Sunlight and mortality from breast, ovarian, colon, prostate, and non-melanoma skin cancer: a composite death certificate based case-control study

D M Freedman, M Dosemeci, K McGlynn

Objectives: To explore whether mortality from female breast, ovarian, colon, and prostate cancer were negatively associated with exposure to sunlight.

Methods: A death certificate based case-control study of mortality was conducted into five cancers: female breast, ovarian, colon, prostate, and non-melanoma skin cancer (as a positive control) to examine associations with residential and occupational exposure to sunlight. Cases were all deaths from these cancers between 1984 and 1995 in 24 states of the United States. Controls, which were age frequency matched to a series of cases, excluded deaths from cancer and certain neurological diseases. Multiple logistic regression was used in a model that included age, sex, race, residential exposure to sunlight (based on region), and socioeconomic status, occupational exposure to sunlight, and physical activity (the last three based on usual occupation).

Results: Residential exposure to sunlight was negatively and significantly associated with mortality from female breast, ovarian, prostate, and colon cancer. Only female breast and colon cancer, however, also showed significant negative associations with jobs with the highest occupational exposure to sunlight (odds ratio (OR) 0.82 (95% confidence interval (95% CI) 0.70 to 0.97) for female breast cancer; OR 0.90 (95% CI 0.86 to 0.94) for colon cancer). For both cancers, the negative association with occupational sunlight was greatest in the geographical region of highest exposure to sunlight and was independent of physical activity on the job. Non-melanoma skin cancer, as expected, was positively associated with both residential and occupational sunlight.

Conclusions: In this exploratory study, unlike mortality from non-melanoma skin cancer, mortality from female breast cancer and colon cancer were negatively associated with both residential and occupational sunlight.

It is well established that exposure to sunlight contributes to non-melanoma skin cancer.1 By contrast, several ecological studies suggest that sunlight may protect against female breast,2–7 ovarian,6 prostate,4 and colon cancer;3 all diseases that contribute to a substantially higher proportion of cancer mortality in the western industrialised world. Some analytical studies, although not all,8–11 also suggest a protective association between circulating vitamin D in blood, which is largely derived from sunlight,12 or dietary vitamin D and colorectal cancer,13–14 female breast cancer,15–16 and prostate cancer.17

To our knowledge, no epidemiological study has examined the relation between ovarian, prostate, or colon cancers and sunlight from non-residential sources, and only one, a recent cohort study,18 has examined these factors for breast cancer. We conducted a set of death certificate based case-control studies of mortality from female breast, ovarian, prostate, colon, and non-melanoma skin cancers in the United States. As an improvement over geography based ecological mortality studies, we assessed potential exposure to sunlight based on occupational data on individual death certificates. The findings for breast, ovarian, colon, and prostate cancer were contrasted with those for non-melanoma skin cancer, which served as a positive control.

Materials and Methods

The National Cancer Institute, the National Institute for Occupational Safety and Health, and the National Center for Health Statistics maintain a database of all deaths in 24 states (1985–95), which codes occupation, state of residence at birth and at death, and other information from death certificates.19 Cases for this study included all deaths from female breast cancer (international classification of diseases, ninth revision (ICD-9), (code 174), ovarian cancer (code 183), colon cancer (code 153), prostate cancer (code 185), and non-melanoma skin cancer (code 173). Non-melanoma skin rather than melanoma was selected as a positive control because the association between sunlight and melanoma is more complex, with age at exposure and intermittent intense exposure thought to have a role.1 A common set of controls was used across a series of case-control studies on cancer and neurological mortality and solar radiation.19 Deaths from cancer (ICD 140–239), multiple sclerosis (ICD 340), and some diseases of the central nervous system (ICD 330–337), were excluded from the controls because of their potential association with exposure to sunlight. Controls were frequency matched by 5 year age group to the combined group of breast cancer, ovarian cancer, prostate cancer, colon cancer, and the other causes of death in the case series. Controls were limited to women for female breast and ovarian cancer, and to men for prostate cancer. The controls represent a one to one ratio with the most common causes of death in the series (colon cancer), but a ratio of about 25 to one with skin cancer.

Residential exposure to sunlight was assessed by state residence and birthplace recorded on the death certificate. We assigned each state one of three levels of solar radiation based...
on data from the United States Weather Bureau. The 24 states reflected all regions of the country (table 1). Subjects were limited to those who resided in the same solar radiation region at birth and at death (about 75%) to exclude those most likely to have varied solar residential histories.

