Research Article

Association between Latitude and Breast Cancer Incidence in Mainland Australian Women

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Aim. To investigate whether breast cancer incidence increases with increasing latitude in mainland Australian women. **Methods.** A cross-sectional study of female breast cancer and cutaneous melanoma incidence 2002–2006 by 5-year age group and local government area. Latitude, Accessibility/Remoteness Index of Australia (ARIA), and Index of Relative Socioeconomic Disadvantage (IRSD) were assigned to local government areas. Latitude was grouped into bands ($\leq 27^\circ\text{S}$; $>27\text{--}30^\circ\text{S}$; $>30\text{--}33^\circ\text{S}$; $>33\text{--}36^\circ\text{S}$, and $>36^\circ\text{S}$), and IRSD was divided into quintiles and ARIA into four categories. Breast cancer rates were age standardized using the direct method. The joint effects of latitude, age, IRSD, and ARIA on incidence of breast cancer and cutaneous melanoma were assessed using multiple logistic regressions. **Results.** At latitudes south of 30°S , rates of breast cancer were over double that north of 27°S (76.4 versus 160.2–176.5). Age-adjusted odds ratios of breast cancer were increased in all latitudes south of 30°S compared with north of 27°S within each IRSD and ARIA category (all $P < 0.001$). After adjusting for age, IRSD, and ARIA, the odds ratio of breast cancer south of 30°S was 1.92 (95% CI 1.84–2.09; $P < 0.001$), whereas cutaneous melanoma was 0.65 (95% CI 0.61–0.68; $P < 0.001$) times north of 30°S . **Discussion.** Increasing latitude is positively associated with breast cancer and negatively associated with cutaneous melanoma incidence. These findings support suggestions that increased risk of breast cancer might be explained by lower ultraviolet radiation-induced vitamin D synthesis.

1. Introduction

Ecologic studies show that the incidence and mortality of breast cancer increase from the equator (latitude 0°) as latitude increases towards the earth's poles (90°) [1–3]. Similarly, the rates of breast cancer have been shown to be inversely associated with the level of ultraviolet (UV) radiation from sunlight [4–9].

For most individuals, solar UV radiation in the B spectrum is the primary source of vitamin D [10]. Exposure of the skin to UV radiation between the wavelengths of 290 and 330 nm causes photolysis of 7-dehydrocholesterol to form previtamin D_3 . In a heat-induced process, previtamin D_3 is then converted to vitamin D_3 , which is subsequently hydroxylated in the liver and the kidneys or in local tissue

such as breast, to form the active form of the vitamin, 25-hydroxyvitamin D_3 [10].

Geographic latitude is an important determinant of cutaneous vitamin D synthesis, as it influences the amount of UV radiation reaching the skin [11]. An increase in latitude causes the solar zenith angle, the angle between the earth's local vertical and the position of the sun at a given moment, to increase. At the equator, the solar zenith angle is at its smallest. The solar zenith angle increases as latitude increases towards the poles, thereby increasing the path that sunlight is required to travel through the atmosphere towards the earth. This results in increased UV scatter and absorption, subsequently reducing the amount of UV radiation that reaches the earth's surface. It follows that the higher UV radiation levels at lower latitudes (closer to the equator)

increase the potential for vitamin D synthesis, compared with the lower UV radiation levels occurring at higher latitudes (further away from the equator), where the potential for vitamin D synthesis is reduced. Although there is little data comparing vitamin D levels according to location in Australia, findings from a 2012 study were consistent with this hypothesis, which showed that vitamin D deficiency is more common in individuals residing south of 30°S in comparison to those closer to the equator [12]. Similarly, we have previously shown that in the winter months when the solar zenith angle is greater there is a higher prevalence of vitamin D deficiency [13].

