Vacations to Waterside Locations Result in Nevus Development in Colorado Children

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Abstract

Nevi are a main risk factor for malignant melanoma, and most nevi develop in childhood. This study examined the relationship between vacations and nevi in 681 White children born in 1998 who were lifetime residents of Colorado. Vacation histories were assessed through telephone interviews of parents, whereas nevus and phenotypic characteristics were assessed through skin exams at age 7. Multiple linear and logistic regression were used to assess the influence of vacations on counts of nevi <2 mm in size and the presence of any nevi ≥2 mm after controlling for other variables. Each waterside vacation ≥1 year before the exam at age 7 was found to be associated with a 5% increase in nevi <2 mm. Waterside vacations <1 year before the skin exam were not related to nevus count (<2 mm); regardless of timeframe, waterside vacations were not related to the presence of nevi ≥2 mm. UV dose received on waterside vacations, number of days spent on waterside vacations, and nonwaterside vacations were not significantly related to nevi <2 or ≥2 mm. These results suggest that there is a lag of at least 1 year in the development of new nevi after vacation sun exposure. It appears that a threshold dose of UV exposure is received quickly on each waterside vacation. Parents of young children should exercise caution in selection of vacation locations to reduce melanoma risk. (Cancer Epidemiol Biomarkers Prev 2009;18(2):454–63)

Introduction

The incidence of malignant melanoma has been increasing at an alarming rate in Caucasians around the world (1). This increase has been attributed to lifestyle changes including outdoor activities and clothing/appearance preferences (2). Risk factors for melanoma include skin color, skin propensity to burn, freckles, blue or green eye color, light hair color, history of severe sunburns, family history of melanoma, and prevalence of numerous melanocytic nevi (3-5).

In particular, the total number of benign nevi, the number of large nevi, and the presence of atypical nevi have shown strong relationships to the development of melanoma even in children (3, 6-9). With the exception of congenital nevi, found in ~1% of infants, most children are born without any melanocytic nevi (10); rather, they are acquired through the influence of genetic and environmental factors (11-13). Most nevi are acquired in childhood (14), and UV sun exposure is the primary influence aside from genetic factors (15-20). Sunburns, which are evidence of intense sun exposure, have been related to nevus development in several studies (17, 18, 20-25). Studies have also found that nevus counts are related to the amount of time spent outside on a daily basis, on weekends, and at the beach (26, 27). Several studies have examined the relationship between vacations to sunny locations and development of nevi, with most finding a positive relationship (16, 22, 24, 25, 28, 29).

Most studies of the relationship between vacations and nevus development have been conducted in European populations, where the pattern of sun exposure typically involves a low level of daily UV exposure at the place of residence (e.g., Germany and Great Britain) and a relatively intense exposure while on holiday (e.g., at Mediterranean locations). No such studies regarding the relationship between vacations and nevi have been reported for North American populations, where residential and vacation sun exposure patterns are likely to be different. The present study addressed this topic in a cohort of children who were lifetime residents of Colorado. Colorado is characterized by high altitude (>5,000 ft elevation) and a sunny climate (>300 days a year of sunshine); thus, the population receives relatively high levels of sun exposure. We hypothesized that total UV dose (UVD) accumulated on high UV intensity vacations, number of days on vacation to high UV intensity locations, and total number of vacations to high UV intensity locations would be related to nevus counts. We examined these relationships for two sizes of nevi (<2 and ≥2 mm) and for vacations occurring ≥1 and <1 year before nevus counts to explore a potential time lag between vacation exposure and the appearance of nevi. We further examined the relative effect of daily routine sun exposure compared with vacation exposure with respect to nevus development.

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Materials and Methods

This study used data collected as part of a randomized controlled sun protection intervention study to examine the relationship between vacation histories (birth to age 7) and nevus development in a cohort of 681 children. Demographic, sun exposure, and sun protection data were acquired through phone interviews in 2003, 2004, and 2005 and phenotypic and nevus data were obtained in a comprehensive skin exam in 2005. The study was reviewed and approved by the Colorado Multiple Institutional Review Board.

