Geographical patterns in melanoma incidence across Australia:
can thickness differentials reveal the key drivers?

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Background: Australia has the highest rates of melanoma incidence in the world, but these vary across the country. It is unclear what drives the observed variation, but one potential cause could be differences in early detection. To investigate this, our study sought to determine the small-area melanoma patterns by thickness.

Methods: Bayesian hierarchical models were applied to all primary invasive melanoma cases diagnosed during 2010–2014 in Australian residents aged 15+ years to model rates across 2,148 small areas based on the Australian Statistical Geography Standard framework. A multivariate spatial model which included all 4 thickness categories [thin (≤1 mm), intermediate (>1–2 mm), thick (>2 mm) and missing] was used to examine geographic patterns by thickness and correlation between thicknesses.

Results: The majority (62%) of melanomas diagnosed were thin melanomas. The highest rates of melanoma diagnosis were across south-east Queensland and northern NSW, and these areas were consistently above the national average for each thickness category. In contrast, much of northern, central and western Australia tended to be below the national average diagnosis rate, and these geographical patterns were also largely consistent across all thickness categories.

Conclusions: The general consistency of geographical patterns of melanoma incidence across thickness categories suggests that the overall patterns are more likely to be due to the underlying population risk profile than differences in diagnostic practices.

Keywords: Melanoma; Bayesian; spatial geography; diagnosis; multivariate

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Introduction

While Australia has the highest incidence rates of melanoma in the world (1), there is substantial variation in these rates across the country (2). The Australian Cancer Atlas (3) divided the country into 2,148 small, populated geographical areas and highlighted the high concentration of areas in south-east Queensland and northern New South Wales (NSW) with a melanoma incidence rate higher than the Australian average. In contrast, the melanoma incidence rate in most areas in central, north Western and southern Australia was substantially lower than the Australian average.

The factors that increase the risk of developing melanoma are well established, including higher age, the presence of more melanocytic naevi, fair skin and blonde/red hair, sun exposure, previous sunburns and numbers of solar keratoses (4). While these will vary between geographical regions, other potential factors that could explain the observed geographical variation in melanoma incidence include higher exposure to solar radiation—the strongest known environmental risk factor for melanoma, high public awareness of skin cancer and better access to diagnostic services resulting in higher rates of melanoma detection (5). Given that higher prevalence of clinical whole body skin examination is associated with higher incidence of thinner melanomas and lower incidence of thicker melanomas (6), examining how the geographical patterns vary by thickness may provide indirect evidence of the diagnostic practices across the country, and greater insights into the potential drivers of the observed geographical variation in melanoma incidence.

By using information about melanoma thickness, this study aims to describe how the small-area patterns of melanoma incidence vary across Australia overall and by broad thickness categories, and how the correlation between thinner and thicker melanomas varies across Australia.

Methods

Data

Information on all diagnoses of first primary invasive melanoma (ICD-10 C43) during 2010 to 2014 was obtained from the Australian Cancer Database (ACD), with appropriate ethics and legislative approvals (see Table S1). Cancer is a notifiable disease in Australia and the ACD contains information on all cancers registered nationally, with the exception of keratinocyte cancers.

Information on melanoma thickness is routinely collected from pathology reports by all Australian population cancer registries. The definitions of thin (≤1 mm), intermediate (>1–2 mm) and thick (>2 mm) have been previously used (7), and are used in the current edition of the American Joint Committee on Cancer melanoma staging, representing T1, T2 and T3-T4, respectively (8).

Location of the patient’s residence was supplied as a Statistical Area 2 (SA2) using the 2011 Australian Statistical Geography Standard (ASGS) (9). This is an administrative region designed to represent communities that interact together, and is the smallest area with readily available annual population estimates. Out of a possible 2,196 physical SA2s that cover Australia without gap or overlap, areas that had no resident population (n=28), nominal resident population (of <5 people on average per year, n=17) or were a remote island >500 km from the Australian mainland (n=3) were excluded, meaning estimates were calculated for 2,148 SA2s. The median population among included SA2s in 2014 was 9,211 (range: 4–54,773). The land area of SA2s also varied substantially (range: 0.8 to 519,520 km²). The SA2s can be aggregated to form larger regions, and the 15 Greater Capital City Statistical Areas (9), are also used in this paper.

Population estimates for 2010 to 2014 by 5-year age groups (0–4,…, 85+), sex (male, female) and 2011 ASGS boundaries for SA2s were obtained from the Australian Bureau of Statistics (10).

