Short Communication

The Effect of a School-Based Sun Protection Intervention on the Development of Melanocytic Nevi in Children: 6-Year Follow-up

Dallas R. English,1 Elizabeth Milne,2 Peter Jacoby,2 Billie Giles-Corti,3 Donna Cross,4,5 and Robyn Johnston4

1Cancer Epidemiology Centre, Cancer Council Victoria, Melbourne, Australia; 2Telethon Institute for Child Health Research; 3School of Population Health, University of Western Australia; and 4School of Nursing and Public Health and 5Vario Health Institute, Edith Cowan University, Perth, Australia

Abstract

Because nevi share risk factors with melanoma and are strong risk factors for melanoma, they are suitable biomarkers for evaluating sun protection programs. Kidskin was a trial of a school-based sun protection program in Western Australia that included high and moderate intervention groups and a control group. Schools were assigned nonrandomly to groups. The primary outcome was number of nevi on the back. Nevi were counted at baseline, after 4 years intervention and again 2 years later. Linear growth models, allowing for correlated data within schools and children were fitted to the data. The primary analysis included 639 control children, 414 in the moderate and 355 in the high intervention group. Compared with the control group, the relative increase in number of nevi on the back was 0.89 (95% confidence interval, 0.81-0.99) for the high intervention group and 0.94 (95% confidence interval, 0.86-1.04) for the moderate group (P = 0.09). In subgroup analyses of nevi on the back, the association was stronger in boys (P < 0.001) than in girls (P = 0.7), although the test for interaction was not significant (P = 0.11). For the chest, examined in boys, the associations were similar to that for nevi on the back in boys. Associations were weak for nevi on the face and arms (P = 0.2); for this site, there was weak evidence of heterogeneity by sex. Overall, there was weak evidence that the Kidskin intervention reduced the number of new nevi over a 6-year period, but there was stronger evidence of an effect on the trunk in boys. (Cancer Epidemiol Biomarkers Prev 2005;14(4):977–80)

Introduction

The risk factors for nevi are largely the same as those for melanoma (childhood sun exposure, low tanning ability, and pale skin color) and nevi are strongly related to risk of melanoma (1). Therefore, nevi are suitable biomarkers for evaluating interventions to reduce sun exposure.

In a randomized trial of sunscreen in Vancouver, the children who received sunscreen developed fewer nevi than did controls (2). The Kidskin study was a school-based trial of an intervention to reduce sun exposure in Perth, Western Australia (3). Nevus counts at follow-up in 1999 were slightly lower in the two intervention groups than in the control group.

We report here the results of further follow-up of the Kidskin cohort to 2001.

Materials and Methods

Study Design. The study was a nonrandomized trial conducted from 1995 to 1999 that included a control group of 14 schools, a “moderate” intervention group of 11 schools and a “high” intervention group of eight schools (3). Schools were selected from within geographic clusters. Schools were not randomly assigned to treatment groups because of concerns about contamination and because costs were reduced by designating clusters closest to the center of Perth as eligible for the high intervention group, whereas clusters located farthest from the center of Perth were designated as control group clusters. Random sampling of schools was stratified by an index of socioeconomic status to ensure even distributions (4). All grade 1 children in participating schools were initially recruited, but children of non-European ancestry were later excluded.

The human research ethics committees of the University of Western Australia and Curtin University of Technology approved the study and parents gave written consent.

Intervention. Control schools taught the standard Health Education curriculum (5). Intervention schools taught a specially designed sun protection curriculum from 1995 to 1998 (6) and were given guidelines on school sun protection policies (7).

Outcome Assessment. The main outcome was the number of nevi of any size on the back, although nevi of any size on the face and arms and, in boys, the chest, were also counted. Nevus were not counted on the lower limbs because children have few nevi on these sites (8). Nevus were counted at baseline (1995), in 1999 and in 2001.

Nevi were counted in winter to minimize confusion with freckles and in accordance with a protocol that details methods to distinguish nevi from freckles (9). Under bright light, lay observers trained by dermatologists counted nevi on the face.
and arms. After marking anatomic landmarks, slide photographs of the back, and of boys’ chests, were taken.

All slides of each child’s trunk were projected side by side onto a whiteboard. A lay observer, trained by a dermatologist and blind to study group, identified and marked all preexisting nevi on the baseline slide and new nevi on the 1999 and 2001 slides. Nevi that had disappeared or been excised were also marked (only two excisions were identified). We excluded the shoulders, which are often freckled. The observer indicated whether freckling or poor slide quality made counting difficult.

