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Original Contribution

Decreased Risk of Prostate Cancer after Skin Cancer Diagnosis: A Protective Role of Ultraviolet Radiation?

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Ultraviolet radiation causes skin cancer but may protect against prostate cancer. The authors hypothesized that skin cancer patients had a lower prostate cancer incidence than the general population. In the southeastern part of the Netherlands, a population-based cohort of male skin cancer patients diagnosed since 1970 (2,620 squamous cell carcinomas, 9,501 basal cell carcinomas, and 1,420 cutaneous malignant melanomas) was followed up for incidence of invasive prostate cancer until January 1, 2005, within the framework of the Eindhoven Cancer Registry. The incidence rates of prostate cancer among skin cancer patients were compared with those in the reference population, resulting in standardized incidence ratios. Skin cancer patients were at decreased risk of developing prostate cancer compared with the general population (standardized incidence ratio (SIR) = 0.89, 95% confidence interval (CI): 0.78, 0.99), especially shortly after diagnosis. The risk of advanced prostate cancer was significantly decreased (SIR = 0.73, 95% CI: 0.56, 0.94), indicating a possible antiprogression effect of ultraviolet radiation. Patients with a skin cancer in the chronically ultraviolet radiation-exposed head and neck area (SIR = 0.84, 95% CI: 0.73, 0.97) and those diagnosed after the age of 60 years (SIR = 0.86, 95% CI: 0.75, 0.97) had decreased prostate cancer incidence rates. These results support the hypothesis that ultraviolet radiation protects against prostate cancer.

cohort studies; neoplasms, second primary; prostatic neoplasms; registries; skin neoplasms

Abbreviations: CI, confidence interval; SIR, standardized incidence ratio.

Ultraviolet radiation causes skin cancer, but it has been hypothesized to protect against prostate cancer development and possibly progression. If this hypothesis were true, one would expect skin cancer patients to have a lower prostate cancer incidence than the general population and, more specifically, to have a lower incidence of advanced stage prostate cancer.

A striking epidemiologic feature of prostate cancer is a gradient of increasing mortality rates among Caucasians with latitude (i.e., inverse correlation between geographic distributions of ultraviolet radiation and prostate cancer mortality). Mortality from prostate cancer was found to increase with latitude in the United States (1–3) and Europe (4). This is consistent with the hypothesis of an ultraviolet radiation-induced ''protective'' effect on prostate cancer incidence and/or survival, because annual average ultraviolet radiation levels decrease with increasing latitude. A case-control study conducted in the United Kingdom found the risk of prostate cancer to be two thirds less in men with high than in men with low lifetime sun exposure (5, 6), and the risk of advanced prostate cancer was reduced by half in the group with the highest quintile of sun exposure index compared with the lowest quintile in a San Francisco Bay area population-based case-control study (7). The risk of prostate

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cancer among White men was decreased by about one third for men with a high solar radiation at their place of longest residence and was halved for men with a high solar radiation at the place of birth in a follow-up study conducted in the United States (8).

Most of these studies used measures of residential sun exposure (1, 2, 4, 8), sometimes combined with job histories (3, 7), as indicators of individual sun exposure, whereas individual behavior can hugely influence the amount of sun exposure received. The case-control study (5, 6) collected individual sun exposure data by use of questionnaires, in which recall bias may influence exposure estimates.

In this study, we compared the incidence of prostate cancer in the general male population with the incidence of prostate cancer in cohorts of male skin cancer patients. It is generally accepted that the majority of skin cancers are caused by exposure to ultraviolet radiation (9, 10). Therefore, although we do not have individual information on sun exposure, we may assume that these skin cancer cases had on average a higher ultraviolet radiation exposure than did the general population in the same area. The association with ultraviolet radiation is most straightforward for squamous cell carcinomas of the skin (9), which are related to cumulative ultraviolet radiation exposure. The association is less strong for basal cell carcinomas of the skin, which have been hypothesized to be etiologically more similar to melanoma (9). Intermittent exposure to sunlight, especially during childhood, is thought to be the main risk factor for cutaneous malignant melanoma (11), particularly for people with a light skin phototype. Generally, skin cancers occurring in the head and neck region and those diagnosed at an older age are associated with chronic exposure, and skin cancers occurring at other body sites and at younger ages are associated with intermittent exposure and probably have a larger genetic component (12, 13). To our knowledge, no previous study has investigated prostate cancer incidence after skin cancer, taking into account the body site of the skin cancer, the age at and time since skin cancer diagnosis, and the prostate cancer stage.