Statistical analyses

All data were stored on and analyses performed within the SURE (Secure Unified Research Environment) facility, maintained by the Sax Institute. Initial data manipulation and calculation of the input data for the spatial models were conducted in Stata version 14.1 (StataCorp, College Station, Texas, USA).

Bayesian hierarchical models were used to examine small-area variation. These models have been demonstrated to perform well for disease mapping (11,12), but they require specific assumptions on the form of smoothing. This is determined by the choice of the prior distribution on the spatial random effect term. Based on a detailed assessment of options (13), the Leroux conditional autoregressive (CAR) prior (14) was adopted. This prior smooths across adjacent areas and is robust even when data are sparse.

Two forms of Bayesian hierarchical models were used: (I) a univariate model run on melanoma combined and...
(II) a multivariate model including all thickness categories to directly examine patterns by thickness and correlations between thickness. All statistical models were run using CARBayes v5.0 package (15) in R software v3.4.1 (16). This uses Markov chain Monte Carlo (MCMC) for computation. For each model 150,000 iterations were sampled, with the initial 50,000 discarded as burn-in and every 10th iteration kept, resulting in a total of 10,000 monitored samples. MCMC convergence was assessed using the Geweke diagnostic (17) for all areas (with P<0.01 considered indicative of lack of convergence) and visualisation of a subsample of trace and density plots.

Univariate model

The data comprise counts of a relatively rare disease, promoting the adoption of a Poisson likelihood, i.e.,

\[ Y_i \sim \text{Poisson}(E_i e^{x_i}) \text{ for } i = 1, \ldots, 2148 \text{ areas} \]  

where \( Y_i \) is the observed number of melanomas diagnosed in the \( i^{th} \) area, and the expected counts (\( E_i \)) in each area are calculated as the age- and sex-specific rates for Australia multiplied by the age- and sex-specific populations in each area, then summed together.

The modelled log standardised incidence ratio (SIR, \( \mu_i \)) comprises two components: an intercept (\( \alpha \)), and an area-specific random effect (\( \phi_i \)), as follows:

\[ \mu_i = \alpha + \phi_i. \]  

The spatial random effect (\( \phi_i \)) is described by a Leroux CAR prior (14). This has the advantage of having just one random effect term for each area, but still allowing smoothing to occur over \( j \) nearby areas (with spatial dependence weight \( \rho \)) and also towards the Australian average (with unstructured dependence weight \( 1-\rho \)). The parameter \( \rho \) can range from 0 (reflecting independence) to 1 (reflects complete spatial dependence), as determined by the data. This is formulated as:

\[ \phi_i | \phi_j \sim \text{Normal} \left( \frac{\rho \sum w_{ij} \phi_j}{\rho \sum w_{ij} + 1 - \rho}, \frac{\sigma^2}{\rho \sum w_{ij} + 1 - \rho} \right) \]  

where \( \rho \sim \text{Uniform}(0,1) \) and \( \sigma^2 \sim \text{InverseGamma}(1,0.01) \). Together, the weights \( w_{ij} \) define the spatial adjacency matrix \( W \). Typically \( w_{ij} \) is binary, with \( w_{ij}=1 \) indicating that areas \( i \) and \( j \) are classified as neighbours, otherwise \( w_{ij}=0 \).

Multivariate model

This model was proposed by Kavanagh and colleagues (18) and is based on that from Gelfand and Vounatsou (19). The key difference from the univariate model above is the use of a multivariate Leroux CAR prior for the random effects \( \phi_k \) for each area \( i \) and melanoma thickness \( k=1,2,3,4 \), representing thin, intermediate, thick and missing. This means that \( \phi_i=(\phi_{1i},\phi_{2i},\phi_{3i},\phi_{4i}) \) denotes the quartet of all thickness levels for the \( i^{th} \) area as follows:

\[ \phi_i | \phi_j \sim \text{Normal} \left( \frac{\rho \sum w_{ij} \phi_j}{\rho \sum w_{ij} + 1 - \rho}, \frac{\Sigma}{\rho \sum w_{ij} + 1 - \rho} \right) \]  

where \( \Sigma \sim \text{InverseWishart} [4, 1] \) and is the 4x4 conditional between-thickness covariance matrix, and other terms are as defined before. Note that \( \rho \) does not vary by melanoma thickness level.

Correlation

The conditional covariance matrix can be transformed into between-thickness correlation by dividing the covariance by the product of the standard deviation of the respective thickness level \( \phi_k \) terms (i.e., \( \sigma_k \) for each \( k \)). Correlation was calculated at each MCMC iteration, and can range between -1 and 1.

