On the other hand, smoking is associated with reduced risk of melanoma,^{6,31,32} and melanoma rates continue to increase, in agreement with the effect of smoking on melanoma risk.

However, there must be additional differences to explain why the skin cancer-other cancer relation varies between sunny and less sunny countries. One reason could be that in less sunny countries less of the body is exposed to solar UV, thereby reducing the amount of vitamin D produced. A study in Norway found that the second most common site for SCC for men was the ear.³⁴ In Sweden, the highest rates of SCC were found for chronically sun-exposed sites.^{35,36}

Another possibility is increasing use of sunbeds in less sunny countries starting in the early 1980s.³⁷ A study of SCC trends in Sweden suggested that the increases between 1961–65 and 1996–98 might be due to intentional tanning.³⁶ However, incidence rates for normally-covered sites were about 10% of those for sun-exposed sites, and rates for covered sites for males were 3–4 times higher for males than females. In addition, the age at which incidence rates started to rise dramatically was about 65 years. Since females outnumber males in sunbed use by about a factor of two, and the average age of sunbed users is 20–30 years, the results of this study do not support a role of sunbed use in affecting the skin cancer-other cancer relation in less sunny countries. Melanoma rates for covered body sites among Swedes have been dramatic since the early 1960s.³⁸ However, the slope of incidence rates on the trunks of males or females is well described by a linear fit, supporting the hypothesis that increased travel,^{39,40} as well as use of sunscreen that does not adequately protect against UVA,^{17,41} rather than sunbed use, explains the trends.

Another important reason that risk of skin cancer might be decoupled from risk of internal cancers in less sunny countries is that skin cancers can arise from sunburning and excess tanning, especially in youth,⁴² and that those who develop skin cancers tend to avoid the sun later in life⁴³ when vitamin D plays a more important role in cancer prevention.

In conclusion, the interesting results presented in Tuohimaa et al.¹ can generally be understood in terms of the decreasing vitamin D production with increasing latitude, different action spectra for BCC, SCC, and melanoma, and the relative effects of UVB/vitamin D, smoking and other risk factors on cancer risk. Thus, such studies, when carefully analysed, can add to our understanding of the role of solar UV and cancer risk, although further work is required to verify that the hypotheses presented here do, indeed, help explain the findings.

Conflict of interest statement

I receive funding from the UV Foundation (McLean, VA) and the Vitamin D Society (Canada) and expect funding from the European Sunlight Association.

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