Review

Does sunlight prevent cancer? A systematic review

H.J. van der Rhee,*, E. de Vries, J.W.W. Coebergh

A Department of Dermatology, Leyenburg Hospital, P.O. Box 40551, Leyweg 275, 2504 LN Den Haag, Zuid-Holland, The Netherlands
b Department of Public Health, Erasmus MC, P.O. Box 1738, 3000 DR Rotterdam, The Netherlands
c Eindhoven Cancer Registry, Comprehensive Cancer Centre South, P.O. Box 231, 5600 AE Eindhoven, The Netherlands

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ABSTRACT

Accumulating evidence for beneficial effects of sunlight on several types of cancer with a high mortality rate makes it necessary to reconsider the health recommendations on sun exposure, which are now mainly based on the increased risks for skin cancer. We reviewed all published studies concerning sun exposure and cancer, excluding skin cancer.

All selected studies on prostate (3 ecologic, 3 case-control and 2 cohort), breast (4 ecologic, 1 case-control and 2 cohort) and ovary cancer (2 ecologic and 1 case-control) showed a significantly inverse correlation between sunlight and mortality or incidence. Two ecologic, 1 case-control and 2 prospective studies showed an inverse relation between sunlight and colon cancer mortality; 1 case-control study found no such association. Ecologic studies on non-Hodgkin lymphoma (NHL) mortality and sunlight gave conflicting results: early studies showing mostly positive and later studies showing mostly negative correlations. Three case-control studies and 1 cohort study found a significant inverse association between the incidence of NHL and sunlight.

The question of how to apply these findings to (public) health recommendations is discussed.

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1. Introduction

The interest in the effects of sunlight and ultraviolet rays on health in man has until now mainly been focused on the negative aspects. The steady rise in the incidence of skin cancer during the last decades, largely caused by increased sun exposure, has in most western countries led to public health recommendations that sun exposure should be avoided.

There is a linear relationship between the degree of sun exposure and squamous cell carcinoma of the skin. The relationship between melanoma, the most aggressive type of skin cancer, and sunlight, however, is more complicated. Intermittent sun exposure at young age causing severe sunburn is the most important exogenous risk factor, whereas a certain degree of chronic exposure might have a preventive effect. Moreover, sun exposure might be associated with increased survival from melanoma.

For many years it has been known that sun exposure has positive effects on bone metabolism. In recent years, a growing list of other possible beneficial effects has been added, such as a reduced risk on multiple sclerosis, diabetes type 1, schizophrenia and several types of cancer.

These new data could make it necessary to reconsider the health recommendations on sun exposure. But first these
new data have to be evaluated. In the present paper, we reviewed all studies concerning sun exposure and cancer other than skin cancer.

2. Materials and methods

2.1. Search strategy

A search was performed in 2 electronic databases: EMBASE (1980 to February 2006) and MEDLINE (1966 to February 2006). Text words (or mesh terms) that were used included cancer (NOT skin cancer) and, separately, the 20 most frequently occurring types of cancer in Western Europe (prostate, bladder, breast, colon, rectal, pancreas, gall bladder, stomach, oesophageal, liver, lung non-small cell, ovary, uterine cervix, uterus, pharynx, larynx, brain, and oral cavity cancer; non-Hodgkin lymphoma, Hodgkin lymphoma and leukaemia), using combinations with text words (or mesh terms) for sunlight or ultraviolet rays. Citation lists of the found studies were used to identify other relevant studies; this did not, however, result in extra studies included in this review.

2.2. Inclusion criteria and review of the studies

Studies concerning the influence of sunlight on the incidence and mortality of cancer, excluding skin cancer, were evaluated.

All titles and abstracts (written in English) found were reviewed by one of the authors. The authors independently reviewed all studies thus found. Disagreements during the review process were resolved by discussion.

Inclusion criteria were ecologic, case-control, and cohort studies with original data which met the following demands: studying the effect of sunlight, description of methodology, containing effect estimates with p-value or confidence intervals.

Reviews, comments and letters, not containing new data, were excluded, as were studies looking exclusively at occupational sun exposure, since the findings of these studies could be heavily confounded by occupational exposure to other risk factors.

A separate search was performed to identify migrant studies looking at colon, prostate and breast cancer, but all these studies focused more on lifestyle and diet differences within migrant populations rather than the latitude of origin. Therefore, it was decided to leave migrant studies out of this review.

