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The North Queensland "Sun-Safe Clothing" Study: Design and Baseline Results of a Randomized Trial to Determine the Effectiveness of Sun-Protective Clothing in Preventing Melanocytic Nevi

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In 1999, the authors began recruitment for a randomized controlled intervention trial aimed at preventing melanocytic nevi (moles) by minimizing sun exposure through the use of sun-protective clothing. The study involves 652 Caucasian children (75.6% response) aged 0–35 months from 25 child-care centers ($n = 13$ intervention and $n = 12$ control) living in the high-solar-irradiance environment of Townsville, Queensland, Australia. Children attending intervention centers wear investigator-provided garments made from fabrics with ultraviolet protection factors rated very good to excellent. Control centers continue to offer usual care. Three-year follow-up of all children will be completed in 2005. The main outcome measure is the number of new melanocytic nevi. At baseline, the two groups were similar with respect to nevi, phenotype, age, demographic characteristics, sun-protection habits, and history of sun exposure, except that more children from control versus intervention centers (2% and 0%, respectively; $p = 0.006$) had experienced painful sunburn with blistering. Higher melanocytic nevus counts were associated with more time spent outdoors and a history of sunburn, while sunscreen use, particularly during the mild winter months, appeared to have a protective effect. These findings further substantiate the hypothesis that nevus development in young children is related to sun exposure.

child; clothing; health behavior; intervention studies; nevus; skin neoplasms; sunlight

Abbreviations: ARPANSA, Australian Radiation Protection and Nuclear Safety Agency; IQR, interquartile range; SD, standard deviation; UPF, ultraviolet protection factor.

Exposure to sunlight, particularly during childhood, is the principal environmental cause of melanoma (1, 2), and melanoma rates in sunny Queensland, Australia, are among the highest in the world (3). Rates of sun-exposure-related squamous cell and basal cell carcinomas also are extremely high in Queensland (4). Past approaches to prevention have included reducing sun exposure by seeking shade and avoiding the sun between 10 a.m. and 2 p.m. In the past, sunscreens reduced only ultraviolet B radiation (wavelengths of 280–315 nm), thus enabling a high ultraviolet A radiation (wavelengths of 315–400 nm) dosage without sunburn (5). Furthermore, compliance with correct application of sunscreens is low (6, 7), while sun protection from clothing, which minimizes exposure to both ultraviolet A and ultraviolet B radiation, has been underutilized.

The most important biomarker for melanoma is an increased number of melanocytic nevi (moles) (2), and children raised in Queensland develop common (8–11) and atypical (12) melanocytic nevi earlier and in higher numbers than children elsewhere. Melanocytic nevi are precursor lesions of a substantial proportion (up to 60 percent) of melanomas (13). Because sun exposure is related to nevus development during childhood (8–11, 14), melanocytic nevi offer a short-term measure of the efficacy of sun-protection interventions.

Few childhood sun-protection intervention studies have been reported. Most of the studies educated children and/or

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their caregivers about sun protection (15–18) or provided high-sun-protection-factor sunscreens (19, 20). To date, we know of only one study that has reported a statistically significant reduction in the development of melanocytic nevi (19).

In this paper, we present the design and baseline results of a sun-protection intervention in child-care centers in Townsville, Australia. The study commenced in 1999 and appears to be the first controlled intervention trial aimed at reducing sun exposure and, hence, the incidence of melanocytic nevi in young children primarily through regular use of sun-protective clothing.

MATERIALS AND METHODS

Ethical approval was given by James Cook University to conduct a randomized controlled intervention trial in child-care centers. The child-care- and home-based intervention is designed to minimize sun exposure in preschool children by providing garments that cover the trunk, upper arms, thighs, and posterior neck and are made from fabrics with ultraviolet-protection-factor (UPF) ratings in the very good to excellent protection categories (21). The study is ongoing in Townsville (lat 19°16′S), North Queensland, Australia, which has a dry, tropical climate and experiences high levels of ambient solar radiation throughout the year (22).

Recruitment

In June 1999, all 26 of the local day-care centers that provided care for infants and children 5 full days a week were invited to participate. Twenty-five (96.2 percent) agreed.

Prior to commencing the study, the availability and quality of shade at each facility was assessed by measuring the ratio of covered to uncovered play areas and the vertical and horizontal penetration of sunlight for at least five shade structures. Results were given to center directors during recruitment.

During random assignment of centers into intervention ($n = 13$) and control ($n = 12$) groups, each intervention center was matched with a control center on the basis of shade provision (three levels) and the socioeconomic status of the suburb by using the SEIFA index (three levels) (23). Permission to obtain enrollment lists comprising the first name, date of birth, and attendance pattern of children less than age 3 years was obtained from center directors. A study information sheet, a questionnaire, and a consent form were sent to the parents of eligible children via the child-care centers.

Participants

The study included all Caucasian (at least two grandparents of European origin) children aged 0–35 months who regularly attended a participating child-care center between November 1999 and July 2002, and whose parents intended to remain in Townsville and gave their written informed consent to participate ($n = 652$).

Clinical examination

At baseline, the first author (S. L. H.) performed full-body examinations (30 body sites excluding the buttocks, genitals, and scalp) for melanocytic nevi of all sizes on all children based on a standard international protocol to define and count melanocytic nevi (24). These examinations are repeated annually for 3 years (to be completed in July 2005).

