BJUI SUPPLEMENTS

Prostate cancer incidence in Australia correlates inversely with solar radiation

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OBJECTIVE

- To ascertain if prostate cancer incidence rates correlate with solar radiation among non-urban populations of men in Australia.

PATIENTS AND METHODS

- Local government areas from each state and territory were selected using explicit criteria. Urban areas were excluded from analysis.
- For each local government area, prostate cancer incidence rates and averaged long-term solar radiation were obtained.
- The strength of the association between prostate cancer incidence and solar radiation was determined.

RESULTS

- Among 70 local government areas of Australia, age-standardized prostate cancer incidence rates for the period 1998–2007 correlated inversely with daily solar radiation averaged over the last two decades.

CONCLUSION

- There exists an association between less solar radiation and higher prostate cancer incidence in Australia.

What's known on the subject? and What does the study add?

Increased sun exposure and blood levels of vitamin D have been postulated to be protective against prostate cancer. This is controversial. We investigated the relationship between prostate cancer incidence and solar radiation in non-urban Australia, and found a lower incidence in regions receiving more sunlight.

In landmark ecological studies, prostate cancer mortality rates have been shown to be inversely related to ultraviolet radiation exposure. Investigators have hypothesised that ultraviolet radiation acts by increasing production of vitamin D, which inhibits prostate cancer cells in vitro. However, analyses of serum levels of vitamin D in men with prostate cancer have failed to support this hypothesis.

This study has found an inverse correlation between solar radiation and prostate cancer incidence in Australia. Our population (previously unstudied) represents the third group to exhibit this correlation. Significantly, the demographics and climate of Australia differ markedly from those of previous studies conducted on men in the United Kingdom and the United States.

KEYWORDS

prostate cancer, solar radiation, sunlight, vitamin D

INTRODUCTION

Prostate cancer incidence and mortality rates vary more than 10-fold worldwide [1]. This striking disparity has been attributed to differences in genetic predisposition, screening intensity and environment. Solar exposure and vitamin D levels have been suggested as risk modifiers, following the observation in one population of men (USA) that prostate cancer mortality correlated positively with latitude and inversely with ultraviolet radiation [2,3]. To our knowledge, this correlation has not been demonstrated before in any other population.

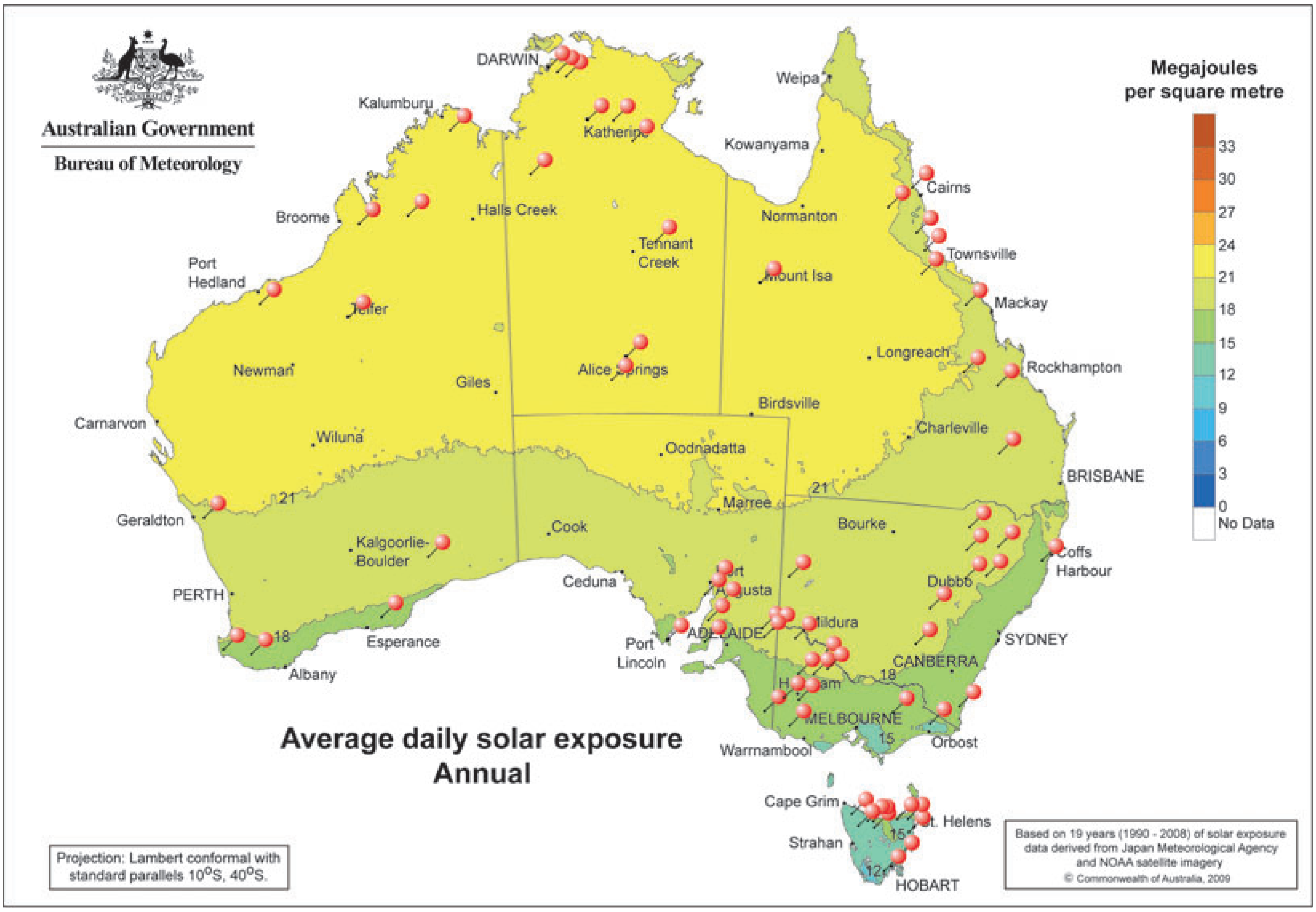
Australia is a geographically diverse country that spans 33° of latitude and includes tropical and desert landscapes as well as more temperate climates. Because cancer is a notifiable disease in all its states and territories, prostate cancer incidence reporting is complete and reliable. Similarly, the centralized Bureau of Meteorology records weather data elements, including daily solar radiation, from over 2000 stations widely distributed across the continent. In most of its stations, decades of historical data are available. The consistency of disease and weather data affords an opportunity to compare geographically disparate populations in a meaningful way.

