

INVESTIGATIVE REPORT

Changes in Body-site Distribution of Common Melanocytic Naevi Among 7-year-old Swedish Children Between 2002 and 2007

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An observational population-based study conducted among 2 sets of 7-year-old children in Sweden in 2002 and 2007 revealed evidence of improved sun protection, also reflected in a significant reduction in the total number of melanocytic naevi. Based on these data-sets, the aim of the current study was to determine whether the overall reduction in naevi had impacted differently on body sites based on their main pattern of sun exposure. In 2002, median naevi counts/m² were highest on intermittently sun-exposed sites: 13.8 (95% CI 8.0–22.7) compared with chronically sun-exposed sites: 11.0 (95% CI 0.0–20.5). In 2007, median naevi counts/m² on intermittently sun-exposed body sites were significantly lower: 8.7 (95% CI 4.7–15.2), $p < 0.0001$, while on chronically exposed sites median naevi counts/m² were unaltered: 10.3 (95% CI 0.0–14.4), $p = 0.9313$. Changes were most evident among boys. Future research can evaluate whether this shift in naevi distribution in Swedish children translates into a reduction in cutaneous melanomas on intermittently sun-exposed body sites. *Key words: children; epidemiology; melanocytic naevus; melanoma; primary prevention; sunlight.*

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Mapping of common melanocytic naevi (CMN) in different geographical regions, by phenotype, age, sex and history of sun exposure, has revealed CMN as the best objective predictor of cutaneous malignant melanoma (CMM) risk (1, 2). The trunk, upper arms and thighs represent body sites generally considered as intermittently sun-exposed associated with high CMN densities and correspondingly high incidence of CMM (3, 4). Studies of children conducted among fair-skinned populations in Europe, Northern America and Australia (5–9) indicate CMN distribution and sex profiles largely consistent with those seen in adults. However, CMN densities in children are readily influenced by changes in sun exposure which was demonstrated in a cross-sectional, population-based study published by our research group

in 2011 (10). In this study 2 sets of 7-year-old children residing in southern Sweden were surveyed in the years 2002 and 2007. Results demonstrated a highly significant reduction in total mean numbers of CMN for 7-year-old children residing in southern Sweden in 2007 compared with 2002. Although sunny holidays abroad have become more common, parental questionnaires demonstrated significant improvements in 2007 in children's use of protective clothing, sun screens and staying in the shade or indoors during peak hours of sunshine. Additional indications of primary sun prevention practices being realized have been demonstrated by Smith et al. in a study of Australian pre-school children having acquired fewer CMN, coinciding with more frequent use of sun screen and swimsuits covering the trunk (11). A decline in the incidence of thin CMM among young people in Australia was recently reported by Iannacone et al. (12), although this has lately been questioned (13).

Based on clinical data for 7-year-old Swedish children in 2002 and 2007, the aim of the present study was to analyse whether the overall lower numbers of CMN had impacted differently in boys and girls and on body sites subjected to different patterns of sun exposure.

MATERIALS AND METHODS

Study design

Two consecutive population-based cross-sectional studies assessing numbers of CMN and sun-protective regimens among 7-year-old children in the municipalities of Falkenberg (57.0°N) and Ljungby (56.9°N) in southern Sweden were conducted in 2002 and 2007, respectively. Total numbers of children enrolled were 1,190 (681 in 2002 and 509 in 2007) corresponding to a response rate of 77.6% for both years. Full details of the study setting, descriptive population data and questionnaire survey results have been published previously (10).

The projects were conducted in collaboration with the school health services and were approved by the Regional Ethical Review Board in Stockholm (01-182, 2006/1466-31/2, 2007/1177-32).

Defining body sites and their main type of sun exposure

The counting of CMN in both years was performed by the same, trained and validated research nurse and followed a protocol from the International Agency for Research on Cancer (IARC) (13). All CMN with a diameter ≥ 2 mm were counted, except for those on the scalp, genitalia, buttocks and abdomen below the umbilicus: the latter being areas naturally delineated by

underwear. The location of each CMN was recorded on an anatomical paper chart divided into 16 body sites (A–P) (Fig. S1¹) as originally presented by Augustsson et al. (14). The classification of the main type of sun exposure within body sites was based on clothing habits and ultraviolet (UV) exposure patterns in the Swedish population and in agreement with a previous study performed by Synnerstad et al. in 2004 (7). Categorized as chronically sun-exposed sites were the face and dorsum of the hands (A and F), and as intermittently sun-exposed sites the back, chest, lateral aspects of the arms, anterior and posterior aspects of the thighs and lower legs and dorsum of the feet (D, G, I, K, L, M, N, O). Rarely sun-exposed body sites were represented only by the medial aspect of the arm, palms and soles, as CMN on the scalp (B), genitalia (H), buttocks/lower abdomen (J) were not counted (see Fig. S1¹).