It was not possible to blind the examiner to the random assignment because of close involvement in the study. However, very high concordance of melanocytic nevus counts was found for 49 children in March 2003 between the study examiner and an experienced visiting dermatologist (14) (concordance correlation coefficient = 0.97, 95 percent confidence interval: 0.95, 0.98) (25).

Height, weight, and hair and eye color were recorded. Skin reflectance of the inner upper arm was determined with a reflectance spectrophotometer (Evans Electroselenium Ltd., model 99; Diffusion Systems Ltd., London, United Kingdom) at 685 nm for melanin discrimination (high skin reflectance correlates with fair skin) and then categorized as fair/medium/olive on the basis of previously used cutpoints (26). Baseline measurements were missing for 56 children because of instrument repairs. Subjective skin color was assigned to these children (53 fair, three medium).

Questionnaire

All parents completed a comprehensive baseline questionnaire covering the children's demographic and pigmentary characteristics, sunburn history, sun exposure, and sun-protection habits. Habitual sun exposure at baseline was assessed by using charts. Parents marked the amount of time that their child usually spent outside in the sun on a line from 6 a.m. to 7 p.m. Information about the hours spent outside on typical weekdays and weekends and the frequency of "playing outside in the sun during the warmer months of the year" was collected. "Total hours spent outside during the warmer months" and "total hours spent playing in water during the warmer months" were estimated from this information.

Sunburn history was assessed with three questions about the frequency of sunburns resulting in "redness without peeling," "redness with peeling," and "pain and blistering." The frequency of each type was weighted 1, 2, and 3, respectively, and was summed to give a combined severity score. Parents were asked to mark, on a body-site diagram, those areas that had been sunburnt. A score for the extent of sunburn was obtained by summing the respective body sites and adjusting according to the surface area affected (27–31). Another combined score of the extent and severity of sunburn was created by multiplying the two scores. Similarly, parents marked the body sites on which "sunscreen was usually applied on a typical day." A score for sunscreen protection was created by summing the number of body sites adjusted for surface area (27–31) and multiplying by frequency of use at home during 1) summer and 2) winter (never = 0, less than half the time = 1, half the time = 2, more than half the time = 3, almost always = 4).

TABLE 1. Summary of all measures conducted for children in control and intervention child-care centers during the nevus intervention study in Townsville, Queensland, Australia, 1999–2005

Both groups	
Shade audit conducted.	
Subjects recruited from intervention and control child-care centers between November 1999 and July 2002 by sending parents a detailed information sheet outlining the relevance (association between melanocytic nevi, childhood sun exposure, and melanoma) and expectations of the study, together with a consent form and questionnaire.	
Baseline phenotypic assessment and melanocytic nevus examination conducted by using International Agency for Research on Cancer protocol (24). Melanocytic nevi recorded separately for 30 body sites.	
Melanocytic nevus examination (30 body sites) repeated annually for 3 years. Parents sent an annual summary of the number of melanocytic nevi their child has.	
Annual phenotypic assessment performed including eye, skin, and hair color as well as measurements of skin reflectance on unexposed and exposed sites.	
Questionnaire and diary completed by a senior staff member in each unit (age group) in each child-care center showing time and duration of outdoor activities and use of various forms of sun protection.	
Regular parental sun-exposure questionnaires.	
Control group	Intervention group
Observations of sun-protective behaviors undertaken at centers when obtaining lists of potential participants and conducting melanocytic nevus examinations.	Observations of compliance/sun-protective behaviors undertaken twice a week when collecting laundry and conducting melanocytic nevus examinations.
Sun-protective clothing *not* distributed (children continued to receive usual care).	Sufficient high-UPF* clothing and legionnaire hats provided to clothe all children.
	Clothing maintained by laundry service. Monitoring of weekly laundry volumes allows prompt investigation of lower-than-usual clothing usage.
	Staff instructed on correct use of high-UPF clothing.
	Parents educated about sun protection and correct use of garments at the center and at home (education session and instruction sheet).
	Legionnaire hats and high-UPF swimwear (long-sleeved UPF 40+ nylon taslon shirt and commercially available UPF 50+ Lycra (nylon elastane) suit with long sleeves with either full or knee-length legs) given to children to use at home (issued at time of recruitment and annually thereafter for 3 years).

* UPF, ultraviolet protection factor.

Scores for hat and swimwear protection were derived from questions about type and frequency of use during 1) summer and 2) winter. A score for hat use was created by multiplying the responses for the following variable: ''What does your child wear on his or her head most often when outdoors?'' (nothing = 0, a cap = 1, a wide-brimmed hat = 2, a legionnaire hat = 3) and the sum of the responses to these questions: ''How often does your child wear this hat when he or she is outdoors during 1) summer and 2) winter?'' (never = 0, less than half the time = 1, half the time = 2, more than half the time = 3, almost always = 4). Likewise, a score was created for swimwear protection by multiplying responses for these variables: ''What does your child wear most often when he or she is playing in water?'' (nothing = 0, shorts/briefs = 1, two-piece swimsuit = 2, one-piece swimsuit = 3, shorts/one-piece/briefs and a T-shirt = 4, Lycra (nylon elastane; E. I. du Pont Nemours & Co., Inc., Wilmington, Delaware) cover-up suit = 5) and ''How often does your child wear this when he or she is playing in water?'' (never = 0, less than half the time = 1, half the time = 2, more than half the time = 3, almost always = 4) for summer and winter.