3. Results

A total of 2431 titles were found. When it was obvious from the title or the abstract that studies were not relevant to our subject, they were excluded. Based on the title and abstract, 94 studies were reviewed completely, of which 27 were selected in accordance with our criteria. Sixty-seven publications were excluded, either because they did not present original data, or because they did not present effect estimates with p-value or confidence intervals, or because they were reanalyses of a data set that had already been included. In the case where one data set was repeatedly analysed, we included the most recent paper studying relevant exposure data and containing usable effect estimates. As regards prostate, breast, colon and ovary carcinoma, the results of the excluded (mainly ecologic) studies showed without exception an inverse association with sunlight.

3.1. Ecologic studies

Latitude is an important determinant of the amount of UV radiation reaching the earth’s surface. Therefore, several authors have compared the risk of cancer in regions of different latitude, many studies using sunlight measurements as well. Some authors corrected in their analyses for some potentially important confounders, such as food habits of different populations and cloud cover. Most of these studies showed associations between latitude and/or sunlight and incidence or mortality, for cancers of the prostate, breast, colon, ovary, and non-Hodgkin lymphomas (mainly ecologic) studies showed without exception an inverse correlation between mortality and UV radiation: bladder, oesophageal, kidney, lung, pancreas, stomach, and uterus cancer.

3.2. Case-control studies

Case-control studies investigating the role of sunlight have been performed on prostate, breast, colon and ovary cancer patients (Table 2). Some of these studies used residential exposure data, others had questionnaire-derived exposure data. One used a sun-exposure index, which is a measure for sun-exposure comparing constitutive skin pigmentation on the upper underarm (a sun-protected site) and facultative pigmentation on the forehead (a sun-exposed site).

3.3. Cohort studies

Few cohort studies (Table 3) have looked at indicators of sun exposure and cancer risk. Three out of 6 cohort studies investigated case-fatality rates of cancer patients, the remaining 3 studies looked at cancer incidence in cohorts of people without a personal history of cancer.

All studies found an inverse relationship between sun exposure and cancer risk.

3.4. Solid tumours

For prostate cancer, as can be seen in the tables, all selected studies, 3 ecologic, 3 case/control and 2 cohort studies, found a significantly inverse correlation between sunlight and mortality or incidence. In Norway, a seasonal influence on the prognosis was found with a significant lower case-fatality in cases diagnosed in summer and fall compared to cases diagnosed during winter for prostate, as well as breast and colon cancer. The absence of a north–south gradient in the mortality is explained by the authors as being the result of dietary traditions in northern Norway, which consists of more vitamin D rich food.
Table 1 – Characteristics and outcomes of ecologic studies investigating the association between sunlight or ultraviolet radiation and cancer risk