The first suggestion that sunlight exposure may lower the risk of cancer was first made by Peller and Stephenson in 1937 [14], after which the observation was made that there is an inverse association between latitude and skin cancer mortality [15]. In 1980, C. F. Garland and F. C. Garland [16] linked low vitamin D status to a higher risk of colon cancer, based on the theory that vitamin D is formed in the skin through solar ultraviolet B (UVB) radiation exposure. A similar association between vitamin D status and breast cancer has since been proposed [4]. It has been demonstrated that geographical incidence and mortality rates of numerous cancers, including breast cancer, are inversely associated with regional UVB radiation exposure [4–9].

The link between the early ecological data showing an inverse relationship between UV radiation exposure and cancer to vitamin D status was the finding that many cell types, including breast cells, contain vitamin D receptors [17]. The theory that vitamin D may be the factor involved in cancer protection is supported by cell studies showing that vitamin D induces differentiation and has antiproliferative and proapoptotic effects [18]. The theory is also supported by animal studies showing that vitamin D reduces tumor growth and size [19, 20]. Additionally, high serum 25OHD has been associated with a reduced risk of breast cancer in some [21–23] but not all [24, 25] studies.

It is well established that exposure to solar UV radiation causes malignant cutaneous melanoma [26]. This seemingly contradictory finding has been explained by the hypothesis that UV exposure to external cells has a mutagenic effect whereas there is a protective effect of UV-induced vitamin D production on internal cells [27]. As such, cutaneous melanoma incidence could be used as a marker of UV radiation exposure to strengthen the assumption that latitude is inversely associated with UV radiation. Furthermore, the average UV radiation striking the ground has been used as a crude surrogate of vitamin D in epidemiological studies. Although this does not take into account individual behaviors related to sunlight exposure, it has been reported to be a useful marker for vitamin D synthesis [28].

The association between latitude and breast cancer has not been examined in Australia. However, there are reports of an inverse relationship between latitude and malignant cutaneous melanoma and noncutaneous melanoma skin cancer [29, 30], with the highest rates of cutaneous melanoma being observed at lower latitudes. That UV radiation exposure is known to cause malignant cutaneous melanoma [31], and it follows that Australian regions with higher rates of cutaneous

melanoma are associated with higher UV radiation levels compared to those with lower rates of cutaneous melanoma.

The aim of this study was to examine the association between latitude and incidence of breast cancer and cutaneous melanoma in mainland Australian women.

2. Methods

2.1. Breast Cancer and Cutaneous Melanoma Incidence Data. Australia is divided into six states and two territories: New South Wales, Victoria, Queensland, South Australia, Western Australia, Tasmania, the Australian Capital Territory, and Northern Territory (Figure 1). This study was approved by state or territory human research ethics committees (New South Wales Population and Health Services Research Ethics Committee, Queensland Health Human Research Ethics Committee, and Human Research Ethics Committee of Northern Territory Department of Health and Menzies School of Health Research) and/or by written approval from the manager or data custodian of Western Australian, Victorian, and South Australian cancer registries.

Female breast cancer (ICD-10 C50) and cutaneous melanoma (ICD-10 C43.9) counts by 5-year age group (15–19 years, 20–24 years, etc., to 85–89 years), for each local government area between 2002 and 2006, were obtained for each state or territory, with the exception of Tasmania for which complete data were not available.

2.2. Population. The Australian 2006 female population, by local government area and 5-year age group, was obtained from the Australian Bureau of Statistics CDATA online database [32]. This was used to calculate age-standardized incidence rates, using the direct method, for breast cancer and cutaneous melanoma. The Australian resident population was used for age standardization.

2.3. Latitude. In latitude, Australia extends from 12°S to 43°S (Figure 1). The latitude of each local government area was obtained by determining the postcode (zip code) of the most populated town in that local government area or, where all towns were highly populated, the most central town (in latitude) was used.