Intervention design

Each of the 13 child-care centers in the intervention group was given enough legionnaire hats and high UPF T-shirts and shorts to clothe all children in their baby and toddler units (which care for children less than age 3 years). Intervention child-care staff members were trained to dress the children in this clothing on arrival each day to ensure that the trunk, posterior neck, upper arms, and thighs were covered when outdoors. Laminated signs on the exit doors of intervention child-care buildings reminded staff to dress all children in the sun-protective clothing before going outdoors. Dirty garments were collected twice a week from intervention centers by research staff, the garments were laundered, and compliance with the intervention was observed (table 1). Weekly laundry volumes were monitored. The parents of children in the intervention group were educated about the appropriate use of protective clothing at the center and at home, and they were given legionnaire hats for home use and garments made of fabrics in the ''excellent'' ultraviolet radiation protection category to wear during water activities.

Children attending control centers do not receive sun-protective clothing but continue with their usual sun protection. They are examined annually for melanocytic nevi for 3 years, and their parents complete the same questionnaires as the parents of the intervention group. Any movement of children and staff between intervention and control centers is monitored. A summary of all measures conducted in control and intervention centers and for the children is provided (table 1).

Clothing design

Advice about suitable fabrics was sought from local clothing manufacturers, their suppliers, and Dr. Peter Gies from the Australian Radiation Protection and Nuclear Safety Agency (ARPANSA). Samples of fabrics with properties usually associated with low ultraviolet radiation transmission (tight weave, darker colors, etc.) (32) were discussed with the staff of the intervention child-care centers. Samples of cotton and nylon taslon (a fine, lightweight, shower-proof fabric) in a range of colors were sent to ARPANSA for UPF testing, and the fabrics with the highest mean UPF measurements were chosen.

Prototype T-shirts, shorts, and long-sleeved shirts in sizes 0–8 were tested on 200 infants and preschool children to ensure that they would adequately cover the trunk, thighs, and upper arms. The T-shirts were made from 100 percent cotton in five colors (sizes were color coded for staff convenience) with UPF ratings in the ''very good'' protection category (a UPF range of 25–39 blocks 96–97.4 percent of ultraviolet radiation) (21). The standard sleeve length for each size was extended by 21 percent to ensure that the sleeves were at least elbow length. The shorts covered the legs to below the knees and were made from water-resistant nylon taslon in five colors, with UPF ratings in the ''excellent'' protection category (a UPF range of 40–49, 50+ blocks $\geq$97.5 percent of ultraviolet radiation) (21). The long-sleeved shirts were made of the same fabric, with contrasting colored cuffs and neckband. To prevent contamination of the control population, these garments were manufactured for the study only.

Outcome measures

Total number of melanocytic nevi was the main target variable for the present baseline assessment. For a more convenient description of main risk factors, melanocytic nevi were dichotomized by using the median ($\leq$1 vs. >1) as the cutpoint, thus enabling multivariate logistic regression analysis to produce effect measures (e.g., prevalence odds ratios) rather than regression coefficients.

Power calculations

Estimation of the required sample size was initially based on achieving a 24 percent reduction in the total number of melanocytic nevi (all sizes) and a 30 percent reduction in melanocytic nevi $\geq$2 mm by 4 years of age, a choice based on reducing the prevalence of melanocytic nevi at age 4 years to that expected for children of that age raised in Sydney, which has less ambient ultraviolet radiation (8). To achieve a power of 80 percent and a significance level of 0.05, two groups of 72 children (standard deviation (SD), 26) were required to detect a 24 percent reduction in mean total number of melanocytic nevi (Townsville = 52.3, Sydney = 40), and two groups of 110 (SD, 10) were required to detect a 30 percent reduction in melanocytic nevi $\geq$2 mm (Townsville = 12.7, Sydney = 8.9) by age 4 years (8, 9). Thus, the study was planned to prevent an average of 12.3 incident melanocytic nevi (all sizes) and of 3.8 incident melanocytic nevi $\geq$2 mm (medians = 12 and 3, respectively) over a 3-year period. A third body-site-specific hypothesis was formulated based on preventing a mean of 3.8 melanocytic nevi (25 percent reduction; median = 3.75, SD, 10.0) on the arms in 3 years (sample size: 110 children/group assuming the same specifications as for the two other hypotheses).

Sample size calculation (adjusted for multiple testing of the three main hypotheses, violation of normality assumptions, and the design effect (1.5) of cluster sampling) estimated a necessary sample size of 230 children per group. Because the Townsville population is transient, the sample size was increased to account for loss to follow-up during the 3-year study period.

Statistical analysis

All numerical variables with a skewed distribution were described by using median values and interquartile ranges (IQRs); approximately normally distributed numerical variables were described by using means and standard deviations. The density of melanocytic nevi was calculated by using the formula suggested by the US Environmental Protection Agency (27).