Occupational exposure to sunlight was based on usual occupation from the death certificate (as reported by next of kin) and classified by an industrial hygienist (MD) into four categories: indoor work, work that combined indoor and outdoor work, outdoor work by non-farmers, and farming (analyzed with dummy variables). Farmers were categorized separately because several studies have suggested that farmers are at increased risk of prostate and other cancers. Those with unidentified occupations or positions that could not be classified were controlled for separately. Occupation was also used to assess occupational history from the death certificate (as reported by next of kin) to have varied solar residential histories.

We used multivariate models of potential occupational and residential exposure to solar radiation that included age, sex, race, socioeconomic status, and physical activity. The models were applied to the entire population; as well as strata based on race, level of physical activity, and years of exposure to sunlight could not be inferred. Other refers to those with unidentified occupations or positions that could not be classified

Table 1 Characteristics of cancer cases and controls (data expressed as numbers of participants, United States, 1984–95)

<table>
<thead>
<tr>
<th>Non-melanoma skin cancer</th>
<th>Breast cancer</th>
<th>Ovarian cancer</th>
<th>Prostate cancer</th>
<th>Colon cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases n=6565</td>
<td>Controls n=153502</td>
<td>Cases n=130261</td>
<td>Controls n=70081</td>
<td>Cases n=39002</td>
</tr>
</tbody>
</table>

Table 2 reports the ORs for residential and occupational exposure to sunlight, as well as physical activity and socioeconomic status, adjusted for age, sex, race, and the other factors in the table. As expected, the odds ratio for non-melanoma skin cancer was greatest in the region of the United States.
with highest exposure to sunlight (OR 1.23; 95% CI 1.14 to 1.33) and among workers with non-farming outdoor jobs (OR 1.30; 95% CI 1.14 to 1.47). Socioeconomic status was not clearly related to risk of skin cancer, but occupational physical activity seemed to be negatively associated with the disease. The association with occupational exposure to sunlight was increased in both white Americans and African-Americans, although the association with residential sunlight was limited to white people (data not shown).

Residential exposure to sunlight was negatively and significantly associated with mortality from female breast, ovarian, prostate, and colon cancer, among those in the highest and medium sunlight region (table 2). Risks in the highest region ranged from OR 0.73 (95% CI 0.71 to 0.74) for colon cancer to OR 0.89 (95% CI 0.75 to 0.93) for prostate cancer. The risks were consistent among white and black people except for prostate cancer, where risk for black men was increased in the highest sunlight region (data not shown).

For occupational exposure to sunlight, however, only female breast and colon cancer showed significant negative associations, and only for non-farming outdoor jobs. The adjusted OR was 0.82 (95% CI 0.70 to 0.97) for female breast cancer, and 0.90 (95% CI 0.86 to 0.94) for colon cancer. The negative associations characterised both white and black cases of breast and colon cancer (data not shown). Farming jobs were associated with increased ORs for prostate cancer, whereas occupational physical activity was negatively associated with each of the cancers except prostate cancer. Each cancer other than skin cancer was positively associated with increasing socioeconomic status.

Table 3 gives the ORs for mortality from non-melanoma skin, female breast, ovarian, prostate, and colon cancer and occupational exposure to sunlight, for each residential strata and for those with jobs with high (high/moderate) and low (low/sedentary) physical activity, also adjusted for sex, race, socioeconomic status, and physical activity. For non-melanoma skin cancer, the OR was increased in each region and physical activity strata for those with non-farming outdoor jobs.

The relation between mortality from female breast cancer and non-farming outdoor employment was most negative in the region of greatest residential sunlight (OR 0.75 (95% CI 0.55 to 1.03)). It remained negative in both physical activity strata (OR 0.90 (low activity) and OR 0.82 (high activity)). Similarly, colon cancer showed a negative association with non-farming outdoor work in the middle and high sunlight regions, which was most pronounced and significant in the highest sunlight region (OR 0.81 (95% CI 0.74 to 0.90)). The association was similarly negative in each physical activity strata.

By contrast, mortality from ovarian cancer was positively, but not significantly, associated with non-farming outdoor jobs in all but the highest sunlight region. It was also increased (OR 1.49; 95% CI 0.86 to 2.58) among those with jobs with low physical activity. Mortality from prostate cancer was highest in the medium sunlight region (OR 1.23 (95% CI 1.18 to 1.28)), although the association with farming jobs was increased in the lowest and medium sunlight regions. There was also no association with non-farming outdoor jobs in the two physical activity strata.