MATERIALS AND METHODS

Cohort

Data on skin cancer patients were obtained from the Eindhoven Cancer Registry, situated in the southeastern part of the Netherlands and serving a population of 2.4 million inhabitants. The Eindhoven Cancer Registry serves more than 12 general hospitals that are served by six pathology laboratories, all participating in the nationwide pathology network known as ''Pathologisch Anatomisch Landelijk Geautomatiseerd Archief'' (PALGA), which also notifies the regional cancer registries. The registry receives lists of newly diagnosed cases on a regular basis from the pathology departments, including cases whose material was sent in by general practitioners. In addition, the medical records departments of the hospitals provide lists of outpatients and hospitalized cancer patients. Following this notification, the medical records of newly diagnosed patients (and tumors), often available only from the outpatient departments, are collected, and trained registrars from the cancer registry abstract the necessary information. Data are checked for duplicate records. Records are assumed to be complete (14, 15). Active follow-up of vital status until January 1, 2005, was conducted through municipal registries and the Central Bureau for Genealogy. The rules of the International Association of Cancer Registries and the International Agency for Research on Cancer for coding multiple tumors were adopted (16). A primary cancer is defined as a cancer that originates in a primary site or tissue and is thus not an extension, a recurrence, or a metastasis. Only patients with a first primary skin cancer were included. Those diagnosed with a cancer before the skin cancer diagnosis were excluded.

Eligible participants for this study were Dutch males with an invasive squamous cell carcinoma ($n = 2{,}752$) and cutaneous malignant melanoma ($n = 1{,}449$) diagnosed in the period 1972–2002; for patients with an invasive basal cell carcinoma, the period of inclusion was 1990–2002 ($n = 9{,}544$), because active follow-up for basal cell carcinoma patients was initiated in 1990. Among the eligible men, we excluded skin cancer patients with zero follow-up time (squamous cell carcinoma: $n = 132$; basal cell carcinoma: $n = 43$; cutaneous malignant melanoma: $n = 29$), as they would have had no ''time'' to develop a second tumor. Patients with zero follow-up time were usually diagnosed with another (usually skin) cancer on the same day as the skin cancer diagnosis, or they were discovered during postmortem examination. We excluded them because they would increase the denominator (number of patients with a second cancer) without contributing any follow-up time and, therefore, would overestimate the relative risk. Included patients were followed for the development of invasive prostate cancer until January 1, 2005. In the case of a diagnosis of another second tumor (not prostate cancer), follow-up ended at the date of diagnosis of this second tumor.

The clinical stage of prostate cancer was recorded according to the tumors, nodes, metastasis (TNM) classification (17). Because the pathologic stage is available only after radical prostatectomy and because treatment decisions are based on clinical stage, only the latter was used (except for lymph node involvement and distant metastasis, which was based also on pathologic stage, because this can still influence treatment decisions). The clinical tumor classification was simplified as T1, T2, T3, T4, or ''unknown'' if sufficient information was not available for accurate staging. Thus, 2,620 patients diagnosed with a squamous cell carcinoma, 9,501 patients diagnosed with a basal cell carcinoma, and 1,420 patients diagnosed with cutaneous malignant melanoma were included for analysis.

Statistical methods

We used the person-years analysis to study the incidence of second neoplasms after diagnosis of skin cancer (18). We compared the incidence of prostate cancer as a second tumor among patients with a diagnosis of skin cancer (the observed incidence) with the prostate cancer incidence in the reference population (the expected incidence), the reference population being the population served by the Eindhoven Cancer Registry. We took into account the amount of time

that had passed between the diagnosis of the first and second tumors, adjusting for age (in 5-year categories) and calendar period of the skin cancer diagnosis. Through the adjusted person-years obtained, we calculated the expected subsequent relative risk for prostate cancer for the general male population. The observed and expected numbers were compared in order to determine the standardized incidence ratio. Statistical significance and 95 percent confidence intervals were calculated using exact Poisson probability (19). Risk estimates were calculated for the total study population, and subanalyses were performed to determine the incidence of skin cancer in the head and neck area (chronically sun exposed) and the other body sites (intermittently exposed), for the age at diagnosis of skin cancer (aged <60 vs. ≥60 years) and for the incidence of prostate cancer by stage (stages I and II compared with stages III and IV). Patients with missing information on body site were excluded from analysis (unknown-location squamous cell carcinoma: $n = 11$, basal cell carcinoma: $n = 32$, cutaneous malignant melanoma: $n = 69$; this exclusion did not significantly influence results).