Bivariate analysis of risk factors for melanocytic nevi initially used standard statistical tests (chi-square test, *t* test, nonparametric Wilcoxon test, Pearson and Spearman correlation coefficients). Bivariate results of parametric tests and chi-square statistics were adjusted for the cluster sampling design by using the survey commands in Stata statistical software, release 8.0 (Stata Corporation, College Station, Texas). Adjustment of nonparametric test results for the cluster sampling design was not directly possible. Therefore, numerical characteristics with skewed distributions were log-transformed to enable comparisons of adjusted transformed mean values. For those characteristics, the untransformed median values and IQR were presented together with the adjusted and unadjusted *p* values. The success of the randomization process was assessed bivariately by comparing children in the intervention group with children in the control group regarding all potential risk factors considered. These comparisons were also adjusted for the cluster sampling design.

Multivariate linear regression and multivariate logistic regression analyses were used to identify risk factors for the prevalence of melanocytic nevi. The log-transformed total number of melanocytic nevi was used as the target variable for the multivariate linear regression analysis. For logistic regression analysis, number of melanocytic nevi was dichotomized by using the median ($\leq$1 vs. >1) as the cutpoint.

TABLE 2. Predictive factors for melanocytic nevi at baseline in 652 young children attending 25 child-care centers in Townsville, Queensland, Australia, adjusted for cluster sampling, 1999–2002

Predictive factor	Total ($n = 652$)	≤1 MN†,‡ ($n = 345$)	>1 MN ($n = 307$)	p value
Phenotypic characteristics				
Mean age in months (SD†)	15.3 (13.8)	11.9 (8.6)	19.2 (6.7)	<0.001
Female sex (%)	46.8	46.7	46.9	0.952
Fair-skinned (%)	95.6	95.7	95.4	0.878
Blue or green eyes (%)	66.0	66.4	65.5	0.540
Fair or blond hair (%)	64.9	59.7	70.7	0.001
Skin "always burns" after 30 minutes of sun exposure (%)	34.7	42.6	26.4	0.001
Skin "never tans" after 30 minutes of sun exposure (%)	15.0	19.9	10.1	0.089
Four Caucasian grandparents (%)	81.8	80.9	82.7	0.569
Demographic characteristics				
At least one parent with a university degree (%)	36.5	37.5	35.3	0.517
Born in the Tropics (%)	90.2	91.6	88.6	0.332
Sun exposure				
Median no. of hours spent outside on a typical day (IQR†)	2.3 (1.2, 4.0)	2.0 (0.9, 3.0)	3.1 (1.7, 4.6)	<0.001
				<0.001*
Median no. of hours spent outside on a typical day during the warmer half of the year (IQR)	2.4 (1.1, 4.0)	2.0 (0.9, 3.1)	3.1 (1.6, 4.6)	<0.001
				<0.001*
Median total no. of hours spent outside during the warmer half of the year prior to examination (IQR)	178.3 (30, 479)	89.1 (3.5, 312)	357.0 (91, 635)	<0.001
				<0.001*
Median no. of hours spent playing in water on a typical day during the warmer half of the year prior to examination (IQR)	2 (1, 3.25)	1.5 (0.5, 3)	2 (1, 4)	<0.001
				<0.001*
Median total no. of hours spent playing in water during the warmer half of the year prior to examination (IQR)	45 (4.5, 175.5)	30 (1, 117)	78 (19.5, 204)	<0.001
				<0.001*
At an outdoor pool "at least once a week" during the warmer months (%)	40.7	33.7	48.5	<0.001
At the beach "at least once a week" during the warmer months (%)	8.8	7.0	10.8	<0.001
Played outside "almost every day" during the warmer months (%)	42.9	29.9	57.3	<0.001
Sunburn characteristics				
At least one sunburn with "redness without peeling" (%)	44.3	33.8	56.0	<0.001

Table continues

After stable models were reached with either linear or logistic regression analysis by using stepwise selection procedures, all remaining variables were considered as potential confounders, and models were adjusted accordingly. All possible interactions between variables of one model were defined and checked for significance in hierarchical models. Results of the linear regression analysis were given as regression coefficients and 95 percent confidence intervals, whereas results of logistic regression analysis were presented as prevalence odds ratios with 95 percent confidence intervals. The results of multivariate linear and logistic regression analyses were adjusted for the cluster sampling design.

RESULTS

Response

Of the 1,136 children invited to participate, 273 were ineligible because of age (>35 months, $n = 22$) or because they were unavailable for follow-up ($n = 221$), were non-Caucasian ($n = 17$), or did not attend child-care regularly ($n = 13$). Of the 863 eligible children, 753 (87.3 percent) participated and were examined for melanocytic nevi at baseline. However, the parents of only 652 of these children completed a baseline questionnaire (response: 75.6 percent).