<table>
<thead>
<tr>
<th>Authors</th>
<th>Country/population</th>
<th>Years + source</th>
<th>UV measure</th>
<th>Characteristics of study subjects</th>
<th>Cancer M/I</th>
<th>Association +M(male) or F(female)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hanchette and Schwartz13</td>
<td>USA</td>
<td>1970–1979, US Environmental Protection Agency, mortality rates on county level</td>
<td>Epidemiologic index: including cloud cover and latitude</td>
<td>Whites</td>
<td>Prostate M</td>
<td>M: $r = -0.25$ ($p &lt; 0.0002$)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>UV count: including altitude and latitude</td>
<td>Prostate M</td>
<td></td>
<td>M: $r = -0.15$ #</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Latitude</td>
<td>Whites</td>
<td>Breast M</td>
<td>M: $r = +0.19$ #</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>DNA-weighted UV-B radiation exposure map obtained by satellite</td>
<td>Whites</td>
<td>Colon M</td>
<td>M: $r = -0.67$ #</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>F: $r = -0.63$ #</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>F: $r = -0.38$ #</td>
</tr>
<tr>
<td>Grant14</td>
<td>USA</td>
<td>1970–1994, Atlas cancer mortality, SEA</td>
<td>Ground based UV-B monitoring stations in weeks without clouds, July</td>
<td>Whites</td>
<td>Breast M</td>
<td>M: $r = -0.30$ #</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Colon M</td>
<td>M: $r = -0.34$ #</td>
</tr>
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<td></td>
<td>F: $r = -0.29$ #</td>
</tr>
<tr>
<td>Ground based UV-B monitoring</td>
<td>Whites</td>
<td>Ground based UV-B monitoring stations in weeks without clouds, July</td>
<td></td>
<td></td>
<td>Rectum M</td>
<td>M: $r = -0.34$ #</td>
</tr>
<tr>
<td>monitoring stations in weeks</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>F: $r = -0.29$ #</td>
</tr>
<tr>
<td>without clouds, July</td>
<td></td>
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<tr>
<td>Ground based UV-B monitoring</td>
<td>Whites</td>
<td>Ground based UV-B monitoring stations in weeks without clouds, September</td>
<td></td>
<td></td>
<td>Breast M</td>
<td>F: $r = -0.75$ #</td>
</tr>
<tr>
<td>monitoring stations in weeks</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Colon M</td>
<td>F: $r = -0.75$ #</td>
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<tr>
<td>without clouds, September</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>F: $r = -0.75$ #</td>
</tr>
<tr>
<td>Authors</td>
<td>Country/Population</td>
<td>Years + source</td>
<td>UV measure</td>
<td>Characteristics of study subjects</td>
<td>Prostate M/ F: Pearson correlation:</td>
<td>Sunlight: β =</td>
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<tr>
<td>Grant(^{18})</td>
<td>20 European countries</td>
<td>Late 1990s WHO mortality database</td>
<td>UV count modeled based on latitude</td>
<td>Prostate M</td>
<td>M: (R^2 = 0.40, \ p = 0.002,) (t = -3.7)</td>
<td>(0.35, p &lt; 0.0001)</td>
</tr>
<tr>
<td></td>
<td>32 Caucasian countries</td>
<td></td>
<td></td>
<td>Prostate M</td>
<td>M: (R^2 = 0.51, \ p &lt; 0.0001,) (t = -5.8)</td>
<td>(0.80, p &lt; 0.0001)</td>
</tr>
<tr>
<td>Garland et al.(^{15})</td>
<td>US</td>
<td>NCI cancer mortality 1950–1969</td>
<td>365-day observation of sunlight measurement</td>
<td>Breast M/Moderately urbanisedOverall</td>
<td>Breast M: R = 0.40, p = 0.002, t = -3.7</td>
<td>F: r = -0.80, p &lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Breast M/Moderately urbanisedOverall</td>
<td>F: r = -0.70, p &lt; 0.002</td>
<td>F: r = -0.51, p &lt; 0.05</td>
</tr>
<tr>
<td>Gorham et al.(^{19})</td>
<td>USSR</td>
<td>Annual age-adjusted breast cancer incidence rates</td>
<td>Total average annual ambient sunlight</td>
<td>Prostate M/Moderately urbanisedOverall</td>
<td>Breast M: R = 0.40, p = 0.002, t = -3.7</td>
<td>F: r = -0.19, p = 0.28</td>
</tr>
<tr>
<td>Grant(^{20})</td>
<td>35 countries</td>
<td>Breast cancer mortality (WHO)</td>
<td>Latitude</td>
<td>Breast M/Moderately urbanisedOverall</td>
<td>Breast M: R = 0.40, p = 0.002, t = -3.7</td>
<td>F: r = -0.70, p &lt; 0.002</td>
</tr>
<tr>
<td></td>
<td>USA non-metropolitan</td>
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</tr>
<tr>
<td>Lefkowitz and Garland(^{22})</td>
<td>USA</td>
<td>Ovarian cancer mortality data NIH and CDC</td>
<td>National Oceanic and Atmospheric Administration, Sunlight data</td>
<td>Ovary, M</td>
<td>Pearson correlation: -0.42</td>
<td>#</td>
</tr>
<tr>
<td>Bentham(^{16})</td>
<td>England and Wales</td>
<td>NHL incidence – atlas of cancer incidence</td>
<td>UV from model with latitude and cloud cover</td>
<td>NHL, I</td>
<td>F+M: r = 0.372, p &lt; 0.001 unadj, 0.289, p = 0.004 adj for social class, employment in agriculture</td>
<td></td>
</tr>
</tbody>
</table>