Standard diagrams were used to assess the level of freckling on the face and arms and on the shoulders when the slides of the back were compared (10).

To permit estimation of inter-rater reliability, the dermatologist counted nevi from 47 randomly selected triplets of slides. Each time nevi on the face and arms were counted, a random sample was assessed by two observers.

**Statistical Analysis.** Proc MIXED in SAS V8 (SAS Institute, Inc., Cary, NC) was used to construct linear growth curves of logged nevus counts for three sites (back, chest, and face and arms combined) with adjustment for confounding variables. We assessed the intervention by comparing models in which each group had its own slope for number of nevi over time with models having a common slope. From the models with separate slopes, we calculated group-specific relative increases in nevi from 1995 to 2001. Secondary analyses included evaluating whether the group-specific slopes differed by gender or level of baseline freckling.

Random intercepts and slopes and covariances between these terms were entered in a stepwise fashion; terms were retained if the likelihood ratio test had \( P < 0.05 \). If no terms were significant, a random intercept was still included. Correlations within children were modeled using a spatial power structure for the error covariance matrix, which allows the covariance of counts from a child to decrease exponentially with the time between the counts. These models fitted better (as measured by Akaike’s Information Criterion) than models with compound symmetrical correlations or with unstructured correlations or with compound symmetrical correlations and better than models with random intercepts and slopes at the person level.

Month of observation, observer (exposed sites only), parental education, tendency to sunburn, ethnicity, hair color, and inner arm skin reflectance were considered as potentially confounding variables (3, 11). Effects of month of observation and observer (exposed sites only) were first removed by performing separate multiple regression models for each year and using the residuals. For the exposed sites, we allowed for different observers in different years by calculating a notional average observer effect for each year. To assess other variables, we then did separate regressions for each child to obtain individual intercepts and slopes over time that were then regressed on the covariates. Those covariates that influenced either the intercepts or the slopes (as assessed by \( P < 0.05 \)) were included in the final analysis. These were sex, inner arm skin reflectance, and hair color.

Inter-rater reliability was assessed by calculating the intraclass correlation coefficient from one-way ANOVA.

**Results**

**Response and Loss to Follow-up.** Of 33 schools selected, 28 agreed to take part in the study. Five replacement schools agreed to participate. None withdrew subsequently. The distribution of the socioeconomic index of the schools was similar in the three groups (data not shown).

Loss to follow-up in 1999 was low and varied little by group (Table 1; \( P = 0.1 \)), but in 2001, the loss was greater and was highest in the control group (\( P = 0.001 \)). Those who last participated in 1999 had similar baseline and 1999 nevus counts on the back, face, and arms to those who continued (baseline means of 15.4 and 16.1, respectively, and 1999 means of 27.4 and 27.3).

Children examined only in 1995 were excluded as were four children assessed in 1995 and 2001 but not in 1999, because they had no measurement of inner arm skin reflectance. A further 45 children were excluded from analyses of nevi on the back because their baseline slides were missing or because counting nevi was impossible due to poor slides or freckling (Table 1).

**Reproducibility of Nevus Counts.** The intraclass correlation coefficient from the analysis comparing the counts of new nevi on the back (1995-2001) by the dermatologist and the observer was 0.94 (95% confidence interval, 0.91-0.97). In 2001, the intraclass correlation coefficient comparing counts of nevi on the face and arms by different observers was 0.91 (95% confidence interval, 0.87-0.95), which was similar to earlier results (11).

**Primary Analyses of Nevi.** At baseline, the moderate intervention group had the lowest mean number of nevi on the back (Table 2). Baseline differences on other body sites were smaller. For all sites, the control group had the largest increase in mean number of nevi during follow-up, but only for the chest was the \( P \) small (Table 2). The high intervention group had the smallest increases in nevi on the trunk.