In the first years after a skin cancer diagnosis, patients are likely to decrease their sun exposure. If the hypothesized protective effect of sun exposure would be effective in the short term, one would therefore expect a more markedly decreased risk of second prostate cancer among skin cancer patients shortly after their initial diagnosis than at a longer follow-up time. Therefore, we performed an additional analysis, calculating standardized incidence ratios for prostate cancer incidence by the time since skin cancer diagnosis divided into six periods: 0–<1, 1–<2, 2–<3, 3–<4, 4–<5, and ≥5 years since skin cancer diagnosis.

RESULTS

We included 13,541 skin cancer cases eligible for analysis, with a total of 75,047 person-years. Table 1 gives the results of the analyses. The average age at diagnosis of squamous cell carcinoma was 73 years; of basal cell carcinoma, 66 years; and of melanoma, 53 years. The average follow-up time was 5.0, 5.6, and 6.0 years, respectively.

For all skin cancers combined, there was a decreased risk of subsequently developing prostate cancer (standardized incidence ratio (SIR) = 0.89, 95 percent confidence interval (CI): 0.78, 0.99). This risk was significantly decreased for patients with a previous diagnosis of nonmelanoma skin cancer (SIR = 0.87, 95 percent CI: 0.77, 0.98) but not for melanoma patients. All male skin cancer patients with a skin cancer diagnosis after the age of 60 years (SIR = 0.86, 95 percent CI: 0.75, 0.97) and those with any skin cancer in the head and neck region (SIR = 0.84, 95 percent CI: 0.73, 0.97) had a significantly decreased risk of subsequent prostate cancer incidence. Among skin cancer patients, advanced prostate cancer (stages III and IV) incidence rates were significantly decreased compared with those of the general population (SIR = 0.73, 95 percent CI: 0.56, 0.94).

After analysis of the cohorts separately for nonmelanoma skin cancer patients and patients diagnosed with a melanoma, the risks remained significantly lower in the group of nonmelanoma skin cancer for those aged more than 60 years at diagnosis (SIR = 0.84, 95 percent CI: 0.73, 0.96) and those with a head and neck nonmelanoma skin cancer (SIR = 0.85, 95 percent CI: 0.73, 0.98). The risk of developing an advanced prostate cancer was especially decreased (SIR = 0.73, 95 percent CI: 0.56, 0.95). Melanoma was positively associated, though not significantly, with subsequent prostate cancer risk (SIR = 1.16, 95 percent CI: 0.71, 1.85), except for head and neck melanomas (SIR = 0.46, 95 percent CI: 0.06, 1.66) and advanced prostate cancer (SIR = 0.69, 95 percent CI: 0.14, 2.03) for which point estimates were smaller than one.

Table 2 describes the results of the analyses by period since diagnosis of nonmelanoma skin cancer, but not for melanoma because of the small numbers of prostate cancer cases after an initial melanoma diagnosis. Although point estimates did not always reach statistical significance, the results clearly demonstrate that the risk of developing prostate cancer was lowest in the time period shortly after nonmelanoma skin cancer diagnosis (during the first year: SIR = 0.53, 95 percent CI: 0.34, 0.78), gradually increasing with time (≥5 years after nonmelanoma skin cancer diagnosis: SIR = 1.10, 95 percent CI: 0.90, 1.34).

DISCUSSION

Our results show that male nonmelanoma skin cancer patients are at a decreased risk of developing invasive prostate cancer. The decreased risk of developing prostate cancer was significant for skin cancers that are assumed to be related to chronic sun exposure: those occurring in the elderly and in the head and neck region. In patients with cutaneous malignant melanoma, which is assumed to be related to intermittent sun exposure (12, 13), a nonsignificantly increased risk of subsequent prostate cancer was exhibited, except for head and neck melanomas, which showed a nonsignificantly decreased risk. Cutaneous melanomas in the head and neck area are, in contrast to other melanomas, assumed to be more related to chronic sun exposure (12, 13).

These observations are in line with the hypothesis that exposure to ultraviolet radiation protects against prostate cancer development and possibly against progression, as the standardized incidence ratios for advanced prostate cancer (stages III and IV) were lower than those for early (stages I and II) disease.

