**Objective:** To investigate risk factors for lentigo maligna melanoma (LMM) compared with superficial spreading melanoma (SSM).

**Design:** Population-based case-control study in Queensland, Australia.

**Setting:** General community.

**Participants:** Population-based sample of 49 patients with LMM and 141 with SSM (in situ or invasive) aged 14 to 86 years at diagnosis in 1979 and 1980 and 232 control subjects. Response rates were 97.1% in cases and 91.8% in controls.

**Main Outcome Measures:** Risks of both subtypes in relation to phenotypic and environmental factors, estimated by multinomial logistic regression.

**Results:** The number of solar lentigines was the strongest determinant for LMM (odds ratio [OR], 15.93; \( P < .001 \) for trend) and significantly weaker for SSM (4.61; \( P < .001 \) for trend; \( P = .04 \) for homogeneity). Skin cancer history was significantly associated with LMM (OR, 2.84) but not with SSM (1.33; \( P = .07 \) for homogeneity). In contrast, the number of nevi was the strongest determinant for SSM (OR, 23.22; \( P < .001 \) for trend) while significantly weaker for LMM (3.60; \( P = .02 \) for trend; \( P < .001 \) for homogeneity). Multiple lifetime sunburns almost tripled the risk for SSM, whereas no association was detected with LMM (\( P = .04 \) for homogeneity). Shared risk factors for both subtypes were the number of solar keratoses (\( P < .001 \) for trend for both) and sun-sensitive complexion (ie, light eye/hair colors, sunburn propensity, and freckling) (2-fold to 5-fold increased risks).

**Conclusions:** A propensity to lentigines is a stronger predictor of LMM, whereas high nevus propensity is a stronger predictor of SSM. Skin cancer history appears to determine LMM risk only, whereas the number of lifetime sunburns determines SSM only. Prevention strategies could be tailored differently given these distinctive points of difference.


CTANEOUS MELANOMA MAY be classified into superficial spreading (SSM), lentigo maligna (LMM), nodular, and acral lentiginous melanoma histological subtypes.1 Although SSM is the most common subtype, LMM accounts for 4% to 15% of all melanomas and 10% to 26% of melanomas on the head and neck.2,3 Incidence of LMM has increased in recent decades,4 and this rise has been attributed to increased amounts of sun exposure.5 Because LMM has been reported to occur predominantly on sun-exposed areas and typically in the elderly,6 most authors accept that it is caused by high cumulative sun exposure and have not explored the etiology of LMM in further detail. Indeed, LMM has been considered a separate entity7 and explicitly excluded from many epidemiological studies. It is important to characterize LMM, however, because other subtypes are known to be associated with heavy sun exposure also.8 In particular, SSM often occurs on the face and can be histologically confused with LMM.9 Our objective, therefore, was to investigate the phenotypic and environmental risk factors for LMM compared with SSM. We tested the hypothesis that LMM is associated with distinct risk factors compared with SSM by using a detailed data set available from a previously conducted population-based case-control study in Queensland, Australia, with an exceptionally high response rate.
The final study sample comprised 49 patients with LMM (with 41 in situ and 8 invasive tumors), 141 with SSM (with 54 in situ and 87 invasive tumors), and 232 controls. Most of the LMMs were located on the head and neck (34 of 49 [69.4%]) and upper limbs (8 of 49 [16.3%]), whereas SSMs were more often found on the back and shoulders (49 of 141 [34.8%]), lower limbs (38 [27.0%]), and chest and abdomen (21 [14.9%]). The mean (SD) age of patients with LMM at diagnosis was 60.7 (11.6) years compared with 44.8 (15.4) years for patients with SSM, whereas controls were 49.8 (16.3) years of age at the interview. Although there were as many male (118 of 232 [50.9%]) as female (114 [49.1%]) subjects in the control sample, there were slightly more women in the SSM group (79 of 141 [56.0%]) than in the LMM group (23 of 49 [46.9%]).