Randomization

Overall, 393 children (60.3 percent) attended intervention centers. They were slightly younger (age 14.6 months (SD, 14.1) vs. 16.4 months (SD, 16.0)) and were less likely to be blond or fair-haired than children in the control group (61.1 percent vs. 70.7 percent) but not significantly so after adjustment for cluster sampling ($p = 0.0977$ and $p = 0.0816$, respectively). Only two significant differences were noted between children in the intervention and control groups: the proportion who had experienced at least one very painful, blistering sunburn (0 percent vs. 2 percent, respectively; $p = 0.0060$) and the proportion who usually wore legionnaire hats (50.1 percent vs. 39.3 percent, respectively; $p = 0.0453$). However, when hat-wearing practices were examined further, we found that similar proportions of children in the intervention and control groups usually wore legionnaire or wide-brimmed hats

TABLE 2. Continued

Predictive factor	Total ($n = 652$)	≤1 MN†,‡ ($n = 345$)	>1 MN ($n = 307$)	p value
At least one sunburn that "burned with peeling" (%)	4.3	3.2	5.5	0.146
At least one sunburn that was "very painful with blistering" (%)	0.8	0.6	1.0	0.584
Median score of history of sunburn weighted according to severity (IQR)	1 (0, 1)	0 (0, 1)	1 (0, 1)	<0.001 <0.001*
Median score of extent of sunburn (IQR)	0 (0, 0.13)	0 (0, 0.07)	0.07 (0, 0.14)	<0.001 <0.001*
Median score of history of sunburn weighted according to extent and severity (IQR)	0 (0, 0.13)	0 (0, 0.07)	0.07 (0, 0.15)	<0.001 <0.001*
Use of sun protection				
Parents ever used sunscreen on their child at home (% of children)	91.7	88.4	95.4	0.004
Use SPF† 30+ sunscreen§ (%)	77.1	77.2	77.1	0.989
Parents "almost always" apply sunscreen to their child at home in summer (% of parents)	47.4	51.3	43.1	<0.001
Parents "almost always" apply sunscreen to their child at home in winter (% of parents)	29.1	32.9	24.8	0.008
Mean no. of body sites (24) on which sunscreen was usually applied (SD)	7.5 (3.4)	7.3 (4.4)	7.7 (2.8)	0.211
Median surface area to which sunscreen was usually applied (IQR)	0.44 (0.27, 0.52)	0.44 (0.27, 0.52)	0.45 (0.28, 0.52)	0.725 0.312*
Median sunscreen protection score weighted by surface area and frequency of use (IQR)	2.0 (0.9, 3.2)	2.1 (0.8, 3.6)	1.9 (0.9, 3.0)	0.315 0.755*
Usually wear a legionnaire hat when outdoors (%)	45.8	43.4	48.5	0.527
Median hat-use score weighted according to hat style and frequency of use (IQR)	16 (8, 24)	16 (8, 24)	16 (8, 24)	0.751 0.847*
Usually wear a Lycra (nylon elastane) cover-up suit when in water (%)	64.9	62.2	67.7	0.482
Median swimwear protection score weighted according to style and frequency of use (IQR)	25 (16, 25)	25 (20, 25)	25 (15, 25)	0.807 0.607*

* The first p value relates to a nonparametric test comparing median values without cluster adjustment; the second p value relates to comparison of mean values of log-transformed variable adjusted for cluster sampling.

† MN, melanocytic nevi; SD, standard deviation; IQR, interquartile range; SPF, sun-protection factor.

‡ Children with a maximum of 1 MN (1 = median no. of MN).

§ SPF 30+ is the maximum protection that can currently be claimed on sunscreen labels in Australia.

when outdoors (79.5 percent vs. 79.4 percent, respectively; $p = 0.9658$).

Description of all children at baseline

A total of 652 children (46.8 percent girls) attending 25 child-care centers participated, and their ages ranged from 1 to 35 months (mean = 15.3 months (SD, 13.8)) (table 2). Almost all (95.6 percent) had a fair complexion. Most children (90.2 percent) were born in the Tropics and had four Caucasian grandparents (81.8 percent). Most questionnaires (93.7 percent) were completed by the children's mothers.

The median number of melanocytic nevi was 1 (IQR = 0, 4), with counts ranging from 0 to 44. The child with 44 melanocytic nevi was a girl aged 35 months with a fair complexion. Almost a third (31.1 percent) of the children had no melanocytic nevi at the baseline clinical examination. Overall, the median density was 2.4 melanocytic nevi/m^2 (IQR = 0, 7.3) with no difference between boys and girls ($p = 0.812$) but with a strong positive regression on age ($p < 0.001$).

Bivariate analyses

The children spent a median of 2.3 hours (IQR = 1.2, 4.0) outside in the sun on a typical day and a median of 178.3 hours (IQR = 30, 479) outside in the sun during the warmer half of the year prior to examination (table 2). Children with more than one nevus were likely to have spent more hours in the sun on a typical day ($p < 0.001$) and during the warmer half of the previous year ($p < 0.001$) and to have spent more hours playing in water on a typical day ($p < 0.001$) and during the warmer half of the previous year ($p < 0.001$). Children whose melanocytic nevus counts were above the median were more likely to play outside in the sun almost daily during the warmer months of the year ($p < 0.001$). Overall, 44.3 percent of children had a history of sunburn with "redness without peeling," and more children with higher-than-median melanocytic nevus counts than other children had experienced this type of sunburn ($p < 0.001$). Children with higher-than-median melanocytic nevus counts also tended to have higher sunburn scores (all $p < 0.001$).

