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Short Communication

Protective effect from solar exposure, risk of an ecological fallacy

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ABSTRACT

Solar exposure, vitamin D, and their possible beneficial effect on cancer risk and cancer prognosis are a topic for research. Despite the distinct nature of sunlight, it has proved difficult to assess the exposure quantitatively in epidemiological studies. Skin cancers, latitude, and sunny climate have been used as proxy indicators of solar exposure above a reference level. The interpretation of such data may still be hampered by incomplete cancer registration, difference in protection against sunbeams, selection mechanisms, and absence of information on potential confounders. A recently published paper—on second primary cancer following the diagnosis of a skin cancer—is discussed to illustrate the difficulties. Further epidemiological studies of potentially protective effects from carcinogenic ultraviolet rays should include individual information on solar exposure and vitamin D levels, as well as on other recognised and relevant risk factors.

Solar energy conveyed by electromagnetic rays is essential for terrestrial life that is dependent on photosynthesis, surface temperature, and the water cycle. The carcinogenic effect of ultraviolet (UV) light is well recognised,[1] as is the vitally important induction of vitamin D production in human skin. There is some evidence that vitamin D might reduce the risk of cancer or improve cancer prognosis, although the nature of the observed associations is not always clear.

In a recent paper, Tuohimaa and colleagues (2007) stated that vitamin D production in the skin 'seems to decrease the risk of several solid cancers (especially stomach, colorectal, liver and gallbladder, pancreas, lung, female breast, prostate, bladder and kidney cancers)'.[2] They followed more than 400 thousand skin cancer patients with record linkage to 13 local or national cancer registries, and studied the pattern of second primary cancers. Such a formidable work with analysis of second primary cancers may be valuable for some cancer forms and for the generation of hypotheses, but we would like to question the authors' aetiological approach in this study.

The diagnosis of skin cancer was taken by Tuohimaa and colleagues to indicate solar exposure above average in the source population.[2] The overall number of second primary cancers was well above that expected from the background population incidence rates, especially following non-melanomas. Similar findings have been reported earlier from some of the participating countries.[3–5] When non-melanoma is taken as an indicator of high cumulative sun exposure, the marked *increase* in second cancer risk appears incompatible with the authors' suggestion that solar expo-

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sure has a *protective* effect. But then the authors changed focus—from the risk following individual sun exposure, to an ecological comparison of differences in second cancer risk ascribed to sunny climate. Standardised incidence ratios (SIR) of skin cancer patients in 'sunny countries' were compared with those in 'less sunny countries' by the calculation of ratios of SIRs.

In 1987, Breslow and Day warned against the use of SIR ratios because serious bias may be introduced when there are differences in age distribution and age-specific rates.[6] Table 1 illustrates the uncertainty of the SIR ratios by showing two possible scenarios: the first with a suggested age distribution (above and below 75 years) based on the number of observed and expected lung cancers from Table 6 in the Tuohimaa paper.[2] The second scenario depicts the situation with an increased number of person-years in the age group 75+ in sunny countries. The SIR ratio changed materially while the age-specific SIRs remained the same. This apparently extreme example may represent a possible scenario given incomplete registration or selection mechanisms in the diagnostic process due to age-specific campaigns or screening for skin cancer.

Incomplete registration of non-melanomas has been a great problem in many cancer registries around the world. In the latest version of Cancer Incidence in Five Continents,[7] the three participating 'sunny countries' in the Tuohimaa paper[2] showed the following figures for a 5-year-period in the 1990s: New South Wales (Australia), 12,603 melanomas and 0 non-melanomas (probably not registered); Zaragoza (Spain), 195 melanomas and 2499 non-melanomas; and Singapore, 69 melanomas and 1261 non-melanomas. If this distribution were representative for the Tuohimaa study, the term 'sunny countries' would largely correspond to a part of Australia for the skin melanoma follow-up; while Zaragoza and Singapore alone would represent the 'sunny countries' in the non-melanoma follow-up.

