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ORIGINAL RESEARCH

Characteristics of 637 melanomas documented by 27 general practitioners on the Skin Cancer Audit Research Database

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ABSTRACT

Background and Objective: Most melanomas (including melanomas in situ), in Australasia, are treated by general practitioners (GPs). Previously undescribed, the characteristics of a series of melanomas treated by multiple GPs are examined.

Patients and Methods: Six hundred and thirty-seven melanomas treated by 27 Australasian GPs during 2013 and documented on the Skin Cancer Audit Research Database (SCARD) were analysed by anatomical site, subtype, Breslow thickness, diameter, associated naevi and linked adverse outcomes.

Results: Most melanomas (59.7%) were on males, mean age at diagnosis being 62.7 years (range 18–96). Most (65.0%) were in situ, with a high incidence of lentiginous melanoma (LM) (38.8%) and 32% were naevus associated. Most LM (86.4%) were in situ, compared to 55% of superficial spreading melanoma (SSM) ($P < 0.0001$). There was male predominance on the head, neck and trunk and female predominance on extremities. There was no significant association between Breslow thickness and diameter, with small melanomas as likely to be thick as large melanomas, and melanomas ≤3 mm diameter, on average, more likely to be invasive than larger melanomas. There was a positive correlation between age and both melanoma diameter and Breslow thickness. Seven cases progressed to melanoma-specific death: Five nodular melanoma (NM) and two SSM, one of which was thin (Breslow thickness 0.5 mm).

Conclusions: A large series of melanomas treated by Australasian GPs were predominantly in situ, with a high proportion of LM subtype. With implications for GP training, NM linked to death was over-represented and there was a novel finding that older patients had larger diameter melanomas.

Key words: anatomical site, Breslow thickness, characteristics, diameter, general practitioner, melanoma, primary care, Skin Cancer Audit Research Database.

INTRODUCTION

While the characteristics of melanoma diagnosed in specialist dermatology practice worldwide have been described,[1] knowledge is limited for primary care.[2–4] This has relevance in Australasia, with the highest incidence of melanoma globally[5,6] and with general practitioners (GPs) managing most skin cancer, including melanoma in Australia.[7,8]

The anatomic distribution of melanoma has been described. A large Australian tertiary care-based study found that sun-exposed sites, such as the female nose and cheek, the male scalp and ear, as well as the upper back in both sexes and posterior leg in women, have the highest incidence of melanoma per unit area (incident rate ratio).[9] A notable exception is the dorsal hand, a highly sun-exposed site with only a fraction of the incident rate ratio compared to melanoma on the face.[9] An association has been described between chronic sun exposure and lentiginous melanoma (LM) limited to sun-damaged skin,[1] and of intense intermittent sun exposure with superficial spreading melanoma (SSM), with a predilection for non-sun damaged sites,[1] including the back in men and posterior leg in women, these subtypes reportedly related to different mutagenic pathways.[1]

The prognostic significance of the anatomic distribution of melanoma was described in a study on 5093 patients,[10] finding that the back, thorax, upper arms, neck and scalp had a significantly higher mortality risk compared to the face, lower trunk, lower limbs and distal upper limbs. The nodular melanoma (NM) subtype, with a predilection for head and back sites[9] has a disproportionate impact on adverse outcomes, including death.[11]

In this retrospective observational cross-sectional study of 637 melanomas managed by 27 GPs in Australasia during 2013, we evaluated characteristics, including the anatomic site, lesion diameter, subtype and Breslow thickness as well as details of any associated naevus. We also analysed the characteristics of melanomas directly linked to adverse outcomes, including death.

METHODS

This study is based on a subset of the Skin Cancer Audit Research Database (SCARD) for patients treated during 2013 by GPs who guaranteed that their data were complete.

The SCARD project is a patient safety, lesion tracking, self-audit and research tool, freely available to professionals managing skin malignancies since 2007. Its purposes and workflow have been described.[12] Since 2007 over one million unique lesions from over 415 000 patients have been entered on the database by over 1300 practitioners, the majority being Australasian GPs.[13] With voluntary, unsupervised participation, completeness of data cannot be guaranteed.