Although we did not have individual information on the exposure to ultraviolet radiation of the included cases, it is generally accepted that most skin cancer cases in predominantly Caucasian populations, such as in the southern part of the Netherlands, are caused by high ultraviolet radiation exposure (9, 10). This increased risk is mainly apparent for people with sun-sensitive skin. Other causes of nonmelanoma skin cancer include immunosuppression (20), smoking (21), and exposure to pesticides (22). Apart from some rare familial syndromes, little is known about nonsolar risk factors for melanoma; the effects of contraceptive use (23) and swimming in polluted water (24) have been postulated but not confirmed. All of these nonsolar factors are, to our knowledge, not associated with a decreased risk of prostate cancer and thus cannot explain our observations. Therefore, our findings are in line with the hypothesis that exposure to

TABLE 1. Subsequent prostate cancers observed in a cohort of skin cancer patients diagnosed in 1972–2002, Eindhoven Cancer Registry, the Netherlands

	No. of cases	Median age (years) at diagnosis		Person-years*	Observed no. of prostate cancer patients	Expected no. of prostate cancer patients	Standardized incidence ratio	95% confidence interval
		Skin cancer	Prostate cancer					
All skin cancers	13,541	66.4	69.3	75,047	272	307	0.89	0.78, 0.99
Nonmelanoma skin cancers	12,121	67.4	74.2	66,564	253	291	0.87	0.77, 0.98
Melanoma	1,420	52.7	68.3	8,483	19	16	1.16	0.71, 1.85
Squamous cell carcinoma	2,620	73.2	77.0	13,204	56	66	0.84	0.64, 1.10
Basal cell carcinoma	9,501	65.7	73.0	53,360	197	224	0.88	0.76, 1.01
All skin cancers								
Age at diagnosis								
<60 years	4,650	51.2	61.6	31,886	42	38	1.10	0.80, 1.50
≥60 years	8,891	72.5	75.2	43,182	230	269	0.86	0.75, 0.97
Location								
Head and neck	9,461	68.6	74.8	51,293	197	235	0.84	0.73, 0.97
Others	3,968	59.8	71.4	23,357	75	71	0.85	0.64, 1.10
Prostate cancer stage								
I and II	13,541	67.7	72.7	75,047	188	199	0.94	0.81, 1.09
III and IV	13,541	70.6	74.9	75,047	61	84	0.73	0.56, 0.94
Unknown	13,541	75.6	76.6	75,047	23	24	0.95	0.60, 1.42
Nonmelanoma skin cancers								
Age at diagnosis								
<60 years	3,719	52.1	62.3	25,401	37	33	1.12	0.79, 1.55
≥60 years	8,402	72.6	75.4	41,164	216	258	0.84	0.73, 0.96
Location								
Head and neck	9,197	68.7	74.8	49,871	19	230	0.85	0.73, 0.98
Others	2,881	63.1	71.9	16,426	58	59	0.98	0.74, 1.27
Prostate cancer stage								
I and II	12,121	68.3	72.9	66,564	174	188	0.92	0.79, 1.07
III and IV	12,121	70.6	75.0	66,564	58	79	0.73	0.56, 0.95
Unknown	12,121	75.6	76.6	66,564	21	23	0.92	0.57, 1.40
Melanoma								
Age at diagnosis								
<60 years	931	45.4	58.7	6,465	5	5	1.01	0.33, 2.37
≥60 years	489	69.8	72.1	2,018	14	11	1.23	0.67, 2.06
Location								
Head and neck	264	65.1	75.0	1,422	2	4	0.46	0.06, 1.66
Others	1,087	51.3	68.3	6,931	17	12	1.44	0.84, 2.34
Prostate cancer stage								
I and II	1,420	63.3	67.7	8,483	14	11	1.31	0.72, 2.20
III and IV	1,420	53.7	60.3	8,483	3	4	0.69	0.14, 2.03
Unknown	1,420	73.2	74.6	8,483	2	1	1.49	0.18, 5.39

* No. of person-years of observation between the date of diagnosis of skin cancer and the date of diagnosis of prostate cancer.

ultraviolet radiation would decrease the risk of prostate cancer development.