(continued on next page)
<table>
<thead>
<tr>
<th>Authors</th>
<th>Country/ population</th>
<th>Years + source</th>
<th>UV measure</th>
<th>Characteristics of study subjects</th>
<th>Cancer M/I</th>
<th>Association +M(male) or F(female)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hartge et al. 17</td>
<td>USA</td>
<td>White men, mortality rates</td>
<td>Annual ambient levels of solar UV-B, adjusted for latitude, altitude and cloud cover, in Robertson-Berger (RB) units</td>
<td>NHL, M</td>
<td>M: each RB unit increase -0.16% NHL mortality, R² = 0.339, p &lt; 0.0001</td>
<td></td>
</tr>
<tr>
<td>Hu et al. 23</td>
<td>USA, 6 states with large Hispanic population</td>
<td>State cancer registries, NHL incidence</td>
<td>UV index of National Weather Service</td>
<td>NHL, M</td>
<td>F: each unit: -0.17% NHL mortality, R² = 0.444, p not available</td>
<td></td>
</tr>
<tr>
<td>Langford et al. 24</td>
<td>9 Western European Countries</td>
<td>NHL mortality</td>
<td>Estimated solar UVB radiation</td>
<td>Female NHL, I</td>
<td>M: r = 0.6 (p = 0.2)</td>
<td></td>
</tr>
<tr>
<td>McMichael and Giles 25</td>
<td>22 Caucasian countries</td>
<td>NHL incidence, Cancer Incidence in 5 continents</td>
<td>Estimated day-long UV-B exposure</td>
<td>Male NHL, I</td>
<td>M: r = 0.49 (p = 0.32)</td>
<td></td>
</tr>
<tr>
<td>Uehara et al. 26</td>
<td>Japan</td>
<td>National death registry</td>
<td>Ambient UVB from weather stations, through formula based on UVB data, latitude, global solar radiation, total ozone</td>
<td>NHL, I</td>
<td>M: r = 0.50, p &lt; 0.001</td>
<td></td>
</tr>
</tbody>
</table>

M = mortality, I = incidence; #=p < 0.0001; M = male, F = female.
Table 2 – Characteristics and outcomes of case-control studies investigating the association between sunlight or ultraviolet radiation and cancer risk

<table>
<thead>
<tr>
<th>Authors</th>
<th>Country</th>
<th>Control population</th>
<th>UV measure</th>
<th>Cancer M/I</th>
<th>OR (95% CI)</th>
<th>Corrected for</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freedman et al.27</td>
<td>24 states of US</td>
<td>Common set 97,873 ca, 83,421 co 130,261 ca, 70,081 co 39,002 ca, 70,081 ca, 153,511 ca, 153,502 co</td>
<td>Residence: high versus low exposure, US Weather Bureau data. Males and Females</td>
<td>Prostate, M</td>
<td>0.90 (0.87–0.93)</td>
<td>Age, sex, race, occupation, physical activity, SES</td>
</tr>
<tr>
<td>Bodiwala et al.28</td>
<td>Caucasians, UK</td>
<td>BPH453 ca, 312 co</td>
<td>Mean hours of cum exposure/year Childhood sunburn (y/n) Adult sunbathing score</td>
<td>Breast, M</td>
<td>0.74 (0.72–0.76)</td>
<td>&quot;</td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
<td>Ovarian, M</td>
<td>0.84 (0.81–0.88)</td>
<td>&quot;</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Colon, M</td>
<td>0.73 (0.71–0.74)</td>
<td>&quot;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Prostate, M</td>
<td>0.99 (0.99–1.00)/h</td>
<td>Age at diagnosis</td>
</tr>
<tr>
<td>John et al.29</td>
<td>San Francisco</td>
<td>Random digit dialing 450 ca, 455 co. Cases derived from SEER</td>
<td>Solar radiation in state of birth: high versus low Duration of residence in low-radiation states (not versus &gt;15 years) Lifetime outdoor activities Sun exposure index: high versus low</td>
<td>Prostate, I</td>
<td>1.01 (0.73–1.39)</td>
<td>Age, family history, month of pigmentation measurements. Sun exposure index: difference constitutive and facultative skin pigmentation Age, BMI, family history, aspirin/NSAID, energy intake, vigorous activity, fiber</td>
</tr>
<tr>
<td>Kampman et al.30</td>
<td>US</td>
<td>Population-based 1993 ca, 2410 co</td>
<td>Sunshine exposure (high versus low quintile) Males</td>
<td>Colon, I</td>
<td>0.9 (0.7–1.1)</td>
<td>Age, sex, race, residence, occupational sun exposure, and SES</td>
</tr>
<tr>
<td>Freedman et al.32</td>
<td>24 states of USA</td>
<td>Non-cancer deaths from 24 state mortality database</td>
<td>Females Residence: high versus low exposure, US Weather Bureau data. Males and Females</td>
<td>NHL, M</td>
<td>1.0 (0.8–1.4)</td>
<td>Age, sex, race, occupation, physical activity, SES</td>
</tr>
<tr>
<td>Hughes et al.31</td>
<td>Australia</td>
<td>Electoral rolls, population-based</td>
<td>Outdoor activities highest versus lowest, both sexes Non-working days, both sexes Vacation sun exposure, both sexes</td>
<td>NHL I</td>
<td>0.65 (0.46–0.91)</td>
<td>&quot;</td>
</tr>
<tr>
<td>Smedby et al.33</td>
<td>Denmark, Sweden</td>
<td>Random sampling from population registers</td>
<td>Sunbathing 5–10 years ago 4×/week versus never Sunbathing at age 20 4×/ week versus never Sun vacations abroad &gt;20× versus never</td>
<td>NHL I</td>
<td>0.7 (0.6–0.9)</td>
<td>&quot;</td>
</tr>
</tbody>
</table>