Calculating body surface proportions and density of common melanocytic naevi

Total body surface area (BSA) was calculated from the height and weight of each child using Mosteller simplified formula (15). The numbers of CMN per square metre BSA were thereafter computed separately for the 16 body sites using burn area estimation charts modified for children by Lund & Browder (16). Regional BSAs for 7-year-olds were estimated as the mean of 5 and 10 years. Minor adjustments were made to make full agreement with the outlined areas of the schematic anatomical chart used in this study.

Statistical analyses

Descriptive statistics were presented as mean and median numbers of CMN per square metre BSA and included standard deviations (SD) and 95% confidence intervals (CI), respectively. Both mean and medians were calculated to facilitate comparison with other CMN studies, as both measures are frequently used.

For each body site the proportion of children with at least one naevus ≥ 2 mm illustrated the varying dispersion of CMN between different body regions. Some body sites generally hosted very few CMN and for the final statistical analyses 4 major anatomical sites (face, arms including hands, trunk and legs including feet) were constructed. Also, a merging of body sites according to their main pattern of sun exposure, chronic, intermittent or rare, was performed.

For statistical testing of numbers of CMN per body site, adjusted for BSA, risk ratios were calculated with zero-inflated negative binomial test, or negative binomial test, as appropriate (17, 18). Due to the multiplicity of comparisons (in total 40 tests for numbers of CMN in total, on major anatomical sites and by main type of exposure) Bonferroni correction was performed and *p*-values below 0.00125 were considered statistically significant.

RESULTS

Body-site specific common melanocytic naevus densities in 2002 and 2007

The body-site specific densities of CMN in 2007 showed a reduction in CMN on nearly every body site compared with 2002 (Table S1¹). On large anatomical surfaces, such as the chest and back, the proportion of children with at least one naevus was high (range

72.7–90.9%) while on smaller anatomical sites, such as hands and feet, it was low (range 4.0–8.2% on the palms, 7.9–13.5% on the dorsal hands, 0.8–3.7% on the soles and 8.7–19.8% on the dorsal feet). Changes between years imputed by only a few CMN on these sites must therefore be interpreted with caution.

Significant ($p < 0.00125$) changes in the numbers of CMN were seen for the chest (risk ratio 0.72 (95% CI 0.65–0.80)), back 0.81 (0.72–0.90), anterior aspect of the thighs 0.50 (0.42–0.61), anterior aspect of the lower legs 0.47 (0.33–0.66), posterior aspect of the lower legs 0.38 (0.21–0.66) and dorsum of the feet 0.40 (0.25–0.63) (Table I).

Common melanocytic naevus densities on major anatomical sites and by main type of sun exposure in 2002 and 2007

Compared with 2002, children in 2007 had had a significant reduction, by a total crude median number of 4 CMN: 11 (95% CI 10–12) to 7 (6–7), corresponding to risk ratio 0.68 (0.63–0.74), $p < 0.0001$ (Tables II and SII¹). The boys had had the largest reduction, by a total crude median number of 5 CMN: 12 (95% CI 11–13) to 7 (7–8), risk ratio 0.66 (0.59–0.74), $p < 0.0001$ and the girls by a total crude median number of 3 CMN: 9 (8–11) to 6 (6–7), risk ratio 0.70 (0.62–0.79), $p < 0.0001$.

For the 4 major anatomical sites: face, arms, trunk and legs, CMN densities on the face had remained largely unaltered between years (Table SII¹), corresponding to a risk ratio of 0.92 (95% CI 0.77–1.10), $p = 0.3643$ (Table II). For the arms, trunk and legs, overall highly significant reductions in numbers of CMN were seen ($p < 0.0001$). The highest rate of reduction was noted for the legs, by approximately 50%: risk ratio 0.48 (0.42–0.55).

In 2002, boys had higher median CMN densities on the face: 15.8 (95% CI 13.9–16.8) and trunk 23.7 (22.0–25.5), compared with girls: 0.0 (0.0–0.0) and 17.9 (15.8–20.2), respectively (Table SII¹). Girls had slightly higher median CMN densities on the legs: 6.8 (6.0–8.3) versus 6.2 (5.3–7.4) in boys. Gender profiles did appear more evident in 2007, however not reaching level of significance $p < 0.00125$, except for the trunk in 2002 (Table II). In 2007, the boys had significantly reduced numbers of CMN on the arms, trunk and legs ($p < 0.0001$), while girls had significantly reduced numbers on the trunk and legs ($p = 0.0002$ and $p < 0.0001$, respectively).