After their skin cancer diagnosis, skin cancer patients were likely to be under increased medical scrutiny and to reduce their sun exposure drastically, resulting in lower sun exposure shortly before the prostate cancer diagnosis. If short-term sun exposure were important in determining the risk of developing a prostate cancer, one would expect

TABLE 2. Standardized incidence ratio with 95% confidence interval of second prostate cancer among nonmelanoma skin cancer patients diagnosed in 1972–2002, Eindhoven Cancer Registry, the Netherlands

Time (years) since skin cancer diagnosis	Basal cell carcinoma		Squamous cell carcinoma		Nonmelanoma skin cancer	
	Standardized incidence ratio	95% confidence interval	Standardized incidence ratio	95% confidence interval	Standardized incidence ratio	95% confidence interval
0–<1	0.51	0.30, 0.80	0.58	0.23, 1.20	0.53	0.34, 0.78
1–<2	0.91	0.62, 1.29	0.66	0.26, 1.36	0.85	0.60, 1.17
2–<3	0.65	0.40, 1.00	0.56	0.18, 1.30	0.63	0.41, 0.93
3–<4	0.89	0.57, 1.32	0.97	0.39, 2.00	0.91	0.62, 1.29
4–<5	1.01	0.64, 1.51	0.90	0.29, 2.09	0.99	0.66, 1.43
≥5	1.10	0.87, 1.37	1.13	0.73, 1.66	1.10	0.90, 1.34

the lowest standardized incidence ratios to occur shortly after skin cancer diagnosis, as observed in our analyses: Standardized incidence ratios were lowest in the first year, gradually increasing to reach levels of around 1 after 5 or more years of follow-up. Of interest is the ''drop'' in standardized incidence ratio estimates during the third year of follow-up (2–3 years after diagnosis), possibly an effect of a decreasing intensity of medical surveillance. Because of the increased medical surveillance during the first years after skin cancer diagnosis, one would expect more (prostate) cancer cases to be detected in this period than in the average population. This may have artificially increased the numbers of prostate cancer in our cohorts and diluted our results, but it provides even stronger evidence for a ''real'' decrease in risk shortly after prostate cancer diagnosis.

A few studies have previously looked at the incidence of tumors, among them prostate cancer, after skin cancer diagnosis (25–33) (table 3). Most of these did not find a significant association between skin cancer diagnosis and prostate cancer (26, 27, 29, 30) and did not investigate the effect of body site or the age at diagnosis of the skin cancer cases. Very few gave information on the mean or median age at diagnosis and/or the mean years of follow-up or person-years at risk. None of these studies investigated the associations with prostate cancer stage, and most suffered a problem of small numbers, such as we did when considering only squamous cell carcinoma or melanoma, causing a lack of power to show any statistically significant effects (25–29, 33). One large study investigating prostate cancer incidence after basal cell carcinoma found an increased risk (31). This study had accumulated a mean follow-up time of about 9 years, against 5.6 years in our basal cell carcinoma cohort. As the standardized incidence ratios tended to increase with time since skin cancer diagnosis, this possibly explains the observed increased risk in this study (31). Another study, which did not mention mean follow-up time, found a decreased risk, with estimates very similar to ours (32); the other two studies did not find any significant association (26, 29). None of the studies on basal cell carcinoma gave an indication of the completeness of their registry of (first primary) basal cell carcinomas. In many countries, basal cell carcinomas are not routinely registered, and therefore some of the populations of basal cell carcinoma patients may have been biased toward the clinically more complicated cases. As was the case in our study, all previous studies reporting the incidence of prostate cancer after squamous cell carcinoma (28, 30, 33) and cutaneous malignant melanoma (25, 27) had too low numbers to make reliable estimates. One Danish study observed a nonsignificantly decreased risk of prostate cancer after squamous cell carcinoma, with a standardized incidence ratio very similar to that observed in our study (33). One study found an increased risk of prostate cancer after a diagnosis of cutaneous malignant melanoma (27), and another found an increased risk after cutaneous malignant melanoma for patients younger than 51 years and a decreased risk for patients diagnosed after age 50 years (25).

Unlike the situation in most cancer registries, the reporting of both nonmelanoma skin cancer and cutaneous malignant melanoma to the Eindhoven Cancer Registry occurs routinely (14). A small degree of underreporting cannot be excluded, because a high proportion of nonmelanoma skin cancer cases are treated in office settings where perhaps not all tumor material will be sent for pathology review. However, the material of all first primary basal cell carcinomas and squamous cell carcinomas will be sent for pathology, and it is therefore unlikely that this cohort of patients will have been subject to selection. As nonmelanoma skin cancer generally has a good prognosis, there are no severe biases expected based on survival time.