Latitudes according to postcode were obtained from <http://www.corra.com.au/australian-postcode-location-data/>. When there was no postcode available, Google Earth (<http://www.google.com/earth/index.html>) was used to determine the latitude of the most populated town in that local government area. Latitude was grouped into five bands. Due to the plateau effect in age-standardized breast cancer incidence observed at latitudes south of 30°S, latitude was dichotomized to north or south of 30°S in the multiple logistic regression models.

2.4. Index of Relative Socioeconomic Disadvantage. The measure of socioeconomic status and social disadvantage, as discussed in this report, is the Index of Relative Socioeconomic Disadvantage (IRSD). We obtained IRSDs by postcode from the Australian Bureau of Statistics [33]. We used the

FIGURE 1: Map of Australia showing risk of breast cancer at latitudes south of 30°S versus north of 30°S.

IRSD because it has been shown to be a determinant of vitamin D status [34]. The IRSD focuses on disadvantage and is produced from the Australian national census by the Australian Bureau of Statistics for each postcode using 17 indicators based on education, income, and occupation [35]. We chose to group the IRSD into quintiles for the purpose of our analysis. The lowest IRSD quintile is the most disadvantaged, and the highest quintile is the least disadvantaged. We assigned each local government area an IRSD quintile according to the postcode of the town for which latitude was obtained.

2.5. Accessibility/Remoteness Index of Australia. People living in less accessible regions of Australia are often disadvantaged in their access to health care services. The Accessibility/Remoteness Index of Australia (ARIA) measures remoteness from major metropolitan areas. ARIA values are calculated according to remoteness and based on physical road distance to the nearest urban centre: major cities (ARIA value: 0–0.2), inner regional areas (0.21–2.4), outer regional areas (2.41–5.92), remote areas (5.93–10.53), and very remote areas (>10.54). ARIA values were obtained from Australian Bureau of Statistics geographical divisions by postcode [36]. An ARIA was assigned to each local government area according to the postcode of the town for which latitude was obtained. Due to low population numbers and cancer counts, the outer regional, remote, and very remote categories were

pooled when assessing the joint effects of several risk factors, using multiple logistic regressions.

2.6. Data Deidentification and Aggregation. Following matching of breast cancer and cutaneous melanoma incidence, population, latitude, postcode, IRSD, and ARIA to each local government area, local government areas were deidentified by removing names and postcodes.

2.7. Statistical Methods and Analysis. The statistical software SPSS version 20.0 (Chicago, IL) was used to analyze the data. Two-tailed tests with a significance level of 5% were used throughout. Breast cancer incidence rates were age standardized using the direct method, with the mainland Australian female 2006 population as the reference [32].

The age-adjusted odds ratios of breast cancer and associated 95% confidence intervals (95% CI) by latitude band relative to the most northerly band ($\leq 27^\circ$ S) were calculated within each quintile of IRSD and within each ARIA category. Multiple logistic regression was used to assess the joint effects of latitude band, age group, IRSD, and ARIA category on the incidence of breast cancer and separately for cutaneous melanoma. In order to model the joint effects of several category variables, it was necessary to collapse some of the sparse categories to ensure stable estimates. Specifically, ARIA values were collapsed into three categories (major city, inner regional, and outer regional and beyond), and latitude

was collapsed into two categories due to the plateau in age-standardized breast cancer incidence observed south of 30°S.

3. Results

Table 1 shows the distribution of breast cancer incidence and population at risk for each latitude band according to decade of age, IRSD quintile, and ARIA category. The age-specific incidence of breast cancer generally increased as latitude and age group increased. The age-standardized incidence of breast cancer was 76.4 at latitudes north of 27°S, whereas at latitudes south of 30°S there was a relative plateau with age-standardized rates approximately doubling to between 160.2 and 176.5. A similar plateau effect was observed within each IRSD quintile and ARIA category, with the age-specific incidences at latitudes south of 30°S being approximately twice those at latitudes north of 27°S. The largest proportion of the population at risk tended to reside between latitudes 27°S and 36°S, be less disadvantaged, and reside in a major city (Table 1).