In 2002 the median CMN densities on the intermittently sun-exposed body sites were generally higher than on the chronically sun-exposed sites: 13.8 (95% CI 8.0–22.7) compared with 11.0 (0.0–20.5). In 2007 the median CMN densities were lower on the intermittently sun-exposed body sites: 8.7 (4.7–15.2) compared with 10.3 (0.0–14.4) (Table SII¹). While numbers of

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Table I. Risk ratio (95% confidence interval) for body-site specific numbers of common melanocytic naevi adjusted for body surface area between the years 2002 and 2007 and between girls and boys

Body site (A–P)		2002	2007	2007 vs. 2002	2007 vs. 2002	2007 vs. 2002
		Girls vs. boys	Girls vs. boys	Boys	Girls	All
(A) Face	Risk ratio ^a (95% CI)	0.93 (0.70–1.24)	0.76 (0.54–1.07)	0.99 (0.74–1.31)	0.83 (0.57–1.20)	0.92 (0.77–1.10)
	<i>p</i> -value	0.6304	0.1125	0.9224	0.3099	0.3643
(C) Arms medial	Risk ratio (95% CI)	0.88 (0.65–1.19)	1.60 (1.20–2.14)	0.67 (0.47–0.96)	1.01 (0.76–1.35)	0.85 (0.67–1.08)
	<i>p</i> -value	0.4019	0.0014	0.0279	0.9395	0.1940
(D) Arms lateral	Risk ratio (95% CI)	1.21 (0.95–1.53)	1.40 (0.99–2.00)	0.63 (0.44–0.89)	0.83 (0.62–1.12)	0.68 (0.53–0.89)
	<i>p</i> -value	0.1186	0.0585	0.0083	0.2228	0.0039
(E) Hand palms	Risk ratio (95% CI)	1.35 (0.67–2.74)	0.76 (0.23–2.51)	4.06 (0.82–20.1)	3.95 (0.98–15.9)	3.81 (1.04–14.00)
	<i>p</i> -value	0.4034	0.6511	0.0859	0.0526	0.0436
(F) Hands dorsal	Risk ratio (95% CI)	1.25 (0.44–3.58)	0.93 (0.56–1.54)	1.74 (1.03–2.95)	0.69 (0.28–1.64)	0.96 (0.63–1.48)
	<i>p</i> -value	0.6788	0.7749	0.0384	0.3913	0.8696
(G) Chest	Risk ratio (95% CI)	0.85 (0.75–0.97)	0.90 (0.76–1.07)	0.70 (0.61–0.80)	0.75 (0.64–0.88)	0.72 (0.65–0.80)
	<i>p</i> -value	0.0137	0.2277	<0.0001	0.0003	<0.0001
(I) Back	Risk ratio (95% CI)	0.77 (0.68–0.88)	0.75 (0.60–0.93)	0.80 (0.69–0.92)	0.82 (0.70–0.97)	0.81 (0.72–0.90)
	<i>p</i> -value	0.0001	0.0088	0.0018	0.0193	0.0002
(K) Thighs anterior	Risk ratio (95% CI)	1.29 (1.05–1.59)	1.37 (0.96–1.94)	0.48 (0.35–0.67)	0.51 (0.40–0.65)	0.50 (0.42–0.61)
	<i>p</i> -value	0.0150	0.0829	<0.0001	<0.0001	<0.0001
(L) Lower leg anterior	Risk ratio (95% CI)	1.08 (0.72–1.61)	1.23 (0.78–1.94)	0.45 (0.29–0.70)	0.43 (0.33–0.57)	0.47 (0.33–0.66)
	<i>p</i> -value	0.7228	0.3791	0.0004	<0.0001	<0.0001
(M) Thighs posterior	Risk ratio (95% CI)	1.07 (0.78–1.46)	2.26 (1.08–4.76)	0.35 (0.18–0.70)	2.08 (1.03–4.21)	1.00 (0.51–1.95)
	<i>p</i> -value	0.6898	0.0313	0.0028	0.0403	0.9997
(N) Lower leg posterior	Risk ratio (95% CI)	0.85 (0.55–1.33)	0.93 (0.62–1.40)	0.37 (0.19–0.70)	0.44 (0.20–0.99)	0.38 (0.21–0.66)
	<i>p</i> -value	0.4796	0.7279	0.0023	0.0483	0.0007
(O) Feet dorsal	Risk ratio ^a (95% CI)	0.86 (0.61–1.20)	1.06 (0.58–1.92)	0.26 (0.13–0.53)	1.49 (0.47–4.68)	0.40 (0.25–0.63)
	<i>p</i> -value	0.3711	0.8544	0.0002	0.4948	<0.0001
(P) Feet soles	Risk ratio (95% CI)	0.51 (0.09–3.02)	2.95 (0.13–65.85)	1.81 (0.51–6.41)	0.22 (0.05–0.96)	7.23 (1.00–52.05)
	<i>p</i> -value	0.4613	0.4943	0.3572	0.0446	0.0494