PHENOTYPIC FACTORS

Compared with dark brown/black hair, red/auburn hair was similarly associated with SSM and LMM, although the estimate did not reach statistical significance for LMM (OR for LMM, 2.51 [95% CI, 0.67-9.40]; OR for SSM, 3.49 [1.44-8.49]) (Table 1). A significant association for SSM was also found for blond/brown hair (OR, 2.66). Although eye color was significantly associated with LMM (OR, 5.01 for green/hazel compared with brown eyes) but not SSM, the difference between the 2 subtypes was, at most, marginally significant. We found no independent association between skin color and LMM or SSM. Propensity to freckle was similarly and significantly associated with both subtypes (OR for LMM, 3.65; OR for SSM, 2.51). Although propensity to sunburn appeared more strongly associated with LMM than SSM, there was a gradient of increasing risk only for SSM. Similar positive relationships were observed between the depth of tan after repeated exposure and both subtypes (Table 1). We found a very strong and significant positive dose-response relationship between number of nevi and SSM (OR for 1-10 nevi, 15.68; OR for >10 nevi, 23.22; compared with no nevi, P < .001 for trend), whereas the positive association with LMM was much weaker, with ORs of 2.30 and 3.60, respectively (P = .02 for trend), and the difference in slopes was highly significant (P < .001 for homogeneity).

SUNBURN

Numbers of sunburns during one’s lifetime and before 20 years of age were positively and significantly associated with SSM (P < .001 for trend for both), whereas there was no evidence of an association with LMM, and the differences were significant for lifetime number of sunburns and marginally so for sunburns before 20 years of age (P = .04 and P = .06 for homogeneity, respectively) (Table 2). The risk of SSM increased with the number of sunburns at different body sites, with ORs ranging from 2.02 to 2.83 for 2 or more, whereas the site-specific associations with LMM, although positive, did not approach statistical significance.

DATA COLLECTION

All interviews were conducted in person by a trained physician (A.C.G.) during 1980 and 1981. Basic demographic information and phenotypic factors were collected using a standard questionnaire. Phenotypic factors included hair color at 21 years of age (light or medium blond, light or medium brown, red, auburn, dark brown, or black), eye color (brown, blue, gray, hazel, green, or other), skin color on the left forearm (very pale, pale, fair, medium, olive, dark olive, or dark), propensity to freckle after sun exposure, depth of tan after repeated sun exposure (none, light, medium, or dark), propensity to sunburn when exposed for 1 hour in strong sun for the first time in summer (painful burn and peel, burn first and then tan, or tan without burning), and number of nevi on the left forearm (0, 1-4, 5-10, or >10). Numbers of sunburns throughout life and at different anatomical locations were obtained by asking participants to recall all episodes of severe sunburn accompanied with pain lasting more than 48 hours, with or without blisters. We also collected detailed data on all outdoor occupations practiced for more than 6 months and all recreations ever pursued regularly after 10 years of age. Total hours of sun exposure were estimated by summing reported lifetime occupational and recreational sun hours. On interview completion, a clinical examination of the face and arms was performed, and skin, hair, and eye color were graded against standard color charts. Numbers of nevi on the left forearm and solar lentigines (brown to black-brown macular lesions with well-defined if irregular edges and normal skin surface creases) on the backs of the hands (0, 1-4, 5-10, or >10) were assessed, as well as the presence of skin cancers and solar keratoses on the left forearm and face.

STATISTICAL ANALYSIS

Because of the small LMM sample in our study population, we ignored the matching for the present analysis and coalesced the categories of several phenotypic factors. We estimated odds ratios (ORs) and 95% CIs using unconditional multinomial logistic regression models. All models were adjusted for sex and quartiles of age (<38, 38-49, 50-63, or ≥64 years). When examining risks of LMM and SSM in relation to phenotypic factors, sun exposure, and markers of cumulative actinic damage, models were additionally adjusted for propensity to sunburn. We used homogeneity tests to compare risk estimates over strata. Where relevant, we performed tests for linear trend using an ordinal score for each factor. We performed statistical analyses using commercially available software (SAS statistical package, version 9.1; SAS Institute, Inc, Cary, North Carolina).
REPORTED HOURS OF SUN EXPOSURE

Overall, there was no evidence of an association between total life hours of recreation or lifetime percentage of time spent in the sun in recreation and the occurrence of LMM or SSM. Total sun exposure hours accumulated during outdoor occupations or through life were positively but nonsignificantly associated with LMM and SSM, with higher risk estimates and a marginally significant linear trend for LMM in relation to lifetime sun exposure hours \((P = .08\) for trend) (data not shown).