Within each IRSD quintile and ARIA category, the age-adjusted odds ratios of breast cancer were significantly increased in each latitude band south of 30°S compared with north of 27°S ($P < 0.001$, Table 2). The age-adjusted odds ratio of breast cancer in the most disadvantaged individuals at latitudes between 27°S and 30°S was almost double the odds ratio at latitudes north of 27°S (OR 1.9; 95% CI 1.2–3.0). The corresponding odds ratio in the second and third IRSD quintiles ranged from 1.2 to 1.5 and failed to reach significance in the two least disadvantaged quintiles. A plateau effect was seen for latitudes south of 30°S, in which the age-adjusted odds ratio was approximately double that of the reference category (north of 27°S). Similar results were observed within the ARIA categories. At latitudes between 27°S and 30°S, the age-adjusted odds ratios of breast cancer were 1.6 to 1.7 ($P < 0.001$) within the inner and outer regional categories, respectively, but failed to reach significance for the other ARIA categories.

In the multiple logistic regression model, the effect of IRSD and ARIA seen in the age-adjusted analysis was neutralized, in that there were no significant differences between categories within each variable. However, the increased risk of breast cancer remained significant after adjusting for all other variables, in that the OR of breast cancer at latitudes south of 30°S was almost double that for latitudes north of 30°S (odds ratio: 1.92; 95% CI: 1.84–2.01; $P < 0.001$) (Table 3, Figure 1). As expected, the model for cutaneous melanoma also confirmed that after adjusting for age, IRSD, and ARIA, the odds ratio for cutaneous melanoma decreased for latitudes south of 30°S compared to latitudes north of 30°S. This supports the conjecture that latitude is a marker of sunlight exposure, and as latitude increases, the potential for vitamin D synthesis decreases.

4. Discussion

A latitudinal gradient has been demonstrated in Australia for several diseases, including multiple sclerosis [37] and diabetes

[38]. This is the first study to show an association between latitude and breast cancer incidence in Australia.

Latitude is an important determinant of vitamin D status [11]. We have shown elsewhere that the potential for vitamin D synthesis is higher at more northerly locations, compared to more southerly locations in Australia [39]. Additionally, it has been shown that while vitamin D synthesis can occur throughout the year towards the equator (0° latitude), at a latitude of 40°S (slightly south of Melbourne, VIC (Figure 1)) there is no vitamin D-effective radiation during the winter months [11, 40]. It is unlikely that dietary intake of vitamin D accounts for a substantial difference in vitamin D status in Australians as there are few foods that contain significant amounts of vitamin D. Estimates suggest that Australians consume approximately 80–120 IU vitamin D from foods each day. Additionally, in Australia the only foods that are mandatorily fortified are edible spreads such as table margarines, which contain approximately 40 IU vitamin D per 10 g serve. There is no data regarding variation in vitamin D intake by location in which individuals reside, and this is worthy of further investigation. Furthermore, we are unable to explain the plateau effect in age-standardized breast cancer incidence observed at latitudes south of 30°S, and it may be that there is insufficient vitamin D synthesis beyond this latitude to have a protective effect.

Our results are in accordance with international studies that show a positive association between risk of, or mortality from, breast cancer and latitude [2, 4, 41] or measures of inadequate UV radiation [9, 41, 42]. We found that at latitudes south of 30°S, a line that runs parallel to the equator from north of Perth on the west coast of Australia to approximately midway between Sydney and Brisbane on the east coast of Australia (Figure 1), there was almost double the risk of breast cancer compared with latitudes north of 30°S. Similarly, a study of 9778 USA Caucasian women aged 20–79 years showed that after adjusting for recognized risk and prognostic factors, mortality rates (per 100 000 individuals) among women aged 50–79 years in the west, Midwest, and Northeast were 1.13 (95% CI, 1.04–1.23), 1.08 (95% CI, 1.01–1.16), and 1.13 (95% CI, 1.04 to 1.23), respectively, compared to women in the south of the country [2]. Garland et al. also showed a 1.8-fold range for breast cancer mortality rates in the USA from the south and southwest to the northeast [4], results that are strikingly similar to ours. Another study, which investigated UVB irradiance in 107 countries, found that age-standardized incidence was substantially higher at latitudes furthest from the equator ($R^2 = 0.43$; $P < 0.0001$) [9]. Similarly, a study that looked at sunlight levels found a significant negative association between breast cancer incidence rates and sunlight levels ($R = -0.75$; $P = 0.001$) [42].