We invited GPs who guaranteed complete recording of data during 2013, to make that available. Subsequently, 27 GPs agreed to participate, representing 18.6% of those on

Abbreviations:

GPs	general practitioners
LM	lentiginous melanoma
NAM	naevus-associated melanomas
NM	nodular melanoma
SCARD	Skin Cancer Audit Research Database
SD	standard deviation
SEER	Surveillance, Epidemiology and End Results
SSM	superficial spreading melanoma

the SCARD database in 2013 but contributing 35.6% of the unique melanomas diagnosed during that year (Table S1).

Data drawn directly from the SCARD online database included coded unique patient and lesion identifiers, patient demographics and histopathological diagnosis. Additional data entered during 2020, via a questionnaire built into the GPs' secure SCARD interfaces, included lesion-data (melanoma subtype, diameter, Breslow thickness and details of any associated naevus), as well as outcome details, including metastatic disease and melanoma-specific death.

This being a retrospective, observational study, on de-identified data, ethics exemption #2019000909 was granted by the Ethics Committee of The University of Queensland, Australia.

Statistical analysis

All statistical analyses were performed using GraphPad Prism 9.1.2 software. Proportions of invasive specimens for various subtypes, sex or specimen location were analysed using Fisher exact tests.[14] In the case of specimen location, repeated Fisher exact tests were used and a Bonferroni correction for multiple comparisons applied.[15] Average age at diagnosis for melanomas from different locations or subtypes and average Breslow thickness for melanomas of different subtypes were compared using an ordinary one-way ANOVA with Tukey multiple comparisons test using a single pooled variance. Correlations between Breslow thickness, specimen diameter and age at diagnosis were tested using Spearman correlation tests following appropriate normality testing. Throughout $P < 0.05$ was considered significant and in all cases two-tailed tests were used.

RESULTS

We analysed 637 melanomas (including melanomas in situ), 59.7% ($n = 380$) being on males, 33.6% ($n = 214$) primary invasive, from 589 patients treated by 27 GPs. The mean age at diagnosis was 62.73 years (standard deviation [SD] 15.12, range 18–96).

Considering anatomic distribution, 25.1% of melanomas were located on the head and neck, 35.6% on the torso, 23.1% on the upper limb and 16.0% on the lower limb (Table S2). There was one melanoma on female genitalia (SSM), none on male genitalia, the buttock or hand. Males were more than twice as likely as females to have a melanoma on the head and face, chest, abdomen, back or shoulder. Females were at least twice as likely as males to have a melanoma on the arm or thigh, with incidence on the distal limbs being similar in both sexes (Fig. 1 and Table S2).

There was a significant difference in average age at diagnosis for different sites, this being older for melanomas on the head, face and neck (mean 66 years, SD 14.99), compared to the torso (mean 60.57 years, SD 14.87 $P = 0.0025$), and lower limb (mean 59.08 years, SD 16.16 $P = 0.0015$) (Fig. 2).

Superficial spreading melanoma comprised 50.2% of all melanomas (Table S3). LM (including in situ and invasive lentigo maligna subtype) comprised 38.8%, and mixed LM/SSM 0.8%. Invasive status for SSM and LM was 45.0% and 13.8% respectively (Fig. 3), this difference being highly significant ($P < 0.0001$). NM made up 4.2% of melanomas but comprised 12.6% of primary invasive melanomas and there were nine melanoma metastases (1.4%) (Table S3).

Breslow thickness metrics for invasive SSM and LM and for NM are shown in Figure 4.

We found no significant difference in the proportion of invasive melanomas for males vs. females.

Lentiginous melanoma was more than twice as common as SSM on all sites on the face, but notwithstanding this, most LM (62%) were located at sites other than the head and neck (Table S2). SSM predominated at all other sites where it occurred apart from the scalp and shoulders, where the frequency was similar. NM ($n = 27$) was located on the head and neck ($n = 4$), back ($n = 10$) and limbs ($n = 13$). The unadjusted incidence rate per unit area[9] for NM (n/% body surface area) was highest for the torso (0.34) followed by the head and neck (0.29), upper limb (0.28) and lower limb (0.21).