^aRisk ratios calculated with zero-inflated negative or negative binominal test including 95% CI (confidence intervals). Bonferroni corrected *p*-values <0.00125 (considered statistically significant) marked in bold.

95% CI: 95% confidence interval.

Table II. Risk ratios (95% confidence interval) for numbers of common melanocytic naevi by major anatomical sites and by main type of sun exposure among 7-year-old children in the years 2002 and 2007

		2002	2007	2007 vs. 2002	2007 vs. 2002	2007 vs. 2002
		Girls vs. boys	Girls vs. boys	Boys	Girls	All
Total body	Risk ratio ^a (95% CI)	0.90 (0.81–1.00)	0.95 (0.83–1.08)	0.66 (0.59–0.74)	0.70 (0.62–0.79)	0.68 (0.63–0.74)
	<i>p</i> -value	0.0407	0.4521	<0.0001	<0.0001	<0.0001
Major anatomical site						
Face	Risk ratio (95% CI)	0.93 (0.70–1.24)	0.76 (0.54–1.07)	0.99 (0.74–1.31)	0.83 (0.57–1.20)	0.92 (0.77–1.10)
	<i>p</i> -value	0.6304	0.1125	0.9224	0.3099	0.3643
Arms including hands	Risk ratio (95% CI)	0.99 (0.83–1.17)	1.39 (1.12–1.73)	0.63 (0.51–0.77)	0.89 (0.73–1.08)	0.73 (0.64–0.84)
	<i>p</i> -value	0.8813	0.0033	<0.0001	0.2308	<0.0001
Trunk	Risk ratio (95% CI)	0.81 (0.72–0.90)	0.84 (0.72–0.98)	0.74 (0.66–0.84)	0.77 (0.67–0.88)	0.75 (0.68–0.82)
	<i>p</i> -value	0.0001	0.0265	<0.0001	0.0002	<0.0001
Legs including feet	Risk ratio (95% CI)	1.11 (0.94–1.30)	1.32 (1.06–1.64)	0.43 (0.35–0.54)	0.53 (0.44–0.64)	0.48 (0.42–0.55)
	<i>p</i> -value	0.2301	0.0123	<0.0001	<0.0001	<0.0001
Main type of sun exposure						
Chronic ^b	Risk ratio (95% CI)	0.85 (0.70–1.03)	0.80 (0.59–1.10)	1.03 (0.85–1.25)	0.91 (0.67–1.25)	0.99 (0.84–1.17)
	<i>p</i> -value	0.1043	0.1776	0.7775	0.5655	0.9313
Intermittent ^c	Risk ratio (95% CI)	0.91 (0.82–1.01)	0.99 (0.87–1.14)	0.63 (0.57–0.71)	0.69 (0.61–0.79)	0.66 (0.61–0.72)
	<i>p</i> -value	0.0905	0.9078	<0.0001	<0.0001	<0.0001
Rare ^d	Risk ratio (95% CI)	0.80 (0.63–1.00)	1.46 (1.12–1.89)	0.69 (0.50–0.93)	1.02 (0.78–1.03)	0.86 (0.69–1.07)
	<i>p</i> -value	0.0521	0.0048	0.0169	0.8968	0.1733

^aRisk ratios calculated with zero-inflated negative or negative binominal test including 95% CI (confidence intervals). Bonferroni corrected *p*-values below 0.00125 (considered statistically significant) marked in bold. ^bChronically sun-exposed body sites includes the face and dorsal of hands. ^cIntermittently sun-exposed body sites includes lateral aspect of arms, chest, back, anterior and posterior aspects of thighs and lower legs and dorsal feet. ^dRarely sun-exposed body sites includes medial aspect of the arm, palms and soles.

95% CI: 95% confidence interval.