**DISCUSSION**

This study found inverse associations between both residential and occupational exposure to sunlight and mortality from female breast and colon cancer, which were independent of physical activity on the job. Although mortality from ovarian and prostate cancer were inversely associated with occupational sunlight. As expected, we also found a positive association between mortality from non-melanoma skin cancer, our positive control cancer, and residential and occupational exposure to sunlight.

This study improved ascertainment of exposure over ecological studies by using individual data on occupation, state of birth and residence at death, socioeconomic status, and physical activity. Although the study also benefited from the many cases in this data set, death certificate studies such as this, have recognised limitations. These include potential misclassification on the underlying cause of death, occupation, and residential exposure, where a lifetime residential history is unavailable, as well as lack of information on other sources of exposure to sunlight, such as leisure activities. Also, death certificates require reliance on crude information such as usual occupation for measures of

**Table 2** Odds ratios (95% CIs) for non-melanoma skin, female breast, ovarian, colon, and prostate cancer mortality associated with residential exposure to sunlight, occupational exposure to sunlight, occupational physical activity, and socioeconomic status, adjusted for age, sex, race, and other factors in the table

<table>
<thead>
<tr>
<th>Residence*</th>
<th>OR 95% CI</th>
<th>OR 95% CI</th>
<th>OR 95% CI</th>
<th>OR 95% CI</th>
<th>OR 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Non-melanoma skin cancer</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Med</td>
<td>1.14</td>
<td>1.07 to 1.23</td>
<td>0.84</td>
<td>0.82 to 0.86</td>
<td>0.90</td>
</tr>
<tr>
<td>High</td>
<td>1.23</td>
<td>1.14 to 1.33</td>
<td>0.74</td>
<td>0.72 to 0.76</td>
<td>0.84</td>
</tr>
<tr>
<td><strong>Ovarian cancer</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Med</td>
<td>0.91</td>
<td>0.83 to 1.01</td>
<td>0.95</td>
<td>0.91 to 0.99</td>
<td>0.97</td>
</tr>
<tr>
<td>High</td>
<td>0.91</td>
<td>0.82 to 1.01</td>
<td>0.79</td>
<td>0.76 to 0.82</td>
<td>0.82</td>
</tr>
<tr>
<td><strong>Colon cancer</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Med</td>
<td>0.97</td>
<td>0.87 to 1.08</td>
<td>0.99</td>
<td>0.93 to 1.06</td>
<td>1.00</td>
</tr>
<tr>
<td>High</td>
<td>0.92</td>
<td>0.83 to 1.03</td>
<td>1.28</td>
<td>1.20 to 1.36</td>
<td>1.24</td>
</tr>
</tbody>
</table>

Footnotes as for table 1.
socioeconomic status and physical activity and cannot assess physical activity unrelated to occupation. Thus, there is no independent source of information on socioeconomic status and occupational physical activity and no assessment of recreational physical activity. Furthermore, there is a lack of information on potential confounders, which, for example in the case of breast cancer, includes parity and other reproductive factors, as well as alcohol, diet, and use of oral contraceptives.

Importantly, there is also a potential bias in using deaths rather than population as the study base because exposure patterns among decedents may not reflect those in the total population. However, that skin cancer showed the expected association with exposure to sunlight\(^1\) argues against a substantial study bias. Moreover, socioeconomic status as categorised in this model showed a dose-response relation with the risk of female breast, ovarian, and colon cancer, which is also consistent with the findings of several, although not all, studies.\(^{30-32}\) On the other hand, we found a similar dose-response relation for socioeconomic status and prostate cancer, although differences in socioeconomic status in other studies have been small.\(^{15}\) Thus, there may be a socioeconomic bias among decedents compared with incident cases, which could potentially have distorted our associations.

Our most noteworthy results were the decreased risk for female breast and colon cancer among those with non-farming outdoor jobs, particularly in the regions of highest sunlight. The breast cancer findings resemble the recent NHANES I follow up study\(^{11}\) of risk of breast cancer and both exposure to sunlight and vitamin D intake by John \textit{et al}, which found that several measures of these exposures were associated with a reduced risk of breast cancer in white women. Our study, which relied on cruder exposure data than that used in the NHANES I study, replicated their negative association with residential sunlight, and confirmed it in both white and black women.