Maximum lesion diameter was known for 89.5% ($n = 570$) of melanomas (Tables S3 and S4). Most melanomas (58.9%) were between 6.1 and 20 mm in diameter, 33.3% of these being primary invasive.

No significant correlation was observed between Breslow thickness and lesion diameter either when including all melanomas, only SSM or only invasive melanomas (in situ melanomas were attributed a Breslow thickness of 0.1 mm for correlation testing). Comparison of lesion diameter at different body sites (head, face and neck; torso; upper limb; lower limb) or between anterior chest and back also revealed no significant correlation and lesion diameter showed no association with sex (t test). However, there was a positive correlation between diameter and patient age ($r = 0.28$, 95% CI [0.19, 0.35], $P < 0.0001$) (Fig. 5), and this also applied when considering only SSM ($r = 0.31$, 95% CI [0.19, 0.41], $P < 0.0001$) or only LM ($r = 0.15$, 95% CI [0.01, 0.28], $P = 0.0320$). This was matched by a positive correlation between age and Breslow thickness of only-invasive melanomas ($r = 0.19$, 95% CI [0.05, 0.32], $P = 0.005$) (Fig. S1). This correlation also applied when considering only-invasive SSM ($r = 0.22$, 95% CI [0.06, 0.38], $P = 0.007$) but not only-invasive LM, possibly attributable to an insufficient sample size, there being only a relatively small number of invasive LM.

Melanomas were associated with a naevus in 32.0% of cases, the naevus variously reported as dysplastic/Clark ($n = 115$), dermal ($n = 45$), combined ($n = 17$), Spitz/Reed ($n = 2$) and other ($n = 19$) or unknown ($n = 6$).

Seven patients who had adverse outcomes (one or more of lymph node metastasis, distant metastasis or melanoma-specific death) had a single primary invasive melanoma in 2013 with no prior or subsequent primary melanoma. The subtypes of these single melanomas directly linked to adverse outcomes, including death in every case, were NM ($n = 5$) and SSM ($n = 2$). The average Breslow thickness of these melanomas was 5.6 mm (range 0.5–10 mm) and the