Our results are in accordance with previous investigations that show higher rates of breast cancer for women from higher socioeconomic status backgrounds (Tables 1–3) [43]. In age-adjusted analysis, we found that women from all IRSD quintiles had at least double the incidence (Table 1) and risk (Table 2) for breast cancer at latitudes south of 30°S compared to north of 30°S (Tables 1 and 2). There appeared to be an increasing incidence associated with quintile of

TABLE 1: Age-specific annual incidence rates of breast cancer and female population at risk by latitude band; age-standardized annual incidence rates overall and according to IRSD and ARIA.

Age group (years)	Incidence per 100 000					Total population at risk				
	≤27	>27–30	>30–33	>33–36	>36	≤27	>27–30	>30–33	>33–36	>36
20–29	1.8	1.9	3.7	5.7	6.0	199359	414435	153062	466416	324622
30–39	21.2	24.4	43.6	46.9	45.1	222995	426499	173618	518699	367956
40–49	79.7	86.9	163.2	153.5	153.4	236756	417843	190334	516382	363328
50–59	114.5	139.7	282.1	261.2	246.0	205370	366540	169079	443360	313046
60–69	149.0	181.7	350.3	336.3	302.0	140420	241453	114089	298706	211478
70–79	142.9	185.5	315.9	301.2	301.8	84679	152522	81287	221913	157668
80–89	143.8	189.8	385.1	346.5	344.5	45492	95725	47359	140679	97308
ASR ¹	76.4	92.5	176.5	167.2	160.2	1135071	2115017	928828	2606155	1835406
IRSD quintile ²										
1	75.0	72.5	161.5	155.4	142.7	62160	19907	42684	179403	51863
2	76.2	73.6	169.2	163.2	144.1	220759	115111	108646	324572	155188
3	69.3	67.1	180.7	174.5	159.4	148656	442881	201448	553689	388791
4	77.7	75.1	182.8	176.4	145.3	536473	509836	287409	471260	409174
5	81.6	78.6	197.0	190.4	175.1	165400	1027282	288641	1077231	830390
ARIA ³										
Major city	80.0	84.5	187.2	168.9	162.4	218908	1774388	651472	2166573	1425572
Inner regional	71.0	108.2	179.8	163.6	156.3	375521	256961	193991	285288	349660
Outer regional	76.9	124.7	166.7	163.4	165.4	434993	75341	70788	136897	56678
Remote/very remote	87.2	92.9	176.3	187.2	256.8	105214	8327	12577	17397	3496

¹ ASR: age-standardized rate. ² IRSD: Index of Relative Socioeconomic Disadvantage. ³ ARIA: Accessibility/Remoteness Index of Australia.

TABLE 2: Age-adjusted odds ratio of breast cancer relative to women at latitude $\leq 27^\circ\text{S}$ within each IRSD and ARIA category.