CMN on chronically sun-exposed sites had not changed significantly between years: risk ratio 0.99 (95% CI 0.84–1.17), $p=0.9313$, a highly significant reduction in CMN on intermittently sun-exposed sites was demonstrated: risk ratio 0.66 (0.61–0.72), $p<0.0001$ (Table II). The numbers of CMN on rarely sun-exposed body sites did not differ significantly between years, although lack of information on CMN status on body areas such as the lower abdomen/genital area, buttocks and scalp makes interpretation for this category precarious.

DISCUSSION

This study demonstrated a shift in the anatomical distribution pattern of CMN between 2002 and 2007 among 7-year-old children in southern Sweden. The overall lower total CMN densities in 2007 were mainly due to a reduction in the number of CMN on intermittently sun-exposed sites represented by the trunk and extremities, while CMN densities on chronically sun-exposed body sites, such as the face and dorsal hands had remained unaltered.

The improvements in parental sun protection routines demonstrated in southern Sweden between 2002 and 2007 were principally reported for physical sun protection (10). This is in line with the health authority's recommendations for children, that sun screens are to be used mainly as complementary protection on body parts not covered by long-sleeved clothing. In practice this means that the face and hands, representing chronically sun-exposed areas, are most likely to be protected with sun screens. However, as sun screens are readily wiped off and often insufficiently reapplied, they risk providing inadequate sun protection. Improved physical sun protection of the trunk and limbs may thus be one reason for a differential decrease in CMN on intermittently sun-exposed body sites compared to chronically sun-exposed sites. There may also be biological variations in CMN volatility on different body sites in response to different sun exposure patterns, as has been shown for CMN on the back among adolescents by Oliveria et al. (19).

In agreement with other international studies (e.g. 9, 20), the results demonstrated higher total numbers of CMN in boys compared with girls. The difference had slightly diminished in 2007 due to a proportionately larger decrease among boys, by a median of 5 CMN vs. 3 in girls. To analyse whether this was due to differences in sun exposure in boys and girls, a sub-analysis from the survey data collected in 2002 and 2007 was performed (data not shown). The results did not support any gender differences in basal phenotype characteristics or in reported numbers of sunburns, sunny holidays or sun screen use, but revealed a tendency among boys more often than girls to be protected

with clothing (e.g. a T-shirt) when in the sun and to stay in the shade or inside during peak hours of sunshine. There is some evidence that school-based sun protection intervention programmes have impacted more strongly among boys (21) and that sun avoidance by clothing or staying indoors at mid-day is more effective than sun screen use in preventing the development of CMN in children (22). No single conclusion regarding the differential lowering in CMN counts between boys and girls can be drawn based on the questionnaire surveys. However, other incentives for staying inside or in the shade during peak hours of sunshine, rather than sun avoidance, may be speculated, such as changes in leisure activities in recent years, e.g. playing TV or computer games in the daytime being more common among boys in Sweden (23).

Body-site specific gender profiles demonstrated that boys had more CMN on the face and trunk, while girls had slightly higher numbers of CMN on the lower extremities, which is in agreement with anatomical patterns demonstrated previously in children and adults (5–9). A possible cause of these variations is differences in clothing habits; however, the dress-code among boys and girls in Sweden is very similar and there are no school uniforms. Boys and girls followed identical examination protocols, and age-adjusted BSAs were used to account for any differences in body size. A review of the literature provided little support as to any major differences in site-specific body proportions in this young age group (24). If CMN profiles in 2007 were to be interpreted as representing a more "sun-naïve" state, the results mainly support the hypothesis that native factors influence CMN distribution in girls and boys.

CMN densities on the lateral aspect of the arm or the back have been demonstrated to best correlate with whole-body counts (7, 25). In our study the risk ratio in 2007 vs. 2002 for total numbers of CMN (0.68) best matched with the reduction of CMN on the lateral arms (0.68), chest (0.72) and back (0.81). This suggests that any of these locations could be held candidate sites when aiming to examine a limited body area for following population trends in numbers of CMN as a proxy for sun exposure.

The steadily rising incidence rates of CMM over the last decades have been linked to increased economic prosperity, enabling a life-style combining indoor work with periods of intense recreational tanning, sunny holidays and the use of sun beds (26, 27). This mode of intermittent sun exposure has been implicated as especially detrimental for CMM risk in populations with fair skin photo-types residing within high latitudes, as in Sweden (6, 28, 29). Studying changes in CMN in relation to sun exposure patterns among children residing in these geographical regions may provide valuable input on how sun prevention strategies and

changes in recreational activities have impacted in the population. This study is the first to demonstrate a differential reduction in CMN densities on mainly intermittently sun-exposed body sites in Swedish children. Future research can evaluate whether this change will persist with age and ultimately lead to a reduction in CMM subtypes and localizations associated mainly with intermittent sun exposure.

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