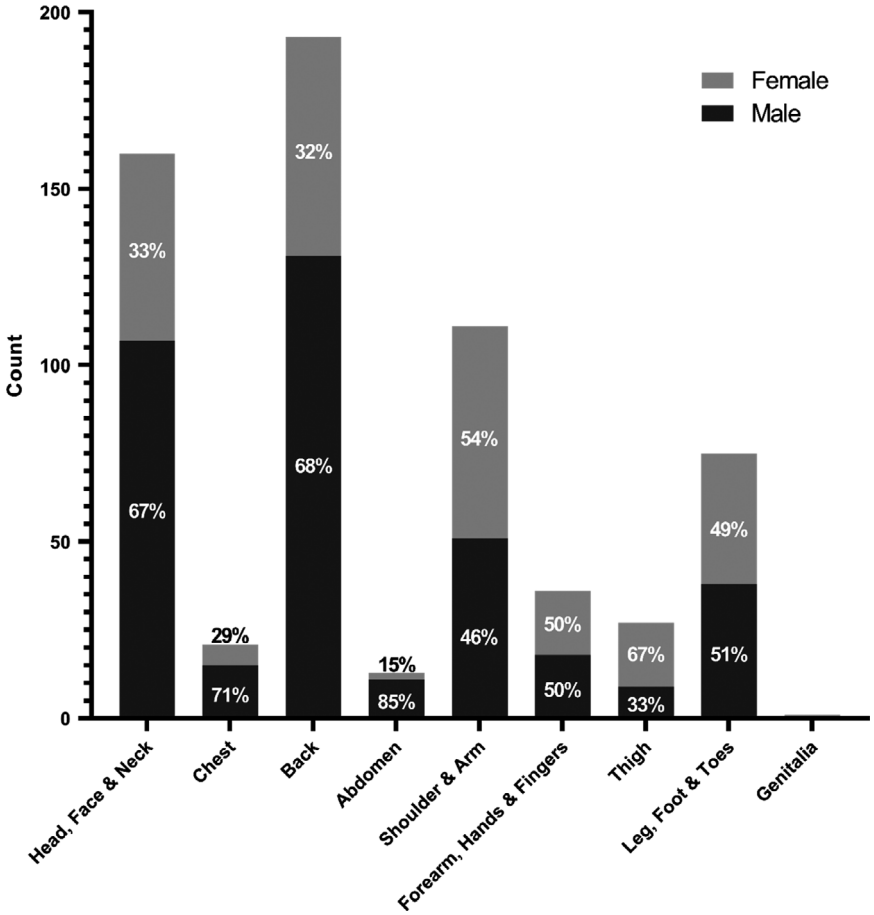

Figure 1 Count of melanomas at different body sites for males and females. Rounded percentage of total at that site is shown labelled on corresponding sections of bars.

average diameter was 15.7 mm (range 10–26 mm). The anatomical site was back (n = 3) followed by other-face (face excluding nose, ear, eyelid and lip), neck, thigh and leg, each with one melanoma.

DISCUSSION

Comparing the anatomical distribution of melanomas in the current study (65.0% in situ) with an Australian tertiary centre study on 5541 melanomas (23.4% in situ),[9] the proportion on the head and neck was similar (25.1% vs. 28.1%) as was the predominance of LM subtype at that location, SSM being more frequent at other locations. Both studies also showed a predominance of melanomas on the head, neck and torso in males and on the extremities in females. However, in the current study, there were more melanomas on the torso (35.6% vs. 28.6%) and upper limb (23.1% vs. 18.7%) and fewer on the lower limb (16.0% vs. 24.6%).

The proportion of NM in the current study was less than in the cited tertiary centre study[9] (4.2% vs. 12.2%). We interpret this to reflect the higher proportion of in situ melanomas in the current study, because if only invasive melanomas are considered, the percentage was similar at 12.6% (Table S3).

The unadjusted incidence rate ratio for NM in the current study was proportionally similar to that in the tertiary centre study,[9] with the exception of the head and neck for which it was lower. This may be a result of the limited absolute number of NM (n = 27) in the current study, with no NM on the ear, a site of high prevalence in the larger study.[9]

Comparing the current study of 637 melanomas, managed in a single year, with a primary care Australian study of 497 melanomas from 380 patients managed between 2000 and 2017 by a single practitioner,[2] the anatomical distribution of melanomas varied, with 25.1% vs. 19.9% on the head and neck, 35.6% vs. 41.9% on the torso, 23.1% vs. 18.1% on the upper limb and 16.0% vs. 19.9% on the lower limb.

A study on 70 605 primary invasive melanomas from the Surveillance, Epidemiology and End Results (SEER) database found that head and neck melanoma made up 21.3% of cases compared with body melanoma and contained older patients (mean age 64.6 vs. 57).[16] This contrasts with the current study, in which the head and neck melanoma cohort made up only 14.0% of primary invasive melanomas. However, as in the SEER study, in the current study these melanomas did occur at an older age than body melanoma (Fig. 2) and additionally they were more likely to be in situ at that location compared to body melanoma