We aim to determine if prostate cancer incidence correlates with solar radiation across Australia.

PATIENTS AND METHODS

Demographic information pertaining to all local government areas (LGAs) in Australia was obtained from the Australian Bureau of Statistics. Any LGA comprising persons living in 'major cities' or 'inner regional' areas (as defined by the Accessibility/Remoteness Index of Australia [4]) was excluded. The 10 largest LGAs (by population) from each state or territory were selected for comparison.

FIG. 1. Average daily solar exposure, annual.



For each selected LGA, the aggregated incidence of prostate cancer for the 10- year period 1998–2007 was sought from the respective cancer registry. The incidence rate was standardized to the Australian Standard Population of 2001 using the direct method. Mean daily solar radiation (in MJ/m^2) was defined as the daily amount of solar energy reaching a specific location, averaged over a 21-year period (1990–2010). This was determined for each LGA by consulting the Bureau of Meteorology. If there was more than one weather station within the boundaries of an LGA, the station that was closest to the geographical centre of the LGA was selected.

The Shapiro–Wilk test was used to confirm the Gaussian distribution of the data. The Pearson product–moment correlation coefficient was calculated to determine whether mean daily solar radiation was linearly associated with prostate cancer incidence, with a $P < 0.05$ accepted to reject the null hypothesis of no linear association.

RESULTS

A total of 561 LGAs were identified from the Australian Bureau of Statistics. There were 291 LGAs that included at least partially areas designated as 'major city' or 'inner regional'; these were excluded. The remaining 270 LGAs had populations ranging from 111 to 175 542, with a mean of 7870. The mean population density was 12.1 persons per square kilometre.

Australia comprises six states (New South Wales, Queensland, South Australia, Tasmania, Victoria and Western Australia) and two territories (the Australian Capital Territory and the Northern Territory). However, as the Australian Capital Territory comprises only one LGA, and this is a major city, 70 LGAs (10 from each of the seven remaining states and territory) were selected for comparison. The locations of these LGAs are indicated on an annual solar exposure map of Australia (Fig. 1). The population totals ranged from 4597 to 158 653, with a median of 13 765. The mean population density was 31.7 persons per square kilometre.