(continued on next page)
All included studies on breast cancer (4 ecologic,\textsuperscript{14,15,19,20} 1 case-control\textsuperscript{27} and 2 cohort\textsuperscript{34,36} studies) also showed a negative correlation with sunlight.

In colon cancer 2 ecologic studies\textsuperscript{14,21} showed a north–south gradient with lower mortality in the south. Two case-control studies gave conflicting results: one finding an inverse relation between colon cancer mortality and sunlight,\textsuperscript{27} the other finding no important association between colon cancer incidence and sunlight.\textsuperscript{30} Two cohort studies\textsuperscript{34,38} found significant inverse correlations between sunlight and case fatality.

In ovary cancer 2 ecologic studies\textsuperscript{14,22} and 1 case control study\textsuperscript{27} were included. All three showed a significantly inverse correlation between sunlight and mortality from this type of cancer.

As to other types of solid tumours, only 2 ecologic\textsuperscript{14,15} studies were included of which 1\textsuperscript{14} found a north–south gradient for oesophageal, kidney, stomach, rectum, bladder, kidney and uterus cancer. No case-control or cohort studies on these tumours were found.

3.5. Haematological malignancies

As can be seen in the tables, a considerable number of studies were performed on non-Hodgkin lymphoma (NHL). The ecologic studies give positive (both significant\textsuperscript{16,25} and non-significant\textsuperscript{23}) as well as negative (both significant\textsuperscript{14,17,26} and non-significant\textsuperscript{23}) correlations between NHL and sun exposure. Three case-control studies\textsuperscript{31–33} found that sun exposure was associated with a significantly reduced risk for NHL. The Swedish cohort study\textsuperscript{37} showed a modest but significant inverse association between the incidence of NHL and latitude.

Two Swedish studies mention other haematological malignancies: one\textsuperscript{37} found no north–south gradient for chronic lymphatic leukaemia. The other,\textsuperscript{33} in addition to an inverse association between NHL and sunlight, reports a similar, albeit weaker, association for Hodgkin lymphoma. No clear differences were found among non-Hodgkin subtypes, although the associations were stronger for B-cell than for T-cell lymphomas. Recently, epidemiological data from Norway indicated that season of diagnosis is a strong prognostic factor for Hodgkin lymphoma: patients diagnosed during autumn have a 20% lower case-fatality compared with those diagnosed in winter.\textsuperscript{39} A Japanese study\textsuperscript{26} reports that among the nine subtypes of leukaemia (ICD-9: codes 200–208) sunlight was found as a significant risk factor for 2 types: ‘other malignant neoplasms of lymphoid and histiocytic tissue’ (ICD 202) and ‘lymphoid leukaemia’ (ICD-204). In this study, for Hodgkin lymphoma (ICD 201) no correlation between sun exposure and mortality was found.

4. Discussion

From our review, it becomes clear that there is an increasing evidence of sunlight having a preventive effect on the initiation and/or progression of different kinds of cancer.

4.1. Prostate cancer

All the eight studies that have been included show an inverse correlation between prostate cancer mortality or incidence and sunlight.