	Latitude ($^\circ\text{S}$)									
	$\leq 27^1$		27–30		>30–33		>33–36		>36	
	OR	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
IRSD ² (quintiles)										
1	1	—	1.9 (1.2–3.0)	0.007	2.1 (1.4–3.0)	<0.001	2.0 (1.5–2.8)	0.001	1.9 (1.3–2.7)	<0.001
2	1	—	1.2 (1.0–1.5)	0.103	2.2 (1.8–2.6)	<0.001	2.1 (1.7–2.4)	<0.001	1.9 (1.6–2.3)	<0.001
3	1	—	1.5 (1.2–1.8)	<0.001	2.5 (2.0–3.1)	<0.001	2.3 (1.9–2.8)	<0.001	2.3 (1.9–2.8)	<0.001
4	1	—	1.1 (1.0–1.3)	0.083	2.3 (2.0–2.6)	<0.001	2.1 (1.8–2.4)	<0.001	1.9 (1.6–2.1)	<0.001
5	1	—	1.1 (0.9–1.3)	0.328	2.3 (1.9–2.8)	<0.001	2.2 (1.9–2.6)	<0.001	2.1 (1.8–2.6)	<0.001
ARIA ³										
Major city	1	—	1.1 (0.9–1.3)	0.258	2.2 (1.9–2.6)	<0.001	2.1 (1.8–2.4)	<0.001	2.0 (1.7–2.3)	<0.001
Inner regional	1	—	1.6 (1.3–1.9)	<0.001	2.4 (2.1–2.8)	<0.001	2.3 (2.0–2.7)	<0.001	2.2 (1.9–2.5)	<0.001
Outer regional	1	—	1.7 (1.3–2.1)	<0.001	2.1 (1.7–2.6)	<0.001	2.1 (1.8–2.5)	<0.001	2.1 (1.7–2.6)	<0.001
Remote/very remote	1	—	1.1 (0.5–2.3)	0.823	2.0 (1.2–3.2)	0.007	2.2 (1.4–3.3)	<0.001	2.9 (1.4–6.0)	0.006

OR: odds ratio. CI: confidence interval. ¹Reference category. ²IRSD: Index of Relative Socioeconomic Disadvantage. ³ARIA: Accessibility/Remoteness Index of Australia. **P** = significant at 95% CI.

TABLE 3: Multiple logistic regression models showing odds ratio of breast cancer and of cutaneous melanoma relative to reference category after adjusting for all other variables in the model.

	Breast cancer		Cutaneous melanoma	
	OR (95% CI)	P	OR (95% CI)	P
Age group (years)				
20–29	0.02 (0.02–0.03)	<0.001	0.28 (0.25–0.32)	<0.001
30–39	0.18 (0.16–0.19)	<0.001	0.48 (0.43–0.53)	<0.001
40–49	0.61 (0.58–0.64)	<0.001	0.70 (0.64–0.77)	<0.001
50–59 ¹	1.00		1.00	
60–69	1.27 (1.21–1.34)	<0.001	1.35 (1.24–1.47)	<0.001
70–79	1.20 (1.14–1.28)	<0.001	1.81 (1.66–1.98)	<0.001
80–89	1.36 (1.27–1.45)	<0.001	1.74 (1.57–1.93)	<0.001
IRSD ² (quintiles)				
1	1.00		1.00	
2	0.99 (0.89–1.10)	0.824	1.16 (0.98–1.38)	0.087
3	1.07 (0.97–1.18)	0.158	1.29 (1.10–1.52)	0.002
4	1.03 (0.94–1.14)	0.521	1.28 (1.09–1.51)	0.003
5	1.16 (1.05–1.27)	0.003	1.39 (1.18–1.63)	<0.001
ARIA ³				
Major city ¹	1.00		1.00	
Inner regional	1.03 (0.98–1.08)	0.289	1.30 (1.20–1.39)	<0.001
Outer regional and beyond	1.05 (0.98–1.13)	0.136	1.16 (1.06–1.28)	0.001
Latitude				
$\leq 30^\circ\text{S}$ ¹	1.00		1.00	
$>30^\circ\text{S}$	1.92 (1.84–2.01)	<0.001	0.65 (0.61–0.68)	<0.001