The significantly decreased prostate cancer incidence in the group of basal cell carcinoma patients can hardly be explained by bias: Patients with a cancer diagnosis are more intensely checked for subsequent tumors and might be regarded as being vulnerable for tumor development. If such higher vulnerability and/or stronger surveillance would play a role, this would have increased the level of prostate cancer detection, especially during the first years after skin cancer diagnosis, and would have diluted our results. In the Netherlands, there is no population-based, prostate cancer-screening program; voluntary prostate-specific antigen screening in this population was quite low and even completely absent in the earlier years of follow-up. However, should skin cancer patients have been under a more frequent and closer medical scrutiny, then diagnosis of a subsequent prostate cancer

TABLE 3. Results of other studies reporting incidence of prostate cancer after skin cancer diagnosis

Country, registry (reference)	Localization and age (years) at skin cancer diagnosis	No. of male skin cancer patients	Age (years) at diagnosis of skin cancer	Mean years of follow-up	Observed no. of prostate cancer cases	Standardized incidence ratio	95% confidence interval
Basal cell carcinoma							
Finland, Finnish Cancer Registry (31)	All basal cell carcinoma	29,727	Not available	9	1,121	1.2	1.2, 1.3
	Head and neck only	20,796	Not available	Not available	839	1.2	1.2, 1.3
Switzerland, Vaud and Neuchatel cancer registries (29)	Basal cell carcinoma	5,947	60–69	Not available	155	1.1	0.9, 1.3
United States, Kaiser Permanente Medical Care Program (26)	Basal cell carcinoma	1,648	45–64	11.3	108	1.1	0.9, 1.4
United Kingdom, South and West Cancer Registry (32)	Basal cell carcinoma	13,961*	Not available	Not available	177	0.85	0.73, 0.99
Squamous cell carcinoma							
United Kingdom, Thames Cancer Registry (30)	Squamous cell carcinoma	16,962	Not available	Not available	389	1.0	0.9, 1.1
Switzerland, Vaud and Neuchatel cancer registries (28)	Squamous cell carcinoma	2,529	60–69	Not available	74	1.1	0.9, 1.4
Denmark, Danish Cancer Registry (33)	Squamous cell carcinoma	3,306	Not available	Not available	49	0.8	0.6, 1.1
Cutaneous malignant melanoma							
Switzerland, Vaud and Neuchatel cancer registries (27)	Cutaneous malignant melanoma	782	60–69	Not available	16	2.1	1.2, 3.4
United States, hospital based (25)	Cutaneous malignant melanoma, $\leq$50	298	Median: 43	6.5	1	1.8	0.0, 7.0
	Cutaneous malignant melanoma, $>$50	$<$150	Not available	Not available	1	0.2	0.0, 0.9

* No separate numbers for males and females were given; prostate risk was calculated separately within the cohort of male skin cancer patients only.

would more likely have occurred at an earlier stage. Because the levels of prostate-specific antigen screening were low in this population during the years of follow-up, any such effect would be minimal. Moreover, if this were true, this would suggest a bias for more medical screening in skin cancer patients and a higher detection rate of prostate cancer in general, which was not the case.

Although biases are unlikely to have caused the observed association, there is some potential for confounding, for example, by physical exercise and/or selenium supplementation. Exercise might be associated with skin cancer through enhancing exposure to ultraviolet radiation and might also be associated with reduced prostate cancer risk. Similarly, selenium supplementation has been found to nonsignificantly increase the risk of recurrent skin cancer, while reducing prostate cancer occurrence (34).

A growing body of evidence, including our findings, supports the hypothesis that ultraviolet radiation protects against the development of prostate cancer, possibly through the formation of vitamin D_3 (1–8), although some plasma studies do not clearly suggest a benefit of vitamin D levels on prostate cancer risk (35, 36). If the hypothesis that ultraviolet radiation has a protective effect against prostate cancer (and possibly other tumors and some autoimmune diseases) is confirmed (37), it will be important to modify public health messages regarding ultraviolet radiation exposure: Levels of ultraviolet radiation that do not result in increased risk of skin cancers should be defined. Additionally, if indeed vitamin D is relevant, then recommendations to increase oral intake of vitamin D through supplementation and/or fortification should be made.

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