ACTINIC DAMAGE AND HISTORY OF EXCISED SKIN CANCER

Although both subtypes were significantly associated with increasing number of solar lentigines \((P < .001\) for trend), the risk estimate for many (>10) solar lentigines on the arm compared with none was higher for LMM (OR, 15.93) than for SSM (OR, 4.61), and slopes were significantly different between subtypes \((P = .04\) for homogeneity) (Table 3). There was a dose-response relationship between risks of LMM and SSM and number of solar keratoses on the arm \((P < .001\) for trend). In contrast, a history of excised skin cancer significantly increased LMM \((OR, 2.84 [95\% CI, 1.39-5.82])\) but not SSM risk \((OR, 1.33 [95\% CI, 0.76-2.32])\) \((P = .07\) for homogeneity).

In the present analysis, a very high propensity to develop solar lentigines was a significantly stronger risk factor for LMM than for SSM, whereas numbers of nevi and lifetime sunburns were significantly more strongly associated with SSM than with LMM. In addition, a history of excised skin cancer strongly determined LMM but not SSM, although the difference between subtypes was only marginally significant.

Propensity to sunburn showed a dose-response effect for SSM not seen for LMM, which was consistent with lifetime sunburns predicting SSM but not LMM. Associations with other factors, such as light hair or eye colors, freckling, the depth of tan, overall sun exposure, and the number of solar keratoses on the arm, were similar for LMM and SSM.
Our results regarding the associations between light hair and eye color and freckling propensity and SSM are generally consistent with those reported in the literature.9-15 The few available studies examining LMM reported similar findings to ours regarding hair color9,10,15 but different results regarding other factors, including lack of previous significant associations with eye color9,16 and freckling10 and an increased risk associated with light skin color.9 Propensity to sunburn and the depth of tan were strongly associated with both subtypes in our study, al-