OR: odds ratio. CI: confidence interval. ¹Reference category. ²IRSD: Index of Relative Socioeconomic Disadvantage. ³ARIA: Accessibility/Remoteness Index of Australia. **P** = significant at 95% CI.

socioeconomic disadvantage for each latitude band (Table 1) although no effect after adjusting for age was seen (Table 2). However, after adjusting for age group, ARIA, and latitude, only those in the highest quintile had a significantly higher risk of breast cancer (OR: 1.16; 95% CI: 1.05–1.27; $P = 0.003$) (Table 3). It is possible that factors that we have not been able to control for, such as diet, physical activity, body mass

index, parity, and hormone use, for example, explain the association we have seen as these factors are known to affect breast cancer risk [44–46]. There is little data available on such factors according to latitude or location of residence of women in Australia. Additionally, variations in screening rates across Australia may account for the association we have observed. For instance, women who reside in remote areas

may not have the same access to screening programs as those in major cities. Our ability to control for remoteness may somewhat control for such variation; however it is possible that residual confounding occurs. These factors are worthy of further investigation.

Findings on the relationship between breast cancer and remoteness have been inconsistent. In age-adjusted analysis, we found that women from all remoteness quintiles had a similar risk of 2 or above for breast cancer at latitudes south of 30°S, although there was no effect of major city, as shown by similar incidence and risk among categories of remoteness (Tables 1 and 2). Similarly, after adjusting for age, socioeconomic disadvantage, and latitude, we found a similar risk of breast cancer, irrespective of whether subjects resided in a major city, inner regional area, or outer regional area and beyond (Table 3). These findings are in accordance with a study by the English, [47] which showed no statistically significant differences in breast cancer risk by remoteness. Conversely, reports from the Australian Institute of Health and Welfare show that those residing in major cities or inner regional areas had significantly higher 5-year relative survival (both 88%) than those from outer regional areas (85%) [43]. These opposing findings in that report may be caused by a confounding effect of latitude, which was not adjusted for in the Australian Institute of Health and Welfare study.

A weakness of our study is that we were unable to take into account individual serum 25(OH)D concentrations or the factors that affect vitamin D concentration, such as sunlight exposure, obesity, age, and skin pigmentation [48]. The strengths of our study include our ability to control for age, socioeconomic disadvantage, and distance from a major city, all of which have been shown to be important determinants of vitamin D status [34].

The association of cutaneous melanoma with increasing UV radiation exposure and lower latitudes at closer proximity to the equator has been well documented internationally [49, 50] and in Australia, [29, 30] and is in accordance with our finding that the risk of cutaneous melanoma is lower at latitudes south of 30°S compared with north of 30°S. However, as has been suggested [40], it is possible that latitude alone is not a good indicator of vitamin D status since other factors such as cloud cover and ozone affect vitamin D synthesis. Nevertheless, our finding that the risk of cutaneous melanoma decreases as latitude increases supports the notion that UV radiation levels decrease with increasing latitude, and therefore the potential for vitamin D synthesis also decreases as latitude increases.

In summary our data show that living at higher latitudes towards the south of Australia, in particular at more than 30°S, is associated with a significantly increased risk of breast cancer compared to latitudes less than 30°S. Further, in multivariate analysis, we showed that the major city effect did not make a difference, but factors such as high socioeconomic status were independently associated with an increased risk of breast cancer.

Our data add to previous ecological evidence suggesting a relationship between latitude and breast cancer incidence, although confounding effects from other factors cannot be totally excluded. Our findings should be interpreted with

caution; they cannot imply causation of breast cancer by low vitamin D as the link between latitude, UV radiation, and vitamin D remains speculative. Further studies involving direct measurement of serum vitamin D are needed to directly test this hypothesis.

Abbreviations

ARIA: Accessibility/Remoteness Index of Australia
IRSD: Index of Relative Socioeconomic Disadvantage.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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