TABLE 3. Predictive factors for melanocytic nevi at baseline in young children (n = 577)* recruited in Townsville, Queensland, Australia, 1999–2002: results of multivariate linear regression using the log-transformed total count of melanocytic nevi as the target variable

Predictive factor	Estimate	95% CI†	p value
Age in months	0.075	0.064, 0.086	<0.001
Red hair color	−0.119	−0.374, 0.136	0.344
Experienced at least one sunburn with "redness without peeling"	0.177	0.046, 0.307	0.010
Interaction between red hair color and sunburn experience‡	−0.472	−0.808, −0.135	0.008
Playing outside in the sun "almost every day" during warmer months of the year	0.200	0.076, 0.324	0.003

* Sample was reduced because the parents of 61 of these very young children were uncertain how their child's skin would react to the sun after 30 minutes of unprotected exposure at the beginning of summer. The ability to address this question with certainty increases with the age of the child.

† CI, confidence interval.

‡ The effects of the original variables can no longer be interpreted if an interaction is in the model. The model was adjusted for the confounding effects of skin's reaction to the sun and the application of sunscreen at home in summer. The multiple correlation coefficient of the model was 0.666. Results were adjusted for the effects of cluster sampling.

When asked about sunscreen use, 47.4 percent of parents reported "almost always" applying it to their child during summer, and 29.1 percent "almost always" did so in winter. Children whose parents "almost always" applied sunscreen to their skin during summer ($p < 0.001$) and winter ($p = 0.008$) had fewer melanocytic nevi than children who used sunscreen less often.

Parents of 45.8 percent of the children reported that their child usually wore a legionnaire hat outdoors and 64.9 percent usually wore a Lycra "cover-up" swimsuit during water activities. These behaviors were more common among boys (both $p < 0.001$).

Results of multivariate linear regression analysis

Increasing age ($p < 0.001$) and playing outside in the sun almost every day during the warmer months ($p = 0.003$) were associated with higher melanocytic nevus counts (table 3). There was a significant protective interaction ($p = 0.008$) for children with red hair who had experienced one or more sunburns with "redness without peeling."

Multivariate logistic regression analysis

Increasing age ($p < 0.001$), a history of sunburn ($p = 0.019$), and applying sunscreen at home in winter up to half the time ($p = 0.025$) were significant predictors of higher-than-median melanocytic nevus counts (table 4). The significance of "playing outside in the sun almost every day during the warmer months" changed from $p = 0.021$ to $p = 0.070$ after adjustment for the confounding variable, reaction of child's skin to the sun. Red hair had a more protective effect than blond or dark hair ($p = 0.002$).

DISCUSSION

Consistent with previous findings (9), higher melanocytic nevus counts were associated with increased time spent outdoors and a history of sunburn, providing further evidence that acute and chronic sun exposure contribute to the development of melanocytic nevi in young children. The prevalence of melanocytic nevi is similar to that reported previously for children from Queensland (10, 33).

Sunscreen appeared to have a protective effect against melanocytic nevi. A slight, nonsignificant protective effect (odds ratio = 0.9) was detected for "almost always" wearing sunscreen when outdoors during summer, while children for whom parents applied sunscreen more than half the time during Queensland's mild winter had significantly fewer melanocytic nevi than children who wore sunscreen less often at this time of year. It is possible that the protective effect of winter sunscreen use was stronger because sunscreen use is generally lower at this time of year and is probably confined to those parents who are very careful to protect their child from the sun. In contrast, summer sunscreen use is common in this community, and it is conceivable that some of these children spend much more time outdoors as a result, thereby reducing the benefits it affords.

Although only cross-sectional, this finding supports those of a Canadian study (19) that showed that schoolchildren who used high-sun-protection-factor sunscreen developed fewer melanocytic nevi than control children did. Although regular sunscreen use reduced the incidence of melanocytic nevi in children from temperate regions with moderate ambient ultraviolet radiation, we were skeptical whether sunscreen use could be improved enough to achieve the same result in Queensland, where an estimated 90 percent (IQR = 25.5, 100) of children attending child care already wear sun-protection-factor 30+ sunscreen (S. L. H., unpublished manuscript).

When we were planning this intervention study, the only findings that showed promise for the prevention of melanocytic nevi were associated with clothing use (34, 35). Enta (34) reported lower mean numbers of melanocytic nevi in a cross-section of Hutterite children (a Christian sect that

TABLE 4. Predictive factors for melanocytic nevi at baseline in young children (n = 577)* recruited in Townsville, Queensland, Australia, 1999–2002: results of logistic regression analysis comparing children with a maximum of one nevus with children who have multiple melanocytic nevi†

Predictive factor	≤1 MN‡ (n = 294)	>1 MN (n = 284)	Prevalence odds ratio	95% CI‡,§	p value
Age in months	Continuous		1.30	1.2, 1.4	<0.001
Hair color					
Dark	83	80	1		
Blond	181	197	0.82	0.5, 1.4	0.473
Red	30	7	0.14	0.04, 0.5	0.002
Playing outside in the sun during warmer months of the year					
Less often	201	120	1		
Almost every day	93	164	1.60	0.96, 2.7	0.070
History of sunburn "redness without peeling"					
No	182	120	1		
Yes	112	164	1.70	1.1, 2.7	0.019
Application of sunscreen at home in winter					
More than half the time	133	101	1		
Half the time or less often	161	183	1.60	1.1, 2.4	0.025
Skin's reaction to the sun¶					
Burn less often	79	120	1		
Burn most of the time or always	215	164	0.84	0.5, 1.4	0.477

* Sample was reduced because the parents of 61 of these very young children were uncertain how their child's skin would react to the sun after 30 minutes of unprotected exposure at the beginning of summer. The ability to address this question with certainty increases with the age of the child.