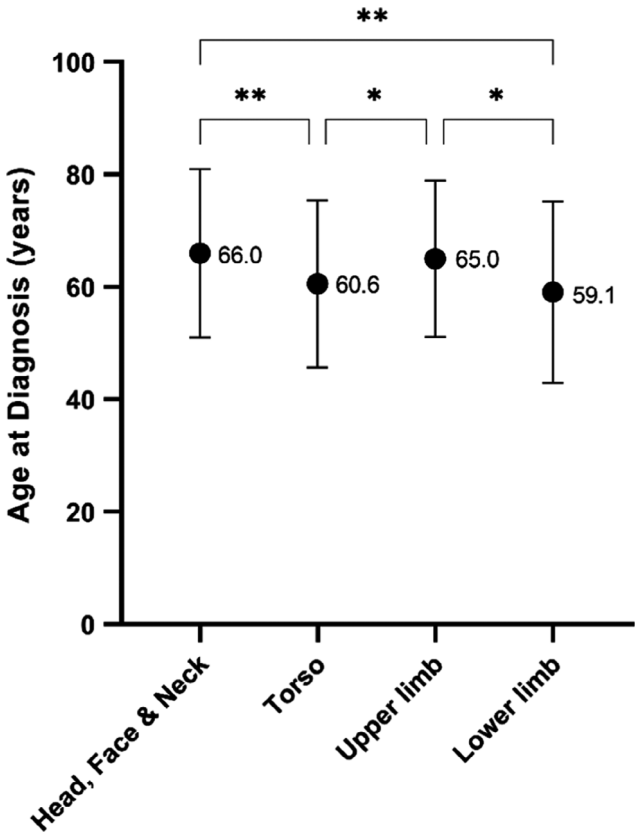

Figure 2 Comparison of age at diagnosis for melanomas at different body sites. Graph shows mean ± standard deviation, with mean (rounded to 1 decimal place) labelled on graph. Statistical analysis was performed using ordinary one-way ANOVA with Tukey multiple comparisons test using a single pooled variance. *$P < 0.05$, **$P < 0.01$.

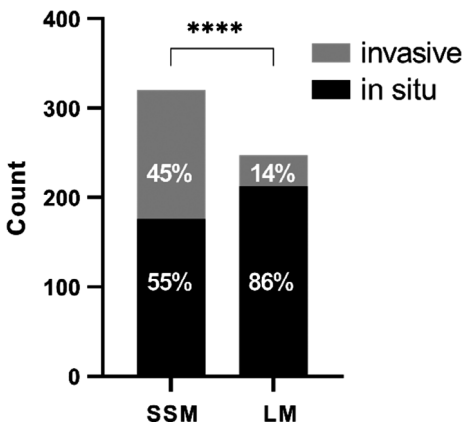

Figure 3 Comparison of proportion of in situ and invasive melanomas for superficial spreading melanomas (SSM) and lentiginous melanomas (LM). Rounded percentage of total for that subtype is shown labelled on corresponding sections of bars. Statistical analysis to compare proportions was performed using Fisher Exact Test. ****$P < 0.0001$.

(Fig. 6). In the current study, this correlated with a higher proportion of LM in these locations (Table S2), having older age of onset (Fig. S2) and having a greater likelihood of being in situ (Fig. 3).

The lack of any melanomas on the dorsal hand in the current study is consistent with a low incidence in other studies.[9,17,18] In the Australian tertiary care study, the incident rate ratio on dorsal hand was 0.1 for males and 0.2 for females, compared with 4.3 and 4.8 for the cheek respectively.[9] The face and hand are practically equivalent with respect to measured insolation.[19] This enigma is a reminder that the relationship between solar radiation and melanoma incidence is complex.

The magnitude by which a greater proportion of SSM were invasive compared with LM, was a notable finding (Fig. 3). Melanoma subtype is infrequently recorded on population registries but an analysis of the SEER database between 1990 and 2000 for 31 977 melanomas which had been subtyped[20] found that invasive status for SSM and LM was 88.7% and 25.1%, respectively, compared with 45.0% and 13.8% in the current study.

While studies have assessed the utility of lesion diameter greater than 6 mm as a diagnostic criterion for melanoma,[21] this metric is not routinely presented in data reported by cancer registries. In the current study, more than a quarter (27.6%) of melanomas were ≤6 mm in diameter, the cut-off diameter of suspicion of melanoma according to the clinical ABCD rule.[22] Significantly, of the 4.9% ($n = 31$) of very small melanomas ≤3 mm in diameter in the current study, 45.2% ($n = 14$) were primary invasive, three being NM. This was a higher proportion of invasive melanomas than for all larger melanomas combined (33.0%) (Table S4).