The overall correlation may disguise discrepancies in correlation occurring in specific areas. To examine if the correlation between melanoma thickness differed across Australia, categories were defined for each area and melanoma thickness. To include the precision of the estimates in the definition of the categories, the categories were classified based on the posterior probability (PP) of the area-specific SIR being above 1.

PP is defined as:

\[ PP = \frac{1}{M} \sum_{m=1}^{M} \left( \exp \left( \mu_i^{(m)} \right) > 1 \right) \]  

where \( \mu_i^{(m)} \) is the \( m^{th} \) MCMC log SIR estimate for the \( i^{th} \) area.

Richardson et al. (20) provided guidelines around using PPs: an area with a PP >0.8 is likely to have a true SIR above 1; conversely an area with a PP <0.2 is likely to have an SIR below 1, and PPs between 0.2 and 0.8 convey insufficient evidence to make a definitive statement.

The correlation categories were calculated for each pairwise combination of ‘thin’ melanomas and one of the
remaining thickness categories (‘intermediate’, ‘thick’ and ‘missing’). The correlation categories were defined as: ‘Unclear’ (one of the thickness categories has a PP within 0.2 to 0.8); ‘High-high’ (both categories have PPs >0.8); ‘High-low’ (PP >0.8 for thin, PP <0.2 for the other thickness category); ‘Low-high’ (PP <0.2 for thin, PP >0.8 for the other thickness category); and ‘Low-low’ (both categories have PPs <0.2).

**Sensitivity analyses**

Sensitivity analyses were undertaken to compare the small-area estimates obtained using separate univariate Leroux CAR models for each melanoma thickness category with those from the multivariate Leroux CAR model. The estimates were found to be similar (see Figure S1).

In the presence of sparse data, it is possible that the hyperprior distributions on the Leroux CAR prior may exert a large amount of influence on the estimates obtained. To examine this, three different versions of hyperpriors were compared for each model. Due to constraints on the specifications allowed in CARBayes, only inverse-Gamma (shape, rate) or inverse-Wishart distributions were available for univariate and multivariate distributions, respectively. The hyperpriors examined for the Univariate model with \( \phi \sigma^2 \) were set either as: (I) IG(1.0,0.01), the CARBayes default; (II) IG(0.1,0.01); or (III) IG(0.5,0.0005), the latter as used by Johnson (21). For the multivariate model the three hyperpriors compared for \( \Sigma \) were: (I) inverse-Wishart (4, 1) [i.e., the identity matrix, with diagonal of 1 and all other elements of 0]; (II) inverse-Wishart (4, 0.1); or (III) inverse-Wishart (4, 0.01). Differences between models were relatively slight, and final results presented in this paper are from option 1 for both univariate and multivariate models.

**Visualisation**

Maps were created in R v3.5.3 (16), with the mapped SIR in each area being the median estimate of \( e^\mu \) from all MCMC iterations. An SIR of 1 represents the Australian average incidence rate and is shaded as pale yellow. The colour scale used in all maps is a continuous colour scale with specific colours specified at the SIR equivalent values of: dark blue (0.67), medium blue (0.80), medium orange (1.25), and red (1.50). Values below 1 are the inverse of values above 1. The colour gradient was defined as linear on the log (base 2) scale. Due to the large numbers of SA2s in the four most populous Australian cities, these are shown as insets and marked on the Australian map as boxes, representing (clockwise, from north-east) Brisbane (Queensland), Sydney (New South Wales), Melbourne (Victoria) and Perth (Western Australia). Areas considered to have no resident population are charcoal coloured.

Maps and graphs of the correlation categories were generated for each pairwise combination of thin melanomas with intermediate, thick and missing categories. These combinations have a colour scheme of pale grey for ‘unclear’ (no clear pattern), red for ‘high-high’, green (high-low), orange (low-high), and blue (low-low).

Additional graphs were created in Stata (StataCorp, College Station, Texas, USA).

**Results**

In Australia, an average of 12,291 invasive melanomas were diagnosed per year during 2010–2014, and 62% of these were thin melanomas. Intermediate, thick and missing thickness melanomas overall comprised 14%, 16% and 7%, respectively. These proportions differed slightly between large regions, ranging from 71% thin and 11% thick diagnosed in Greater Brisbane to 54% thin and 22% thick in the Rest of the Northern Territory (Figure 1).

The highest rates of melanoma diagnosis across small areas based on modelled results were across south-east Queensland and northern NSW (Figure 2). These areas were also consistently above the national average for each thickness category (Figure 3). In contrast, much of northern, central and western Australia tended to be below the national average diagnosis rate, and these general patterns were also largely consistent across all thickness categories (Figures 2, 3).