### Table 2. Risk of LMM and SSM in Relation to History of Sunburn

<table>
<thead>
<tr>
<th>History of Sunburn</th>
<th>Control Group (n=232)</th>
<th>LMM Group (n=49)</th>
<th>Age- and Sex-Adjusted OR (95% CI)</th>
<th>SSM Group, No. (%) (n=141)</th>
<th>Age- and Sex-Adjusted OR (95% CI)</th>
<th>P Valueb</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. of sunburns lifetime</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>87 (37.5)</td>
<td>22 (44.9)</td>
<td>1 [Reference]</td>
<td>32 (22.7)</td>
<td>1 [Reference]</td>
<td></td>
</tr>
<tr>
<td>1-2</td>
<td>94 (40.5)</td>
<td>19 (38.8)</td>
<td>0.96 (0.47-1.95)</td>
<td>49 (34.8)</td>
<td>1.35 (0.78-2.31)</td>
<td></td>
</tr>
<tr>
<td>≥3</td>
<td>51 (22.0)</td>
<td>8 (16.3)</td>
<td>0.95 (0.37-2.41)</td>
<td>60 (42.6)</td>
<td>2.97 (1.68-5.26)</td>
<td></td>
</tr>
<tr>
<td>P value for trend</td>
<td></td>
<td></td>
<td>.91</td>
<td></td>
<td>&lt;.001</td>
<td>.04</td>
</tr>
<tr>
<td><strong>No. of sunburns &lt;20 y</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>118 (50.9)</td>
<td>31 (63.3)</td>
<td>1 [Reference]</td>
<td>45 (31.9)</td>
<td>1 [Reference]</td>
<td></td>
</tr>
<tr>
<td>1-2</td>
<td>71 (30.6)</td>
<td>11 (22.4)</td>
<td>0.92 (0.41-2.06)</td>
<td>47 (32.3)</td>
<td>1.54 (0.91-2.81)</td>
<td></td>
</tr>
<tr>
<td>≥3</td>
<td>43 (18.5)</td>
<td>7 (14.3)</td>
<td>1.08 (0.41-2.26)</td>
<td>49 (34.8)</td>
<td>2.71 (1.54-4.77)</td>
<td></td>
</tr>
<tr>
<td>P value for trend</td>
<td></td>
<td></td>
<td>.94</td>
<td></td>
<td>&lt;.001</td>
<td>.06</td>
</tr>
<tr>
<td><strong>No. of sunburns on head and neck</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-1</td>
<td>207 (89.2)</td>
<td>44 (88.9)</td>
<td>1 [Reference]</td>
<td>109 (77.3)</td>
<td>1 [Reference]</td>
<td></td>
</tr>
<tr>
<td>≥2</td>
<td>25 (10.8)</td>
<td>5 (10.2)</td>
<td>1.23 (0.43-3.55)</td>
<td>32 (22.7)</td>
<td>2.35 (1.30-4.24)</td>
<td>.25</td>
</tr>
<tr>
<td><strong>No. of sunburns on back and shoulders</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-1</td>
<td>171 (73.7)</td>
<td>36 (73.5)</td>
<td>1 [Reference]</td>
<td>70 (49.6)</td>
<td>1 [Reference]</td>
<td></td>
</tr>
<tr>
<td>≥2</td>
<td>61 (26.3)</td>
<td>13 (26.5)</td>
<td>1.44 (0.68-3.05)</td>
<td>71 (50.4)</td>
<td>2.83 (1.78-4.50)</td>
<td>.09</td>
</tr>
<tr>
<td><strong>No. of sunburns on arms</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-1</td>
<td>218 (94.0)</td>
<td>46 (93.9)</td>
<td>1 [Reference]</td>
<td>121 (85.8)</td>
<td>1 [Reference]</td>
<td></td>
</tr>
<tr>
<td>≥2</td>
<td>14 (6.0)</td>
<td>3 (6.1)</td>
<td>1.23 (0.32-4.66)</td>
<td>20 (14.2)</td>
<td>2.37 (1.14-4.90)</td>
<td>.34</td>
</tr>
<tr>
<td><strong>No. of sunburns on legs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-1</td>
<td>212 (91.4)</td>
<td>44 (89.8)</td>
<td>1 [Reference]</td>
<td>117 (83.0)</td>
<td>1 [Reference]</td>
<td></td>
</tr>
<tr>
<td>≥2</td>
<td>20 (8.6)</td>
<td>5 (10.2)</td>
<td>1.47 (0.50-4.29)</td>
<td>24 (17.0)</td>
<td>2.02 (1.06-3.85)</td>
<td>.57</td>
</tr>
</tbody>
</table>

**Abbreviations:** LMM, lentigo maligna melanoma; OR, odds ratio; SSM, superficial spreading melanoma.

a Percentages have been rounded and might not total 100.
b Calculated as a test for homogeneity in adjusted estimates between the LMM and SSM groups.

d Missing values (n = 5) were imputed to the modal category of number of solar keratoses (none).