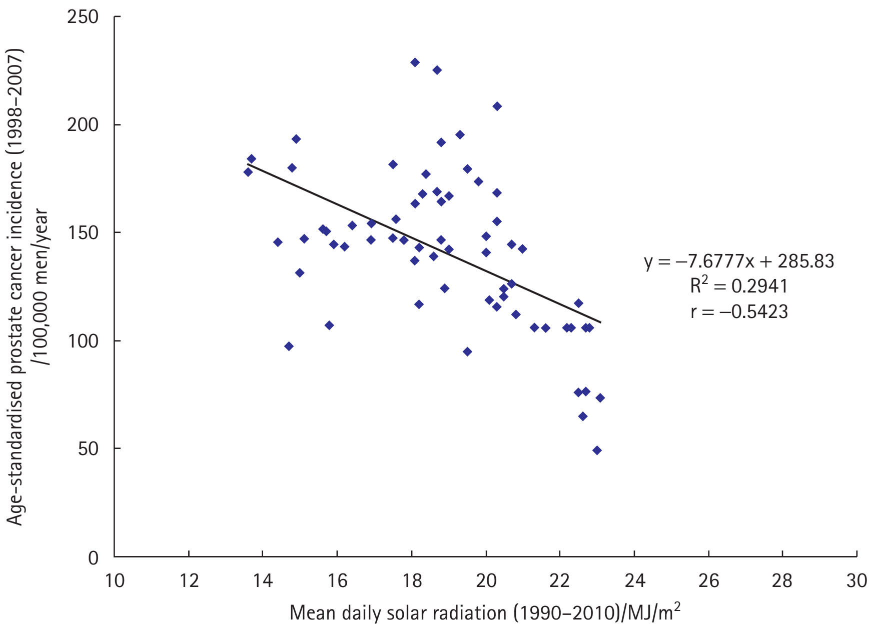
In all 70 reference weather stations, mean daily solar radiation was available for a common 21-year period (1990–2010). We used this period for consistency in comparison.

Prostate cancer incidence rates from 1998 to 2007 standardized to the Australian Standard Population of 2001 were provided by the respective state and territory cancer registries. In the case of the Northern Territory, statistics for this period and to the level of LGAs were not available; we used the rate for the territory over the period 1991–2005 instead. In Queensland and

Western Australia, data for a few LGAs were at the level of the statistical local area (SLA) – a spatial unit that is smaller than the LGA. In these cases (occurring in four instances), the cancer incidence of the most populous SLA was used to represent its LGA.

The mean daily solar radiation ranged from 13.6 to 23.1 MJ/m^2. The age-standardized incidence of prostate cancer ranged from 49.3 to 228.6 per 100 000 men per year. The null hypothesis that these data were normally distributed was not rejected for $\alpha < 0.05$ (Shapiro–Wilk test). Figure 2 is a scatter plot of the LGAs, with prostate cancer incidence and solar radiation as the axes. A line of best fit was derived using least-squares regression. The coefficient of determination (r^2) was 0.294 (95% CI 0.120, 0.468) and the Pearson correlation coefficient (r) was –0.542, with a two-tailed $P < 0.001$.

FIG. 2. Age-standardized prostate cancer incidence vs mean daily solar radiation.



DISCUSSION

Ultraviolet radiation in natural sunlight is a potent catalyst for conversion of 7-dehydrocholesterol to vitamin D. As a result, solar exposure is the chief determinant of serum vitamin D levels [5]. The protective effect of vitamin D in prostate cancer was first postulated more than 20 years ago and was based on the observation that prostate cancer mortality was greater in populations under-exposed to ultraviolet radiation [2,3]. This has been supported by evidence of the inhibitory effect of vitamin D on prostate cancer cells *in vitro* [6–9] and a corresponding clinical effect *in vivo* [10–12].

However, epidemiological studies of vitamin D levels in men with prostate cancer have generated apparently contradictory results. Four case–control studies, conducted in Nordic and North American populations and analysing pre-diagnostic banked serum, have demonstrated a higher risk of prostate cancer in men deficient in 1,25-dihydroxyvitamin D or its pro-hormone 25-hydroxyvitamin D [13–16]. In nine other studies with broadly similar designs, and examining populations from Europe, Hawaii or North America, no correlation was seen [17–25].

These contradictory findings force us to re-evaluate the original evidence for an association between sunlight and prostate cancer. Schwartz and Hulka [2] were the first to observe that prostate cancer mortality was inversely related to ultraviolet radiation in the USA, in an ecological study at the state level ($n = 48$). Hanchette and Schwartz [3] then confirmed this at the level of the county ($n = 3073$), using indices of ultraviolet radiation calculated from latitude, altitude and measured cloud cover. More recently, the same investigators [26] refined the analysis by examining mortality rates over 45 years, utilizing the ultraviolet index (derived from satellite observations, cloud cover data and atmospheric pressure and temperate forecasts, and available for 55 cities) to interpolate values at the county level, and confirming their original findings.