The highest modelled SIRs across all known thickness categories were consistently in coastal NSW, containing the highest SIR for thin (3.01, PP=1.0), intermediate (SIR 2.46, PP=0.9998) and thick (2.00, PP=1.0) melanomas. NSW also had the lowest rates across every melanoma thickness category, including missing [modelled SIRs ranged from 0.21 (thin) to 0.46 (thick), all PPs=0.0].

Overall, there was evidence of strong positive correlation between different thickness levels (Table 1), particularly between thin and intermediate, and intermediate and thick. The positive correlation means that most areas with high incidence of thin melanomas also had high incidence of other categories of melanomas, including intermediate, thick, and missing thickness (Figures 4, 5). These areas (high-high) tended to be north-
eastern NSW, south-eastern Queensland, some of coastal northern Queensland, and small parts of south-west Western Australia (Figure 5). The same held for low rates of thin melanomas being often associated with low rates of each of the other thickness categories considered (low-low), which were mainly in the central and western parts of the country, along with some areas in Victoria and within Sydney (Figure 5). There were some exceptions to this though, with some areas (mainly in NSW) having low rates of thin and high rates of intermediate or thick melanomas (low-high; Figure 5), while less commonly, some areas had high rates of thin melanoma but low rates of either intermediate or thick melanomas (high-low, Figure 5).
Discussion

This population-based study reveals for the first time that the small-area geographical patterns of melanoma incidence across Australia are generally consistent across the different thickness categories. In all thickness categories, melanoma incidence was consistently high around south-east Queensland and northern NSW, as well as parts of northern coastal Queensland and south-west Western Australia. Conversely, it was consistently low across all thickness categories throughout most of the Northern Territory, South Australia, and northern Western Australia.

Apart from age, information on other individual-level risk factors such as hair/skin colour, sunburn history or numbers of melanocytic naevi or solar keratoses were not available, as is the case for most population-based cancer registries. Therefore, it remains possible that geographical variations in any of the above risk factors (apart from age) may explain at least part of the observed geographical patterns.

We found that most of the areas with a lower risk of thin melanoma also had a lower risk of intermediate and thick melanomas. This is consistent with a low overall risk of melanoma within those communities, further supported by noting that the areas with lowest melanoma rates were generally found among areas at low latitude, or those with high proportions of non-English speaking migrants (>25%) (22) or Indigenous Australians (often >40%) (23). Therefore, our results are consistent with the hypothesis that geographic variation is more likely to be driven by the underlying risk of developing melanoma based on the demographic population mix, rather than a difference in diagnostic or early detection practices.

Australians have a generally high awareness of their elevated risk of skin cancer, with the population having been exposed to public health skin cancer prevention and early detection messages since the 1980s (24). That the majority of melanomas diagnosed in Australia during 2010–2014 were ≤1 mm in thickness suggests the importance of early detection is being noted. However, a sizeable proportion of melanomas are still being diagnosed when they are more than 2 mm thick, with the risk being higher in coastal areas of central and southern Queensland and northern NSW. Given the inverse association between melanoma thickness and survival (25), continued efforts to increase the effectiveness of greater skin cancer awareness and early detection activities in these areas are warranted.

Disentangling the impact of increased risk and early detection is difficult. For example the higher overall
Figure 3 Spatial patterns for modelled SIR by melanoma thickness, Australia, 2010-2014. SIR, standardised incidence ratio.
Table 1 Overall correlation (median and 80% credible intervals) between melanoma thickness diagnosis rates, Australia, 2010–2014

<table>
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<th>Melanoma thickness</th>
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<th>Thick</th>
<th>Missing</th>
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<td>Median (80% CrI)</td>
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<td>Thin</td>
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<td>Intermediate</td>
<td>0.71 (0.66, 0.76)</td>
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<td>0.60 (0.51, 0.68)</td>
<td>0.47 (0.36, 0.57)</td>
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<td>0.60 (0.51, 0.68)</td>
<td>1.00</td>
<td>0.42 (0.29, 0.53)</td>
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Figure 4 Overall correlation between thin melanoma small-area modelled SIRs and other thickness SIRs, Australia, 2010–2014. SIR, standardised incidence ratio. Refer to subsection “Correlation” for further details on correlation categories.
Figure 5 Spatial patterns of correlation between modelled SIRs by melanoma thickness, Australia, 2010-2014. SIR, standardised incidence ratio. Note: The categories are the same as shown in Figure 4, and based on the probability of an SIR being above the national average. Refer to subsection “Correlation” for further details on categories.
melanoma incidence in south-east Queensland and northern New South Wales could be explained by these areas also having a high number of dedicated primary care skin cancer clinics and a high awareness of skin cancer in general practice, thus leading to higher detection of melanoma, some of which may not have progressed to cause symptoms (26). However, it is also known that these areas have a predominately Caucasian population and outdoor lifestyle, and this increased population risk may explain the observed results. It is hoped that these results motivate further research efforts to obtain the additional data required to determine the key drivers, including, for example, geographical patterns of skin biopsies for suspected skin cancers. It is also hoped that these results prompt behaviour change in those geographical regions of very high risk.