The absence of any significant correlation between Breslow thickness and melanoma diameter in the current study contrasts with findings in a study in Tuscany of 2071 melanomas, which found a statistically significant, but small correlation ($r = 0.39$).[23] However, they also found that a non-negligible proportion of small melanomas was thick and/or nodular, this being consistent with 34.5% of primary melanomas < 6 mm in diameter in the current study being invasive (Table S4).

As early as 1992, an Australian study found that 31% of 1150 invasive melanomas consecutively treated at the Sydney Melanoma Unit were ≤6 mm, including 47 with a diameter of 3 mm and nine with a diameter of 2 mm.[24] Relevant to recent published exhortations not to excise lesions smaller than 6 mm in diameter,[25] the proportion of invasive, small-diameter melanomas in the current study, as well as in the other cited studies, is clear evidence of the potential harms created by arbitrary admonitions.

While an association between age, Breslow thickness and melanoma mortality has been described,[26] the novel finding of a positive correlation between age and melanoma diameter, independent of LM and SSM subtype, has implications for clinical practice. Speculative explanations include different growth patterns of melanoma at advanced age; delayed detection because older patients have less concern or poorer eyesight; differing clinician threshold

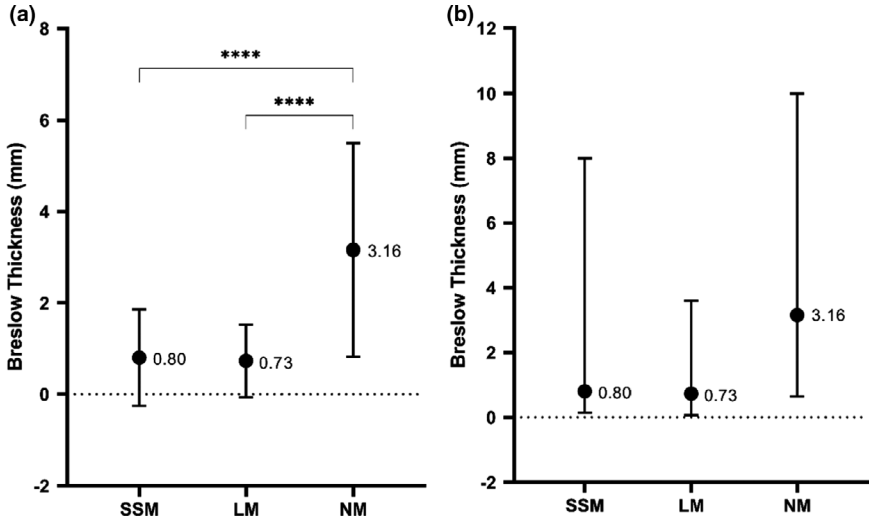

Figure 4 Comparison of Breslow thickness for superficial spreading melanomas (SSM), lentiginous melanomas (LM) and nodular melanomas (NM). Melanomas with unknown thickness or diameter, metastatic melanomas and in situ melanomas were excluded. (a) Graph shows mean ± standard deviation, with mean labelled on graph. Statistical analysis was performed using ordinary one-way ANOVA with Tukey multiple comparisons test using a single pooled variance. ****$P < 0.0001$. (b) Graph shows mean with total range of Breslow thickness shown by lines.