† One nevus was the median of the distribution.

‡ MN, melanocytic nevi; CI, confidence interval.

§ The model predicted 76.0% of the cases correctly.

¶ The model was adjusted for the confounding effects of the skin's reaction to the sun. No significant interactions were detected. Results were adjusted for the effects of cluster sampling.

wears traditional clothing covering the entire body except the face and hands) in Alberta, Canada, compared with non-Hutterite children from central Alberta. Similarly, Autier et al. (35) found fewer melanocytic nevi on the trunks of European children aged 6–7 years in the highest category of clothing use and more truncal melanocytic nevi among children in the highest category of sunscreen use. Given that high-UPF clothing was underutilized and is easier to use to achieve consistent broad-spectrum protection than sunscreens, which are often applied too thinly and not reapplied at appropriate intervals (6, 7, 36), we chose to use clothing. This choice seems appropriate given recent reports of the correlation between the global distribution of ultraviolet A radiation and melanoma mortality rates (37) and evidence that the carcinogenic potential of ultraviolet A radiation has been underestimated (38).

At baseline, children in the intervention and control groups were alike except for very painful sunburns with blistering, where five controls, but no children in the intervention group, had had such an experience. The two groups were also similar in their use of sun protection, except that more children in the intervention group than controls usually wore a legionnaire hat when outdoors. This finding is probably due to ongoing recruitment, because children in the intervention group who were recruited after the clothing had been introduced into the intervention centers would have been given a legionnaire hat from the center's stockpile (provided by the investigators) to wear while at the center. Thus, the response to the question regarding the style of hat usually worn when outdoors may not reflect the baseline situation for children in the intervention group recruited into the study later but is more a measure of compliance with hat wearing in this subset of children. A more accurate assessment of baseline hat-wearing practices would have been obtained by asking about the style of hat worn at home and at child care separately. This situation could have been prevented and the management of annual examinations simplified if the population had been sufficiently large to recruit and examine the entire cohort simultaneously. However, multiple examiners would have been needed, and tracking the movement of children

and staff between child-care centers would have been more difficult.

We are confident that our measures for assessing the effect of the intervention are valid and reproducible. Melanocytic nevi were counted by one experienced examiner using a standard international protocol, and there was high concordance with an experienced dermatologist who was blinded to the randomization. Site-specific sunscreen use and information about other forms of sun protection collected in parental and staff questionnaires will enable us to control for potential confounders (e.g., sunscreen use on unprotected body sites) in the final analysis.

Limitations of the study include the possibility that parents overreported their children's sun-protective practices at baseline because they were aware of our interest in sun exposure and thus reported socially acceptable behavior. Nondifferential classification such as this has the potential to bias the results toward the null hypothesis. In addition, although interaction with control centers has been minimized to avoid altering their sun-protection behavior, in keeping with the guidelines for ethical research, we have been providing the parents of children in both groups with annual feedback on the number of melanocytic nevi their child has. This practice may improve sun-protective behavior among controls and make it more difficult to detect a difference in incident melanocytic nevi between the two groups at the completion of the study. However, because we inflated our sample size beyond that required to detect a 24 percent reduction in incident melanocytic nevi, we should have sufficient power to detect a difference as small as that achieved previously using sunscreens (19) with power in excess of 80 percent, and to answer hypotheses relating to body sites (upper arms, thighs, trunk, and posterior neck) specifically protected by clothing.

In conclusion, the present findings further substantiate the relation between melanocytic nevi and sun exposure. Although it seems likely that sun protection may reduce the number of melanocytic nevi that develop during childhood (and hence the risk of melanoma), the answer to this question awaits completion of the current intervention.