### Table 3. Risk of LMM and SSM in Relation to Actinic Skin Damage and History of Excised Skin Cancer

<table>
<thead>
<tr>
<th>Skin Damage/History of Skin Cancer</th>
<th>Control Group (n=232)</th>
<th>LMM Group (n=49)</th>
<th>Adjusted OR (95% CI)b</th>
<th>SSM Group, No. (%) (n=141)</th>
<th>Adjusted OR (95% CI)b</th>
<th>P Valuec</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. of solar lentigines on left arm</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>155 (66.8)</td>
<td>9 (18.4)</td>
<td>1 [Reference]</td>
<td>38 (27.0)</td>
<td>1 [Reference]</td>
<td></td>
</tr>
<tr>
<td>1-10</td>
<td>50 (21.6)</td>
<td>21 (42.9)</td>
<td>7.16 (2.92-17.57)</td>
<td>64 (45.4)</td>
<td>4.68 (2.75-7.96)</td>
<td></td>
</tr>
<tr>
<td>&gt;10</td>
<td>27 (11.6)</td>
<td>19 (38.8)</td>
<td>15.93 (5.58-46.53)</td>
<td>39 (27.7)</td>
<td>4.61 (2.35-9.93)</td>
<td>.04</td>
</tr>
<tr>
<td>P value for trend</td>
<td></td>
<td></td>
<td>-.001</td>
<td></td>
<td>-.001</td>
<td>.04</td>
</tr>
<tr>
<td><strong>No. of solar keratoses on left arm</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>181 (78.0)</td>
<td>15 (30.6)</td>
<td>1 [Reference]</td>
<td>86 (61.0)</td>
<td>1 [Reference]</td>
<td></td>
</tr>
<tr>
<td>A few</td>
<td>37 (15.9)</td>
<td>17 (34.7)</td>
<td>3.69 (1.55-8.80)</td>
<td>29 (20.6)</td>
<td>2.62 (1.37-4.99)</td>
<td>.07</td>
</tr>
<tr>
<td>≥5</td>
<td>14 (6.0)</td>
<td>17 (34.7)</td>
<td>10.10 (3.71-27.45)</td>
<td>26 (18.4)</td>
<td>7.24 (3.14-16.67)</td>
<td></td>
</tr>
<tr>
<td>P value for trend</td>
<td></td>
<td></td>
<td>-.001</td>
<td></td>
<td>-.001</td>
<td>.43</td>
</tr>
<tr>
<td><strong>History of excised skin cancer</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>181 (78.0)</td>
<td>22 (44.9)</td>
<td>1 [Reference]</td>
<td>105 (74.5)</td>
<td>1 [Reference]</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>51 (22.0)</td>
<td>27 (56.1)</td>
<td>2.84 (1.39-5.82)</td>
<td>36 (25.5)</td>
<td>1.33 (0.76-2.32)</td>
<td>.07</td>
</tr>
</tbody>
</table>

**Abbreviations:** LMM, lentigo maligna melanoma; OR, odds ratio; SSM, superficial spreading melanoma.
a Percentages have been rounded and might not total 100.
b Adjusted for age, sex, and propensity to sunburn.
c Calculated as a test for homogeneity in adjusted estimates between the LMM and SSM groups.
d Missing values (n = 5) were imputed to the modal category of number of solar keratoses (none).

though propensity to sunburn showed a significant trend only with SSM risk. Regarding propensity to sunburn, a recent meta-analysis reported a significantly higher SSM risk with skin that easily burns compared with skin that always tans, whereas the OR for LMM risk was higher but nonsignificant based on the findings of 5 to 7 studies.\textsuperscript{9} In Australia, Holman and Armstrong\textsuperscript{17} showed a strong and significant dose-response relationship between lack of tanning ability and LMM risk, with ORs ranging from 2.32 for a moderate tan to 10.01 for no tan compared with a deep tan. In contrast to our results, the association with SSM risk, although significantly positive, was weaker than that observed with LMM risk.\textsuperscript{17}

Variants of the melanocortin 1 receptor gene (\textit{MC1R}) have been associated with the red hair phenotype, which includes red hair, light skin color, the presence of freckles, and poor tanning ability.\textsuperscript{18} On the basis of the currently available data, it is unclear whether the red hair phenotype or some genetic polymorphisms of the \textit{MC1R} gene are specifically associated with 1 particular melanoma subtype. To date, only 1 study has examined these associations and reported no significant difference in the proportion of melanoma subtypes between carriers and noncarriers of several \textit{MC1R} polymorphisms.\textsuperscript{19} Further genetic investigation may help sharpen our understanding of the true pigmentary risk profile specificities of LMM and SSM.