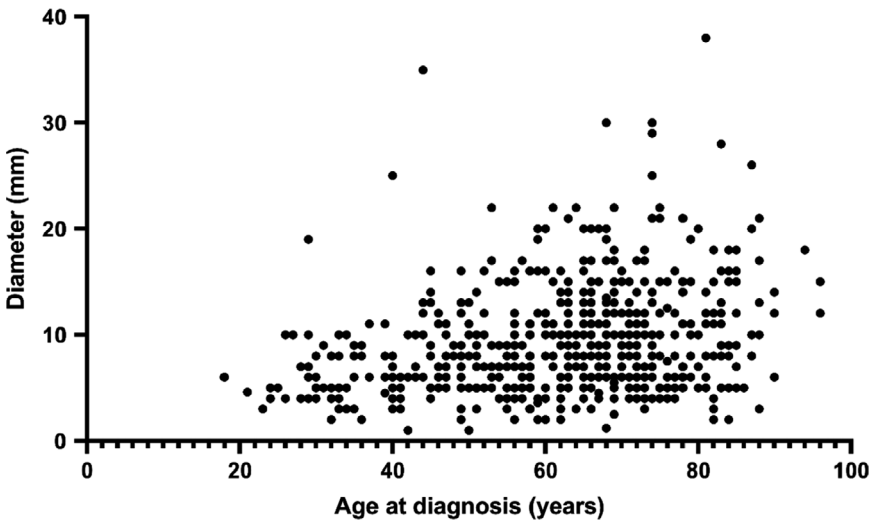

Figure 5 Comparison of melanoma diameter to age at diagnosis, excluding metastatic melanomas and melanomas with unknown diameter. Statistical analysis was performed using Spearman correlation testing.

for excision at advanced age and the possibility that older patients, on average, will have older melanomas.

The incidence of naevus-associated melanomas (NAM) was assessed in a review of 25 studies to be 36%,[27] compared with 32% in the current study. Assessment of naevus subtype is challenging because there is no uniform classification of naevi. One study which addressed this, and which controversially classified intradermal naevi as acquired, looked at 13 of 38 studies which distinguished between congenital and acquired naevi, finding that 22.6% of NAM were congenital and 77.4% acquired.[28] Considering only the acquired naevi, NAM were more frequently associated with intradermal naevi (54%) than with junctional or compound remnants. Of 15 studies reporting dysplastic status of naevi which were associated with melanoma, there was an increased prevalence of non-dysplastic naevi (56.7% vs. 43.3%).[27] This contrasts with the current study, in which the naevus component of NAM was reported as dysplastic/Clark in 56.4% of cases. There is poor intra- and inter-observer concordance among pathologists in grading dysplasia of naevi,[29] and it is possible that current pathology reporting practices in Australasia have influenced the prevalence of dysplastic naevus remnants in the current study. Also, given that concordance is particularly poor with respect to severe dysplasia vs. melanoma in situ,[29] it is quite possible that

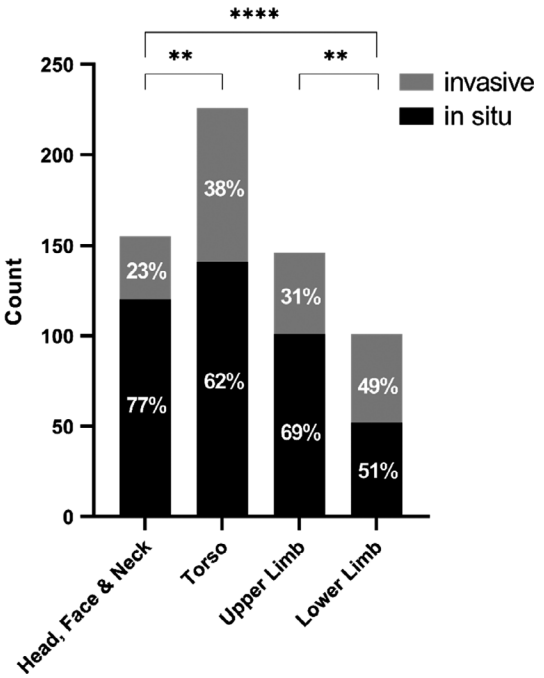

Figure 6 Comparison of proportion of in situ and invasive melanomas at different sites. Rounded percentage of total for that site is shown labelled on corresponding sections of bars. Statistical analysis to compare proportions was performed using repeated Fisher exact tests with a Bonferroni correction for multiple comparisons. $^{**}P < 0.01$ $^{****}P < 0.0001$.

portions of de-novo melanomas were incorrectly diagnosed as (dysplastic) naevus.