Just as we found, John \textit{et al} generally found low or no association with sunlight among women who lived in the region of lowest exposure to sunlight. They also generally found that risk reductions were greatest in the region of highest solar radiation, and intermediate in regions of intermediate exposure. This is consistent with findings that vitamin D is not synthesised in winter in regions of lowest solar radiation in the United States.\(^9\)

Only a few studies have analyzed the risk of breast cancer associated with blood concentrations of vitamin D. Although Janowsky \textit{et al} found no case-control differences in 25(OH)D in blood, they found significant mean differences in 1,25-dihydroxyvitamin D\(^{3}\) (1,25(OH)\(_2\)D) concentrations between cases of breast cancer and controls.\(^{33}\) By contrast, Hiatt \textit{et al} compared serum concentrations of 1,25(OH)\(_2\)D before diagnosis among cases of breast cancer and non-cases, and found no association.\(^{34}\)

Analytical epidemiological data on colon cancer do not include estimates of exposure to sunlight. Although several cohort studies reported negative associations between dietary vitamin D intake and colon or colorectal cancer,\(^{35-37}\) the few case-control studies have been inconsistent.\(^{4\text{a, b}}\)\(^3\)

Recent experimental studies suggest biological plausibility of a protective effect of vitamin D on cancer, particularly for breast and colon cancer. Most notably, hormonal vitamin D, 1,25(OH)\(_2\)D, has been shown to promote cell differentiation and retard or terminate proliferation of human cancer cells in vitro,\(^{40,41}\) including breast\(^{42}\) and colon cancer cells.\(^{43}\)

The mechanisms by which 1,25(OH)\(_2\)D may produce an anticarcinogenic, prodifferentiation effect include inhibition of growth, angiogenesis,\(^{44}\) and metastasis.\(^{45}\) Evidence in support of the growth inhibition mechanism has been reported from studies of experimental carcinogenesis in several tumour types. For example, 1,25(OH)\(_2\)D has been shown to suppress formation of breast tumours after

### Table 3

<table>
<thead>
<tr>
<th>Occupational exposure to sunlight</th>
<th>Residence: low sunlight OR (95% CI)</th>
<th>Residence: medium sunlight OR (95% CI)</th>
<th>Residence: high sunlight OR (95% CI)</th>
<th>Low physical activity OR (95% CI)</th>
<th>High physical activity OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-melanoma skin cancer:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inside</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Mixed</td>
<td>1.02 [0.86 to 1.21]</td>
<td>1.03 [0.91 to 1.18]</td>
<td>0.97 [0.82 to 1.14]</td>
<td>0.92 [0.82 to 1.03]</td>
<td>1.03 [0.93 to 1.14]</td>
</tr>
<tr>
<td>Outside</td>
<td>1.24 [0.92 to 1.67]</td>
<td>1.41 [1.14 to 1.76]</td>
<td>1.19 [0.91 to 1.54]</td>
<td>1.39 [0.83 to 2.33]</td>
<td>1.25 [1.10 to 1.42]</td>
</tr>
<tr>
<td>Farmer</td>
<td>0.84 [0.60 to 1.18]</td>
<td>1.20 [0.97 to 1.49]</td>
<td>1.26 [0.94 to 1.69]</td>
<td>–</td>
<td>1.08 [0.94 to 1.24]</td>
</tr>
<tr>
<td>Female breast cancer:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inside</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Mixed</td>
<td>1.05 [0.93 to 1.19]</td>
<td>0.92 [0.83 to 1.03]</td>
<td>1.09 [0.95 to 1.25]</td>
<td>0.90 [0.83 to 0.97]</td>
<td>1.19 [1.09 to 1.30]</td>
</tr>
<tr>
<td>Outside</td>
<td>0.94 [0.64 to 1.41]</td>
<td>0.87 [0.65 to 1.17]</td>
<td>0.75 [0.55 to 1.03]</td>
<td>0.90 [0.56 to 1.44]</td>
<td>0.82 [0.69 to 0.98]</td>
</tr>
<tr>
<td>Farmer</td>
<td>1.24 [0.83 to 1.86]</td>
<td>0.78 [0.58 to 1.04]</td>
<td>0.90 [0.65 to 1.24]</td>
<td>–</td>
<td>0.89 [0.73 to 1.06]</td>
</tr>
<tr>
<td>Ovarian cancer:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inside</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Mixed</td>
<td>0.95 [0.81 to 1.12]</td>
<td>1.03 [0.90 to 1.18]</td>
<td>1.14 [0.96 to 1.36]</td>
<td>0.92 [0.83 to 1.01]</td>
<td>1.16 [1.03 to 1.30]</td>
</tr>
<tr>
<td>Outside</td>
<td>1.14 [0.70 to 1.87]</td>
<td>1.17 [0.80 to 1.71]</td>
<td>0.55 [0.33 to 0.91]</td>
<td>1.49 [0.86 to 2.58]</td>
<td>0.87 [0.68 to 1.10]</td>
</tr>
<tr>
<td>Farmer</td>
<td>1.36 [0.81 to 2.29]</td>
<td>1.07 [0.72 to 1.61]</td>
<td>1.14 [0.75 to 1.74]</td>
<td>–</td>
<td>1.07 [0.85 to 1.36]</td>
</tr>
<tr>
<td>Prostate cancer:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inside</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Mixed</td>
<td>1.03 [0.97 to 1.09]</td>
<td>0.96 [0.91 to 1.00]</td>
<td>1.02 [0.96 to 1.08]</td>
<td>0.98 [0.95 to 1.02]</td>
<td>1.04 [1.01 to 1.08]</td>
</tr>
<tr>
<td>Outside</td>
<td>1.04 [0.93 to 1.15]</td>
<td>1.04 [0.96 to 1.14]</td>
<td>0.95 [0.86 to 1.04]</td>
<td>1.02 [0.83 to 1.26]</td>
<td>1.01 [0.97 to 1.06]</td>
</tr>
<tr>
<td>Farmer</td>
<td>1.28 [1.16 to 1.42]</td>
<td>1.21 [1.12 to 1.31]</td>
<td>1.01 [0.91 to 1.12]</td>
<td>–</td>
<td>1.18 [1.12 to 1.24]</td>
</tr>
<tr>
<td>Colon cancer:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inside</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Mixed</td>
<td>1.01 [0.97 to 1.06]</td>
<td>0.94 [0.90 to 0.98]</td>
<td>1.00 [0.95 to 1.06]</td>
<td>0.94 [0.91 to 0.97]</td>
<td>1.00 [0.97 to 1.04]</td>
</tr>
<tr>
<td>Outside</td>
<td>0.99 [0.90 to 1.09]</td>
<td>0.92 [0.85 to 1.00]</td>
<td>0.81 [0.74 to 0.90]</td>
<td>0.92 [0.76 to 1.12]</td>
<td>0.89 [0.85 to 0.93]</td>
</tr>
<tr>
<td>Farmer</td>
<td>1.09 [0.99 to 2.13]</td>
<td>1.04 [0.97 to 1.11]</td>
<td>1.06 [0.95 to 1.17]</td>
<td>–</td>
<td>1.01 [0.97 to 1.06]</td>
</tr>
</tbody>
</table>