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REFERENCES

1. Armstrong BK, Kricker A. How much melanoma is caused by sun exposure? Melanoma Res 1993;3:395–401.
2. Armstrong BK, English D. Epidemiologic studies. In: Balch CM, Houghton AN, Milton GW, et al, eds. Cutaneous melanoma. Philadelphia, PA: J B Lippincott Company, 1992:12–26.
3. MacLennan R, Green AC, McLeod GRC, et al. Increasing incidence of cutaneous melanoma in Queensland, Australia. J Natl Cancer Inst 1992;84:1427–32.
4. Buettner PG, Raasch BA. Incidence rates of skin cancer in Townsville, Australia. Int J Cancer 1998;78:587–93. (Erratum in Int J Cancer 2001;93:302–3).
5. Diffey BL, Farr PM. UVA filters in sunscreen preparations. Lancet 1989;2:170–1.
6. Stokes R, Diffey B. How well are sunscreen users protected? Photodermatol Photoimmunol Photomed 1997;13:186–8.
7. Pincus MW, Rollings PK, Craft AB, et al. Sunscreen use on Queensland beaches. Australas J Dermatol 1991;32:21–5.
8. Kelly JW, Rivers JK, MacLennan R, et al. Sunlight: a major factor associated with the development of melanocytic naevi in Australian schoolchildren. J Am Acad Dermatol 1994;30:40–8.
9. Harrison SL, MacLennan R, Speare R, et al. Sun exposure and melanocytic naevi in young children in Townsville, Queensland. Lancet 1994;344:1529–32.
10. Harrison SL, MacKie RM, MacLennan R. Development of melanocytic nevi in the first 3 years of life. J Natl Cancer Inst 2000;92:1436–8.
11. Green A, Siskind V, Hansen ME, et al. Melanocytic nevi in schoolchildren in Queensland. J Am Acad Dermatol 1989;20:1054–60.
12. Rivers JK, MacLennan R, Kelly JW, et al. The eastern Australian childhood nevus study: prevalence of atypical nevi, congenital nevus-like nevi, and other pigmented lesions. J Am Acad Dermatol 1995;32:957–63.
13. Bauer J, Garbe C. Acquired melanocytic nevi as risk factor for melanoma development. A comprehensive review of epidemiological data. Pigment Cell Res 2003;16:297–306.
14. Sander Wiecker T, Luther H, Buettner P, et al. Moderate sun exposure and nevus counts in parents are associated with development of melanocytic nevi in childhood. Cancer 2003;97:628–38.
15. Milne E, English DR, Cross D, et al. Evaluation of an intervention to reduce sun exposure in children: design and baseline results. Am J Epidemiol 1999;150:164–73.
16. MacKie RM, Turner S, Harrison SL, et al. A comparison of the rate of development of naevi in infants in Scotland and Australia. (Abstract). Melanoma Res 1997;7:S4.
17. Girgis A, Hancock L, Perkins J, et al. Community action: does it impact on sun protection practices in rural communities. (Abstract). Melanoma Res 1997;7:S17.
18. Milne E, Johnston R, Cross D, et al. Effect of a school-based sun-protection intervention on the development of melanocytic nevi in children. Am J Epidemiol 2002;155:739–45.
19. Gallagher RP, Rivers JK, Lee TK, et al. Broad-spectrum sunscreen use and the development of new nevi in white

children: a randomised controlled trial. JAMA 2000;283: 2955–60.
20. Whiteman D, Green A, Hayward N, et al. Natural history and prevention of melanocytic naevi (''moles'') in early childhood. Brisbane, Queensland, Australia: Queensland Institute of Medical Research, Cancer and Population Studies Group. Last modified November 30, 2003. (http://www.qimr.edu.au/research/labs/adeleg/melanoma.html). Accessed April 20, 2004.
21. Sun protective clothing—evaluation and classification. Sydney, Australia: Standards Australia, 1996. (Publication no. AS/NZS 4399:1996).
22. Hornby F. The Townsville region: a social atlas. Townsville, Australia: Townsville City Council, 1986.
23. 1996 Census of population and housing—socio-economic indexes for areas (SEIFA). Canberra, Australia: Australian Bureau of Statistics, 1996. (Catalog no. 2033.0).
24. English DR, MacLennan R, Rivers J, et al. Epidemiological studies of melanocytic naevi: protocol for identifying and recording naevi. Lyon, France: International Agency for Research on Cancer, 1990. (IARC internal report no. 90/002).
25. I-Kuei Lin L. A concordance correlation coefficient to evaluate reproducibility. Biometrics 1989;45:255–68.
26. Harrison SL, Buettner PG. Do all fair-skinned individuals consider themselves to be fair? Prev Med 1999;29:349–54.
27. US Environmental Protection Agency. Exposure factors handbook. Final report. Washington, DC: Office of Health and Environmental Assessment, 1989. (EPA/600/8-89/043).
28. Boyd E. The growth of the surface area of the human body. Institute of Child Welfare monograph series 10. Minneapolis, MN: University of Minnesota Press, 1935:53–60.
29. Berkow SG. A method of estimating the extensiveness of lesions (burns and scalds) based on surface area proportions. Arch Surg 1924;8:138–48.
30. Lund CC, Browder NC. The estimation of areas of burns. Surg Gynecol Obstet 1944;79:352–8.
31. Harrison SL, Buettner PG, MacLennan R. Body site distribution of melanocytic nevi in young Australian children. Arch Dermatol 1999;135:47–52.
32. Gies P, Roy C, McLennan A, et al. Ultraviolet protection factors for clothing: an intercomparison of measurement systems. Photochem Photobiol 2003;77:58–67.
33. Whiteman DC, Brown RM, Purdie DM, et al. Prevalence and anatomical distribution of naevi in young Queensland children. Int J Cancer 2003;106:930–3.
34. Enta T. Melanocytic nevi in sun-protected Canadian Hutterite children. Arch Dermatol 1998;134:379–81.
35. Autier P, Dore J, Cattaruzza M, et al. Sunscreen use, wearing clothes, and number of nevi in 6–7 year old European children. J Natl Cancer Inst 1998;90:1873–80.
36. Stenberg C, Larko O. Sunscreen application and its importance for the sun protection factor. Arch Dermatol 1985; 121:1400–02.
37. Garland CF, Garland FC, Gorham ED. Epidemiologic evidence for different roles of ultraviolet A and B radiation in melanoma mortality rates. Ann Epidemiol 2003;13:395–404.
38. Agar NS, Halliday GM, Barnetson RS, et al. The basal layer in human squamous tumors harbors more UVA than UVB fingerprint mutations: a role for UVA in human skin carcinogenesis. Proc Natl Acad Sci U S A 2004;101:4954–9.