Anatomical sites have prognostic implications with respect to adverse outcomes. In addition to the findings of a German study that the back, thorax, upper arms, neck and scalp were high-risk sites,[10] an Australian study of 3570 primary invasive melanomas found that the posterior scalp and neck had a high relative risk compared to other anatomical locations in both sexes.[30] Four of the seven melanomas directly associated with death in the current study were from high-risk locations as defined in these studies (back $n = 3$, neck = 1).[10,30]

Nodular melanoma cause a disproportionate number of deaths[11] and thin melanomas can also lead to death.[16] Consistent with this, in the current study, five NM and two SSM, one with a Breslow thickness of 0.5 mm and a diameter of 10 mm, were directly linked to patient death.

Limitations

Limitations of this study include the analysis being based on a subset of a database, which might introduce bias because the data from GPs who volunteered may differ from that of others. Completeness and accuracy of data were not independently verified. There was a significant excess of Australian vs. New Zealand GPs, and the absolute number of melanomas was small, as a proportion of the total managed by GPs in Australasia in 2013. Laterality and anterior/posterior sub-units of limbs were not discriminated, which limited calculations of incidence rate per surface area to unadjusted values.

CONCLUSIONS

This study showed that anatomical distribution of melanoma and proportions of melanoma subtypes detected by GPs, in comparison with tertiary care studies, were similar, except for a higher proportion of LM, with a propensity for the head and neck, most being in situ. SSM was significantly more likely to be invasive on presentation, which has implications for dermatoscopic recognition. There was no significant correlation between melanoma diameter and Breslow thickness, small melanomas being invasive as frequently as large ones, which would caution against dismissal of, and recommend dermatoscopic examination of, smaller lesions. We were able to directly correlate death to a single primary invasive melanoma in seven cases, five being NM and two SSM, one of these being a thin melanoma. Of relevance to clinical practice and GP training was the novel finding that older patients have larger diameter melanomas. Further studies in the primary care setting are warranted.

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AUTHORSHIP

Authors Jimenez Balcells, Hay, Keir, Coetzer-Botha, Wilson, Clark, Kittler and Cliff Rosendahl made substantial contributions to conception and design, acquisition of data, analysis and interpretation of data, were involved in drafting and critically revising and finally approving the manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of the work have been appropriately investigated and resolved. Nikita Rosendahl prepared the Tables and Figures and performed the statistical analyses and takes responsibility for data analysis, made substantial contributions to conception and design, was involved in drafting and critically revising and finally approving the manuscript and agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of the work have been appropriately investigated and resolved. The other authors were all involved in data acquisition, were involved in critically revising and finally approving the manuscript and agree to be accountable for relevant aspects of the work in ensuring that questions related to the accuracy or integrity of the work have been appropriately investigated and resolved. All authors have participated sufficiently to take public responsibility for appropriate portions of the content.

ETHICAL APPROVAL

The Human Ethics Research Office of The University of Queensland, Australia, provided ethics exemption for this study.

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Supporting Information

Additional Supporting Information may be found online in Supporting Information:

Table S1. Comparison between count of doctors and melanomas in the SCARD pool in 2013 and in the current study.
Table S2. Melanoma characteristics by anatomical location: in situ status, sex distribution and subtype.
Table S3. Characteristics for (all and primary) melanomas: Subtype, diameter, Breslow thickness.
Table S4. Melanoma diameter related to subtype and Breslow thickness.
Figure S1. Comparison of melanoma Breslow thickness to age at diagnosis for invasive melanomas only, excluding metastatic melanomas and melanomas with unknown thickness. Statistical analysis was performed using Spearman correlation testing.
Figure S2. Comparison of age at diagnosis for superficial spreading melanomas (SSM), lentiginous melanomas (LM) and nodular melanomas (NM). Graph shows mean ± standard deviation, with mean (rounded to 1 decimal place) labelled on graph. Statistical analysis was performed using ordinary one-way ANOVA with Tukey multiple comparisons test using a single pooled variance. $^{**}P < 0.01$, $^{****}P < 0.0001$.