Consistent with our findings, the number of nevi has been shown repeatedly to determine SSM risk, with strong dose-response trends,\textsuperscript{11-17,20,21} whereas risk estimates for LMM in previous studies have been of lower magnitude, and associations have not been consistently significant.\textsuperscript{15-17,20,22} Indeed, LMM has been associated with significantly reduced numbers of nevi compared with other subtypes of melanomas occurring on the trunk.\textsuperscript{9} This is consistent with experimental evidence that SSM exhibits greater proliferative activity of melanocytes compared with LMM.

Taken together, these data suggest that the number of nevi is a more important component of SSM than LMM etiology. This is in agreement with the divergent pathway hypothesis, which proposes a nevus pathway associated with high nevus counts, younger age and anatomic sites that are not usually exposed to the sun, and a sun-exposure pathway associated with low nevus counts, later age, and sites with chronic sun exposure.\textsuperscript{6} Exploration of this model has shown that SSM is associated with contiguous nevus remnants, whereas the LMM subtype is associated with dermal elastosis, a marker of excessive sun exposure.\textsuperscript{23}

**SUNBURNS**

It has been proposed that LMM is caused by increased DNA damage in melanocytes\textsuperscript{25} and thus that a history of painful sunburns as a marker of high amounts of UV radiation exposure should confer greater LMM risk.\textsuperscript{26} Our data do not confirm this hypothesis, however, because we found no evidence of an association between the number of sunburns and LMM. The number of lifetime sunburns was significantly more strongly associated with SSM than with LMM in our study. In addition, the ORs were systematically higher for SSM than for LMM regarding the number of sunburns at different body sites, although the difference was not statistically significant. In contrast to our findings, most previous studies found similar associations between sunburn history and the risk of LMM and SSM,\textsuperscript{9,20} although the risk estimate for LMM was not statistically significant in the meta-analysis.\textsuperscript{9}

We were not able to examine sunburn severity in relation to LMM or SSM risk. Previous research on these relationships yielded inconsistent findings, sometimes suggesting a stronger association with LMM than for SSM\textsuperscript{20} or, in the opposite direction, with SSM but not for LMM\textsuperscript{10} or no significant association for either subtype.\textsuperscript{27}

**SUN EXPOSURE**

Similar to our findings, mean annual hours of bright sunlight during one’s lifetime was nonsignificantly and positively associated with both LMM and SSM risks in an Australian case-control study,\textsuperscript{28} whereas there were no significant associations between LMM or SSM risks and high vs low intermittent or continuous sun exposure in the meta-analysis.\textsuperscript{9}

Although nonsignificant, our observation of an increased risk for both subtypes with total hours of occupational sun exposure is in agreement with the significantly positive relationships described in a German study, in which risk estimates were stronger for LMM than for SSM,\textsuperscript{17} whereas the finding by Holman et al\textsuperscript{20} of a positive association for LMM compared with the inverse for SSM was nonsignificant.

**MARKERS OF ACTINIC DAMAGE AND HISTORY OF SKIN CANCER**

The number of solar lentigines reflects excessive cumulative sun exposure given a particular skin type.\textsuperscript{29,30} The fact that this measure was significantly more strongly associated with LMM risk than with SSM risk in our study is consistent with the lentiginous nature of LMM and suggests that this inherent propensity combined with excessive sun exposure plays a stronger role in LMM than in SSM etiology. This is coherent with solar lentigines being very common contiguous lesions with lentigo maligna.\textsuperscript{31}

Our result is consistent with the report by Holman and Armstrong\textsuperscript{28} in which 89% of LMMs were associated with moderate to severe solar elastosis compared with only 16% of other melanoma subtypes. Those authors also reported a higher risk of LMM than SSM with a higher grade of actinic damage, as measured by cutaneous microtopography.\textsuperscript{28} Our finding is further consistent with the results of yet another Australian study showing an association between dermal elastosis (a histological marker of chronic sun exposure) and LMM but not SSM.\textsuperscript{29}