Internationally, studies from the United States suggest that areas having a high density of general practitioners (26,27) were associated with higher rates of thin melanoma diagnoses, while not affecting the diagnosis of thick melanomas. A similar area-level association with higher numbers of skin biopsies (28,29) was also found in the United States. While Australian-specific small-area screening data are not available, it is known that whole-body skin examination reduces the incidence of thick melanoma in Australia (6).

While definitive causes are not possible to determine using these data, areas with a low incidence of thin melanomas and a high incidence of thick melanomas (low-high), would be consistent with insufficient access to and/or use of early detection methods. Conversely, areas with a higher than average incidence of thin melanomas, but lower than average thick melanomas (high-low) would be consistent with either very effective early detection practices, or it could relate to the difficulty of distinguishing between benign lesions and early melanomas (30). Further investigation into the ethnic mix and medical workforce density in each geographic area is needed to gain more definitive insights into the reasons for these patterns.

There are important challenges associated with analysing data at the small area level. Small populations and case numbers result in sparse data that are particularly prone to random fluctuations, in addition to the privacy and confidentiality constraints. Unless appropriately accounted for, this can lead to unreliable rate estimates and undue sensitivity to missing data requiring data suppression. While there are other methods available, for example data zone design using criteria such as population equity and minimum number of cases (31), spatial smoothing such as Bayesian spatial models has been increasingly demonstrated (32) to be an effective way of addressing these challenges with small-area data.

Visualising results across Australian small areas is difficult due to the large difference in size between areas. It is known that people’s attention is drawn to larger regions, which are more sparsely populated, than to smaller regions, which are more densely populated (33). One approach to circumvent this is to distort the map into a cartogram. Several forms are possible: for instance, each area could be represented by the same size and shape (e.g., a hexagon), or areas could be proportional to the population size (34). Australia is perhaps uniquely challenging in attempting this, due to the massive variation in size between small areas, and the resulting disfiguration of the resulting cartogram compared to the easily recognisable map of Australia. Although beyond the scope of this paper, it is an area worthy of future investigation.

Study limitations include the substantial proportion (7%) of melanomas with missing information about tumour thickness. Generally, we found that the geographical pattern of melanomas with missing thickness was reasonably similar to that for the known thickness categories. Given the increasing centralised pathology labs, it is unlikely that different measuring or reporting practices would explain the patterns in missing data. The patterns for males and females were not examined separately, but sex was standardised in the input data, and the Australian Cancer Atlas showed similar geographic patterns of melanoma incidence for both sexes (2). Although the best possible data were used, the methods used and accuracy of assigning SA2s varied between different Australian states and territories. However, this process was independent of the melanoma thickness so is unlikely to impact on the observed geographic patterns. Although the input data were standardised by age, so that results were not influenced by differing age structures between small areas, data sparsity prevented examining whether geographic patterns differed by age groups. This could be an interesting area for future research.

Strengths of this study include the comprehensive national population coverage and completeness of the data from the cancer registries across Australia, and the use of Bayesian spatial hierarchical models to generate robust estimates at high geographical resolution, enabling far more detailed examination of the geographical patterns than before.

In conclusion, the general consistency of geographical patterns of melanoma incidence by thickness categories
suggests that the overall patterns are more likely to be due to the underlying population risk profile than differences in diagnostic practices. For this to be confirmed, there is an urgent need to examine geographical variation in early diagnostic procedures, such as the number of skin biopsies and excisions of potential skin cancers. Given the strong association between thickness at diagnosis and survival, the areas with higher rates of thicker melanomas highlight the need for interventions aimed at reducing the incidence of thick melanomas in these regions.

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**Footnote**

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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**References**


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Figure S1: Spatial patterns for univariate modelled SIR by melanoma thickness, Australia, 2010–2014. SIR, standardised incidence ratio.
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Note: Although the Australian Cancer Database combines data from each registry and conducts additional checks, including removing duplicate records, each State and Territory Cancer Registry remain as data custodian for their data.