Grant [27] studied the same population (USA) but at the level of the state economic area ($n = 506$) and using satellite data from the month of July 1992 to estimate ultraviolet B radiation for each area. He concluded that the mortality rate of prostate cancer (as well as that of 12 other cancers) was inversely related to ultraviolet B radiation. More recently, St-Hilaire *et al.* [28] confirmed the negative correlation between short wave radiation and prostate cancer incidence at the county level. Short wave radiation was derived from sun-slope geometry and interpolated diurnal temperature ranges.

In contrast, investigators [29–32] from Staffordshire (UK) conducted case–control studies using a validated questionnaire to ascertain the magnitude of ultraviolet radiation exposure of individual men with prostate cancer or benign prostatic hypertrophy (controls). Parameters that were associated with decreased prostate cancer incidence were longer cumulative exposure, more frequent sunbathing, childhood sunburning and regular holidays in hot countries. The case–control design has also been used by John *et al.* [33] in a US population based study which identified residence in southern states as well as birth in states with high solar radiation as risk factors for prostate cancer.

The current study has found an inverse correlation between solar radiation and prostate cancer incidence in Australia. This corroborates findings from the aforementioned studies of essentially two populations: men from across the USA [2,3,26–28,33] and a select group of men in Staffordshire, UK [29–32]. Our study population represents the third group to exhibit this correlation. Significantly, the demographics and climate of Australia differ markedly from those of previous studies.

Our methodology is noteworthy in two regards. First, we have benefited from the availability of direct measurements of solar radiation. Mean daily solar radiation for each location was calculated by the Bureau of Meteorology using hourly visible radiation measured by a geostationary meteorological satellite [34]. The accuracy of these calculated values has been confirmed by comparisons with readings from conventional ground instruments (pyranometers) [35]. In order to reflect long-term solar radiation, the daily solar radiation was integrated over a 21-year period from 1990 to 2010. We posit that a direct measurement of solar radiation over a long duration is more accurate than interpolated values, measurements over short durations or indirect surrogate measures such as latitude, cloud cover, skin types and recalled behaviours.

Second, we have chosen the LGA as the unit of comparison. The advantages are (1) it is large enough to minimize sampling error (the median population is approximately 12 000), (2) it is compact meaning that solar radiation is uniform within its boundaries (the median land area is 5669 km^2) and (3) urban LGAs can be excluded from analysis. This exclusion is important as city dwellers spend a greater portion of their days indoors and hence shaded from the sun [36]. Meteorologically measured solar radiation in these locations would not reflect individuals' exposures. Moreover, urban environments attenuate solar radiation significantly, such that even if city dwellers were outdoors their exposure would be substantially less than that measured due to the 'urban canyon' effect. An *in vitro* model predicts a greater than 75% reduction in vitamin D synthesized [37].

There are weaknesses evident in this study. As an ecological study it is vulnerable to the fallacious reasoning that, if populations receiving less solar radiation tend to have higher incidences of prostate cancer, then individual men who receive less solar radiation have a higher risk of prostate cancer. Correlations observed for groups are not necessarily true for individuals [38].

Ecological studies also suffer from systematic bias introduced by confounding. The population distribution in Australia is asymmetric, with most of its inhabitants clustered in the more temperate (and less sun-exposed) areas. Denser populated areas have better access to medical care, and life expectancy is longer. As prostate cancer is the quintessential disease of the elderly, these areas will have higher crude (non-age standardized) rates of prostate cancer. Moreover, intense PSA-based screening in urban populations [39,40] will result in more diagnoses of prostate cancer. We have attempted to correct for these two confounders by age standardization and by excluding from comparison areas that are designated 'major cities' or 'inner regional'.

Other known risk factors for prostate cancer are family history and race (higher in African Americans and lower in Asians [41] and indigenous Australians [42]). Familial prostate cancer is estimated to account for 10–20% of all cases [43], but there is no evidence to suggest an uneven geographical distribution of prostate cancer families. Similarly, disproportionate representation of indigenous Australians in LGAs that receive more solar radiation would certainly bias the findings in the direction observed. However, in the 57 (of 70) LGAs for which the Bureau had data, the indigenous population represented only 6.9% of the population (statistics on other ethnicities are not recorded by the Bureau). It is not likely that excluding indigenous Australians from the analysis would have changed the findings.

We acknowledge that the ideal investigation to establish an association between solar radiation and prostate cancer would be a prospective controlled cohort study of individuals. Within the limitations of its design, this analysis of a previously unstudied population adds to the existing body of evidence in support of a protective effect of solar radiation in prostate cancer. We hope this will serve as impetus to continue research into the role of vitamin D as the most likely responsible agent of this effect.

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CONFLICT OF INTEREST

None declared.

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Abbreviations: **LGA**, local government area; **SLA**, statistical local area.