Results from other studies have reported a less clear distinction between LMM and SSM regarding solar lentigines.\textsuperscript{9,16} In the French study,\textsuperscript{20} risks of LMM and other melanomas were significantly associated with the number of solar lentigines (which they termed \textit{senile lentigines}) on the hands but not the forearms. Other markers of actinic damage (ie, cutis rhomboidalis nuchae and gut-
tate hypomelanosis) were positively and similarly associated with risks of LMM and other melanomas, consistent with the similar association between the number of solar keratoses and the risk of LMM and SSM in our study.

Our results of a stronger association between a history of skin cancer and LMM risk rather than SSM risk are in agreement with the results from 2 previous studies. Holly et al also reported a significantly increased risk of SSM in people with a history of nonmelanoma skin cancer, but no risk estimation was performed for LMM.

STRENGTHS AND LIMITATIONS

Strengths of our study include the objective measurement of phenotypic factors, the exceptionally high participation rates in cases (97.1%) and controls (91.8%), and the ascertainment of all tumors through pathology reports. Although a potential weakness is that sun exposure and protection habits were likely quite different when the study was conducted 3 decades ago compared with present-day Australia, the possible difference in prevalence of, for instance, lifetime sunburns is unlikely to detract from the validity of the observed associations with SSM. Another limitation is the small size of our LMM sample. However, because LMM occurs at significantly later ages compared with other subtypes that may usually be under study, most previous studies of different melanoma subtypes also included small numbers of LMM cases. Indeed, only 1 other study sample to date, containing 86 cases, has been larger, and thus our study should not be dismissed in terms of number of LMM cases. Another limitation that is inherent to retrospective designs is the possibility of recall bias. However, this bias was minimized by the fact that data were collected through clinical examinations and face-to-face interviews that were performed by the same investigator in cases and controls, although the interviewer could not be totally blinded to the case/control status of the participants. More saliently, the comparison between the 2 histological subtypes should have been very little affected by difference in recall. Because age distributions of persons with LMM and SSM differ and given that lentigines and skin cancer history are strongly age dependent, we wanted to ensure that the method of controlling for age in our analyses was adequate. We checked this in 2 ways, including the addition of other age-related covariates (eg, age squared) to the models, and by confining analysis to those 55 years or older. Neither made any substantive difference to our results.

CONCLUSIONS

Our data support the hypothesis that LMM and SSM have distinct etiologies. This study suggests that an inherent high propensity to solar lentigines is more predictive of LMM than SSM and that history of excised skin cancer is a distinguishing risk factor for LMM not shared with SSM, whereas the number of nevi is more predictive of SSM and high lifetime sunburns is a distinctive risk factor for SSM not shared by LMM. Thus, it could be suggested that, beyond the influence of having sun-sensitive complexion and sun exposure patterns on the risk of both subtypes, LMM occurs in individuals prone to lentiginous pigmented lesions who additionally experience excessive cumulative doses of sun exposure during their lifetimes, whereas SSM tends to occur in individuals with a high nevus propensity who additionally experience a high number of acute sunburns. Given these different risk profiles, specific prevention strategies could be developed to reduce the risks of LMM and SSM. For example, people of any age with high nevus counts could be particularly counseled to avoid sunburn to lower their risk of SSM, whereas medical practitioners caring for people with many solar lentigines and a history of skin cancer could be alerted to these patients’ increased risk of LMM.

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Author Contributions: Dr Kvaskoff had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Green. Acquisition of data: Green. Analysis and interpretation of data: Kvaskoff, Siskind, and Green. Drafting of the manuscript: Kvaskoff and Green. Critical revision of the manuscript for important intellectual content: Kvaskoff, Siskind, and Green. Statistical analysis: Kvaskoff. Obtained funding: Green. Administrative, technical, and material support: Siskind and Green. Study supervision: Green.

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