The quantitative relationship between sunlight and mortality from prostate cancer seems to follow a dose–response curve: the more sunlight received, the higher the preventive effect. This is suggested by the north–south gradients in the ecologic studies and by the finding that increased chronic exposure gives increased protection.\textsuperscript{28,29} Moreover, features of acute exposure, such as childhood sunburn, regular foreign holidays and a high adult sunbathing score, were demonstrated to have a reducing effect on risk.\textsuperscript{28}

The effect of sunlight on prostate cancer risk seemed to be influenced by both geno- and phenotype. The effect was modulated by polymorphisms in Vitamin D receptors.\textsuperscript{29,40} Concerning phenotype: among individuals with low or intermediate sun exposure those with skin type 1 (burns easily, never tans) had a significantly reduced risk compared with those with skin type 4 (rarely burns, easily tans), who are partially deprived from the effects of sunlight by their increased level of pigmentation.\textsuperscript{28,29} Similarly, black American men had a higher incidence of prostate cancer than white American men\textsuperscript{14} and carcinomas of the prostate and the breast behaved more aggressively in black Americans than in white Americans.\textsuperscript{10}

From all these data, we conclude that there is a strong evidence that sunlight has a preventive effect on prostate cancer.

4.2. Breast cancer

All the seven studies that have been included show a beneficial effect of sunlight on breast cancer incidence or mortality.
<table>
<thead>
<tr>
<th>Authors</th>
<th>Country</th>
<th>Population</th>
<th>UV measure</th>
<th>Outcome</th>
<th>Cancer</th>
<th>RR (95% CI)</th>
<th>Corrected for</th>
</tr>
</thead>
<tbody>
<tr>
<td>Robsahm et al.</td>
<td>Norway, cancer registry</td>
<td>Norwegians born 1900–1966, diagnosed with cancer of breast, prostate or colon between 1964–1992</td>
<td>Latitude and climatic differences, RR for residential sun exposure level VIII (highest) versus level I (reference)</td>
<td>Case-fatality</td>
<td>F: breast</td>
<td>0.95 (0.86–1.05)</td>
<td>Age at diagnosis, birth cohort, period of diagnosis, stage at diagnosis, occupational sun exposure, childbearing pattern, educational level</td>
</tr>
<tr>
<td>John et al.</td>
<td>USA, NHANES I</td>
<td>3414 white men without history of prostate cancer who completed baseline questionnaire. 153 prostate cancer cases in follow-up</td>
<td>Residential sun exposure at region of residence South versus North-east</td>
<td>RR</td>
<td>M: prostate</td>
<td>0.96 (0.83–1.10)</td>
<td>Age, family history of prostate cancer, fat and calcium intake</td>
</tr>
<tr>
<td>John et al.</td>
<td>USA, NHANES I</td>
<td>5009 white women without history of cancer, with completed dietary and dermatological exams, 191 breast cancer cases in fu</td>
<td>Residential sun exposure at region of residence South versus North-east</td>
<td>RR</td>
<td>F: breast</td>
<td>0.71 (0.49–1.09)</td>
<td>Age, education, age at menarche, age at menopause, BMI, frequency of alcohol consumption, physical activity</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>F: colon</td>
<td>Around 0.7</td>
<td></td>
</tr>
</tbody>
</table>

(continued on next page)
We therefore conclude that there is also substantial evidence for a preventive effect of sunlight on this type of cancer.

4.3. Colon cancer

Five out of 6 (2 ecologic, 1 case-control and 2 cohort) studies investigating the relationship between sunlight and colon cancer showed a preventive effect of sunlight, whereas 1 case-control study showed no effect. The latter is the only publication on the effect of sunlight on these 4 types of solid tumours that did not show any preventive effect. A possible explanation, as given by the authors, for this divergent finding is that in most studies exposure to sunlight was assessed for the period many years before diagnosis, while in this study exposure from a recent past was assessed. Possibly, the protective effect only occurs in early stages of tumour development. Our conclusion therefore is that the data that were found mainly support the hypothesis that sunlight plays a role in the prevention of colon cancer.

4.4. Ovarian cancer

For ovary cancer the evidence is small but conclusive. However, since 2 out of the 3 studies are ecological studies and only 1 case-control study was identified, more studies on ovarian cancer would be needed to make a more firm statement about the association with sunlight exposure.