*Region is as identified in table 1; †low physical activity includes those jobs described as sedentary or involving low physical activity, whereas high physical activity includes those jobs described as involving moderate or high physical activity.
induction in rats by both nitrosomethylurea and 7,12-dimethylbenz[a]anthracene. Similarly, formation of colon tumours has been suppressed by 1,25(OH)2D in nude mice implanted with a colon cancer cell line.

As John et al note, however, these relations do not establish the biological plausibility of the protective effect of sunlight on cancer. Unlike 25(OH)D, a precursor vitamin D metabolite which is highly correlated with levels of sunlight, serum 1,25(OH)2D concentrations are tightly regulated, and not closely tied to levels of sunlight, at least at high levels of exposure. If sunlight is protective against some cancers by a mechanism involving vitamin D, presumably exposure to sunlight may be linked to the endogenous hormonal vitamin D dose at the tissue level or risk of cancer may be connected to 25(OH)D.

Much remains to be explained about the biology of sunlight and cancer. Although this study is exploratory, with necessarily unrefined sunlight and other exposure categorisations, our findings of significant negative associations between both residential and occupational exposure to sunlight and mortality from female breast and colon cancer warrant additional study. The hypothesis that sunlight may reduce the risk of female breast cancer and colon cancer should be investigated using incident cases with more refined measures of sun exposure for both leisure and work.

ACKNOWLEDGEMENTS
We gratefully acknowledge the thoughtful comments of Dr Aaron Blair and Dr Robert N Hoover on the study.

REFERENCES
12 Holick MF. Environmental factors that influence the cutaneous production of vitamin D. Am J Clin Nutr 1993;51(suppl):638S–45S.


Sunlight and mortality from breast, ovarian, colon, prostate, and non-melanoma skin cancer: a composite death certificate based case-control study

D M Freedman, M Dosemeci and K McGlynn

Occup Environ Med 2002 59: 257-262
doi: 10.1136/oem.59.4.257

Updated information and services can be found at:
http://oem.bmj.com/content/59/4/257

These include:

References
This article cites 40 articles, 19 of which you can access for free at:
http://oem.bmj.com/content/59/4/257#BIBL

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections
Articles on similar topics can be found in the following collections
Other exposures (1023)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/