**Subgroup Analyses of Nevi.** The association for the chest prompted us to perform subgroup analyses by sex for the other sites (Table 2). Although the statistical evidence for different effects in girls and boys was weak (back, \( P = 0.11; \}

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Table 1. Number of children examined each year and included in the analysis of the primary outcome (nevus on the back) by study group

<table>
<thead>
<tr>
<th>Total, ( n ) (%)</th>
<th>Control, ( n ) (%)</th>
<th>Moderate intervention, ( n ) (%)</th>
<th>High intervention, ( n ) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invited to participate</td>
<td>2,529</td>
<td>1,247</td>
<td>727</td>
</tr>
<tr>
<td>Agreed</td>
<td>1,776 (70)</td>
<td>816 (65)</td>
<td>533 (73)</td>
</tr>
<tr>
<td>European origin</td>
<td>1,623</td>
<td>749</td>
<td>472</td>
</tr>
<tr>
<td>Examined</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1995</td>
<td>1,615 (100)</td>
<td>744 (100)</td>
<td>470 (100)</td>
</tr>
<tr>
<td>1999</td>
<td>1,453 (90)</td>
<td>659 (89)</td>
<td>433 (92)</td>
</tr>
<tr>
<td>2001</td>
<td>1,116 (69)</td>
<td>484 (65)</td>
<td>354 (75)</td>
</tr>
<tr>
<td>Included in analysis of nevi on the back</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1,408 (87)</td>
<td>639 (86)</td>
<td>414 (88)</td>
</tr>
<tr>
<td>Data for all years</td>
<td>1,081 (67)</td>
<td>471 (63)</td>
<td>338 (72)</td>
</tr>
<tr>
<td>Data for 1995 and 1999 only</td>
<td>327 (20)</td>
<td>168 (23)</td>
<td>76 (16)</td>
</tr>
</tbody>
</table>
face and arms, $P = 0.19$), the associations for the back seemed different in boys and girls. In boys, the relative increase was least in the high intervention group, but in girls, the three groups had similar relative increases. This also occurred for the face and arms in girls, but boys in both intervention groups had smaller relative increases than the control group.

**Effect of Freckling.** There was no evidence that the group-specific slopes in nevus counts on the back ($P = 0.3$) or face and arms ($P = 0.6$) varied by degree of baseline freckling. For the chest, the relative increase was higher for freckly children in the high intervention group but not in the moderate group ($P = 0.01$).

**Discussion**

In both sexes combined, we found only weak evidence that the increase in number of nevi during follow-up was lower in the two intervention groups. In boys, the high intervention group had the smallest increase in number of nevi on their chests and the control group the largest increase. In secondary analyses, similar associations were observed for the back in boys. In girls, there was no evidence of any differences among the groups for any site. Although these sex-specific findings should be interpreted with caution because we had no prior hypothesis of different effects in boys and girls and the interactions between sex and group had high $P$s, they are consistent with an effect of the intervention that was most pronounced for nevi on the trunk in boys and which may have been stronger for the high intervention group.

These findings are subject to some potential limitations. The study was not randomized and there were baseline differences among groups. For those sites where there was evidence of different slopes in the three groups (i.e., the back and chest in boys), the high intervention group had the highest initial counts as well as the lowest increases over time. Given the high within-person correlations over time, one might have expected the group with the highest mean baseline count to have the greatest slope. Loss to follow-up may have compromised validity. The loss was differential with respect to intervention group but was unrelated to the number of nevi that children had.

Gallagher et al. reported that after 3 years of intervention, the median increase in nevi in the group given sunscreen was 85% as great as in the control group, which was a stronger association than we observed overall. That trial was individually randomized, making it a stronger design, and because it was conducted in Vancouver, where sun protection programs are less widespread than in Australia, would have been subject to less contamination. However, its results may be subject to regression to the mean that would lead to overestimation of the effect of the intervention (12), because there seemed to be baseline differences between groups in nevus counts, and the number of nevi at baseline was not included in the statistical analysis. Regression to the mean may also partly explain the finding of a stronger effect in freckly children, because baseline freckling was strongly associated with baseline nevi. We found no evidence of a stronger effect in children with more freckling at baseline.

Overall, these results confirm our previous conclusion that the Kidskin intervention had, at most, a modest effect on the
development of nevi, although this analysis, with further follow-up, provides reasonable evidence of a stronger effect in boys. The stronger association in boys is difficult to explain because the intervention seemed to have similar effects in boys and girls with respect to sun protective behaviors such as covering the trunk (13). These weak associations occurred despite early indications of a favorable effect on sun protection behavior and the level of suntan (14, 15). One explanation for this apparent inconsistency was that insufficient time had elapsed for behavior change to affect nevi (15). This now seems unlikely to be the explanation. It is more likely that nevi may not be sensitive indicators of sun exposure within populations. Thus, any effect of the Kidskin intervention on sun exposure may have been insufficient to have a substantial effect on nevi, especially in view of high levels of awareness in Australia about the importance of sun protection.

References
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