4.5. Non-hodgkin lymphoma

The results for NHL are conflicting. Most early (mainly ecologic) studies, based chiefly on the hypothesis that sunlight is a risk factor for NHL, show a positive correlation with sunlight exposure, while more recent (in particular case-control and cohort) studies found inverse relationships. If there is a relationship between sunshine and NHL, these conflicting results might also, at least partially, be explained by the different lymphoma classifications used in the various studies: some mention ICD-codes 7, 8, 9 and 10, some studies mention no classification at all. Others do not mention which ICD code was used and only mentioned to have included histologically verified cases. Due to improving diagnostic techniques, ICD codes for haematological malignancies have changed substantially over the last few decades and are not completely comparable.

4.6. Other malignancies

Other types of solid tumours or haematological malignancies have not been studied to the degree that any conclusion can be drawn as to a possible effect of sunlight.

From the data discussed here, it can be concluded that there is increasing and conclusive evidence that sunlight has a preventive effect on the initiation and/or progression of prostate and breast cancer, colon and possibly also ovarian cancer.

As in all review studies, our findings might be influenced by publication bias, since regarding prostate, breast, colon and ovary carcinoma nearly all studies that have been pub-
lished show the same result: an inverse relationship between sunlight and/or UVR dose and cancer incidence and/or mortality. This possibility, however, is contradicted by the conflicting results for non-Hodgkin and Hodgkin lymphomas.

As an explanation for the preventive effect of sunlight on cancer, usually the role of UVB in Vitamin D (Vit D) synthesis is given. Most humans obtain 80–90% of their requirement for Vit D from sunlight; very few types of food (mainly oily fish) naturally contain Vit D and only in fish-consuming populations a major part of Vit D is ingested with fish oil.

Vit D3 is synthesised from its precursor 7-dehydrocholesterol in the skin by the direct action of sunlight. The steroid hormone 1,25(OH)2D3 is much more active than its precursors and is produced of Vit D3 by 25-hydroxylation in the liver, followed by 1α-hydroxylation in the kidney. Consequently, Vit D is a potential candidate for cancer regulation.

Higher rates of cancer mortality have been found among African-Americans and obese and overweight people, each associated with lower circulating Vit D levels. Only colorectal, prostate and breast cancer have been examined directly in relation to Vit D status. The evidence that colorectal carcinogenesis is inhibited by Vit D is substantial. Both epidemiological and biological data support a role for Vit D in the prevention of breast cancer. The biological evidence for an anticancer role of Vit D is also strong for prostate cancer, but the epidemiological data are inconclusive. The observed associations may be caused by other confounding risk factors such as calcium and Vitamin A and, additionally, other effects of UVB than Vit D synthesis may be responsible for the presumed preventive effect. In comparison with the quantitative relationship between sunlight and its preventive effect, for Vit D this relationship is less clearly elucidated; the optimal levels of Vit D for a preventive effect are still unknown. Many authors assume that these levels are considerably higher than the levels recommended to prevent osteoporosis, although a Finnish study found an increased risk for prostate cancer both for low and high levels of Vit D. It is therefore questionable if Vit D synthesis is the only mechanism by which sunlight exerts its preventive effect on cancer. In this regard, it has been suggested that the effect of sunlight on circadian rhythm could have a beneficial influence too.

There is now an increasing evidence that (at least moderate) sun exposure may have a preventive effect on several forms of cancer, even on melanoma, the most aggressive type of skin cancer. However, intensive exposure to the sun can also cause all types of skin cancers by a direct mutational effect on epidermal cells. In countries with a moderate climate like the Netherlands, the absolute mortality of prostate, breast and colon cancer is almost 20 times higher than that of skin cancer.

The question remains as to how to apply these findings to (public) health recommendations. Until recently, recommendations on sun exposure were only given from the viewpoint of its deleterious effects. The authors of this review believe that from the data available promotion of moderate sun exposure should be considered, besides warning against intensive (over-)exposure to sunlight. This would particularly apply to people living in countries with a moderate climate and to individuals without known risks for skin cancer.

More definite data are needed to decide definitely if the advantages of sun exposure exceed the disadvantages to the extent that a further adaptation in health recommendations becomes advisable.

**Conflict of interest statement**

There is no conflict of interest. The researchers have not been funded by any external organisation.

**REFERENCES**


46. DeLeo VA. The vitamin D and sunlight controversy – we will wait and see. Cutis 2005;76:229.