The distribution of person-years according to age would further depend on age at diagnosis and life expectancy, and, indeed, the authors stated that the age at diagnosis of non-melanoma non-basal cell carcinomas was 7 years lower in 'sunny countries' than in 'less sunny countries'. Overall, the situation does not seem to justify the featuring of the non-melanoma follow-up as the study's key finding, flagged in the title.[2]

Needless to say, climate alone cannot fully explain time trends or differences in cancer rates, not even for skin cancer where the effect from sunshine is known to be important. The crucial question for skin cancers is—perceive it as simple or complex—to what extent and how people allow susceptible skin to be exposed to UV rays. Latitude, altitude, season, temperature, cloudiness, and time of the day, are of course fundamental factors, but equally important are hereditary characteristics such as skin type, clothing, sunbathing habits, or solar protection used during outdoor activities. Additionally, the skin's own protection against UV damage, known as tan, is highly time- and exposure-dependent (resulting from recent solar exposure), and may strongly modify the effect of the most harmful carcinogenic rays. People's behaviour on sunny days may be determined by local or national traditions, by fashion, or personal preference, and these factors may be further associated in various time- and age-dependent ways with other cancer relevant factors, such as smoking, fertility pattern, diet, physical activity, and occupation—depending on nationality.

In an editorial comment on an earlier study of second primary cancers following basal-cell carcinomas, Schottenfeld warned that patterns should be interpreted with caution in the absence of information on confounders.[8] In some countries, skin cancers are more common in people of high socioeconomic class, implying that even a complete population-based sample of skin cancer patients would represent a selection.[9,10] The risk pattern for other cancers in such a selected group should not be expected to follow the average population, and clearly these selections and deviations need not be the same across national borders. The claim that the differences in cancer risk are related to regional UV doses or vitamin D levels is not immediately plausible.

The complexity of some group-related differences is illustrated by a large registry-based study of cancer in four Nordic countries (Denmark, Finland, Norway, and Sweden), whose cancer incidence weigh heavily among the 'less sunny countries' in the Tuohimaa study.[2] Andersen and colleagues (1999) demonstrated marked differences in risk between occupational groups from the 1970 censuses.[11] The largest group of

Table 1 – Scenarios showing the effect on SIR ratios from changes in the number of person-years in a certain age group

Scenario 1				Scenario 2			
	Age < 75	Age ⩾ 75	All ages[a]		Age < 75	Age ⩾ 75[b]	All ages
Observed(S)[c]	47	33	80	Observed(S)	47	330	377
Expected(S)	59	18	77	Expected(S)	59	180	239
SIR(S)	0.80	1.83	1.04	SIR(S)	0.80	1.83	1.58
Observed(L)[d]	1112	1950	3062	Observed(L)	1112	1950	3062
Expected(L)	690	1482	2172	Expected(L)	690	1482	2172
SIR(L)	1.61	1.32	1.41	SIR(L)	1.61	1.32	1.41
SIR(S) / SIR(L)	0.47	1.48	0.74	SIR(S) / SIR(L)	0.47	1.48	1.12

a Column 'All ages' in Scenario 1 is taken from Table 6, reference [2].
b Number of 75+ person-years in sunny countries in Scenario 2 has been increased.
c (S), Sunny countries.
d (L), Less sunny countries.

economically active women, clerical workers, constituting 10% of all women, had increased risks (SIRs) of skin melanoma, squamous cell carcinoma of the skin, breast cancer, colorectal cancer, and lung cancer compared to the background average. In contrast, the largest group of economically active men, farmers, constituting 9% of all men, had lower than expected risks for the very same cancers, inclusive of the rare male breast cancer.

For some western countries, the striking rise in skin cancer incidence (melanoma and non-melanoma) over the last decades has been comparable to that of lung cancer. Both lung and skin cancers largely result from human choice of lifestyle, aggressively supported by fashion, commercials, and movies. Unlike tobacco smoking, the choice of unfavourable solar exposure is not influenced by randomly distributed chemical addiction. The more likely it would appear that unhealthy behaviour in sunny weather may be associated with a number of other choices of habits and modern lifestyle that might increase or decrease the risk of cancer.

For cancer forms with no known or suspected causal factor, the pattern of second primary cancer could be more informative. This may involve prostate cancer,[12] although differences in diagnostic pressure within national or regional populations may severely complicate the interpretation. Many developed countries have experienced a substantial increase in incidence rate in the wake of the introduction of tests for prostate specific antigens (PSA).[13,14] The uncertainty and variability linked to the diagnosis of this cancer might represent a huge problem for aetiological research for this common disease.

If a general protective effect from sunshine does exist, as suggested by Tuohimaa and colleagues, it could be extremely important, as it might affect more than 50% of the cancers diagnosed in developed countries.[2] On the other hand, the possible absence of such a beneficial effect should call for more consideration in the choice of message conveyed to the public, as long as the exposure is known to be carcinogenic and does affect very large population groups. We would rather look for studies with individual information on solar exposure, vitamin D levels, and well-known and relevant risk factors.

Conflict of interest statement

None declared.

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