Participants. In 2003 and 2004, 1,145 children born between January and September 1998 were recruited to a sun protection intervention study via private pediatric offices, a large managed care provider, and various community locations in the Denver-Boulder-Colorado Springs area of Colorado. The main objective of the study was to test a behavioral intervention to reduce skin cancer risk. Children were assigned to an intervention or control group; parents in the intervention group received four newsletters promoting sun protection accompanied by a sun protective swim shirt and sunscreen in the spring of 2005. The control group received standard care. This analysis of vacation sun exposure was limited to White children (both non-Hispanic and Hispanic) who were lifetime residents of Colorado. These restrictions were placed because (*a*) other racial groups are known to have significantly lower nevus counts than Whites (1) and (*b*) we desired to examine the effect of sun exposure during vacations on nevus development while holding residential sun exposure, which is high in Colorado, as a constant. Only children whose parents or guardians completed the enrollment interview (in 2003 or 2004), follow-up interviews in both 2004 and 2005, and a skin exam in 2005 were included in the present analysis. Of the 1,145 children enrolled in the study, 1,010 (88%) were reported by parents to be of White race. Of these, 868 (86%) were lifetime residents of Colorado. Of these, 681 (78%) completed all required interviews and the skin exam and were included in the analysis.

Parent Interviews. Telephone interviews required 20 to 30 min for completion and were conducted by trained interviewers using a computer-assisted telephone interviewing system with up to 20 calls to reach each family. Enrollment interviews were conducted between October 2003 and July 2004. Follow-up interviews were conducted in the summer months of 2004 and 2005 (June-September). At each time point, the parent who reported providing the primary care of the child was interviewed. Enrollment interviews collected demographic data, sunburn history, and vacation history from birth. The subsequent phone interviews in 2004 and 2005 assessed daily sun exposure and sun protection practices and updated sunburn and vacation history information.

Skin Exams. The skin exam was conducted in 2005, between June and September. Height and weight measurements were used to provide an estimate of the child's body surface area. Eye color was designated into one of four categories, blue, green, brown, or hazel, using an eye color chart. Hair color was determined to be red, blonde, light brown, dark brown, or black by comparison with hair samples. Degree of freckling was determined using a previously established 10-level chart (30). Base pigmentation was measured using a Minolta Chroma Meter CR-400 on the unexposed, upper medial arm. Five measurements were taken and averaged, using the L scale, which measures color from white to black. Higher scores represent lighter skin color (31, 32).

Nevus examinations were done by a team of seven physicians, nurses, and nurse practitioners, all of whom were trained to perform a standardized nevus examination. Consistency across the seven examiners was assessed by duplicate exams. Among the attendees of the skin exam sessions, 48 children were assessed separately by two examiners who were each blinded to the results of the other exam. Both exams were conducted on the same day. Interrater reliability was 0.79 [95% confidence interval (95% CI), 0.66-0.92]. During exams, a nevus was defined as any size pigmented macule or papule, flat or raised, dark brown in color, with regular borders, and not occurring in patches. These characteristics were sufficient to distinguish nevi from freckles, café-au-lait macules, and warts. Congenital nevi were recorded although excluded from analysis because they are not induced by sun exposure. Exams were full body, with the exception of the scalp, genitals, and buttocks. Nevus size was determined using a plastic stencil with cutouts for <2, 2 to <5, and ≥5 mm. Nevi were recorded by size on a body map.

Construction of Key Variables

UVD and Vacations. At enrollment, parents were asked to provide information about all vacations their children had taken to "sunny locations" away from their residential location, from birth up to the interview in 2003 or 2004. The location, season, and number of days spent at the location were recorded. This information was then updated in subsequent interviews in 2004 and 2005.

The vacations reported by participants were screened to include only locations outside of the Denver-Boulder-Colorado Springs metropolitan areas. The longitude and latitude of each vacation destination were determined to the nearest 0.5°. Vacation locations that spanned a large area were assigned the latitude and longitude of their geographical center. The daily seasonal average UVD for each location was determined using the online TEMIS archive of data.[6] UVD is defined as the level of UV radiation received by a person in a specific location on a given day, accounting for cloud cover, measured in kJ/m^2. Daily data were obtained from the satellite GOME and from the SCIAMACHY instrument aboard the satellite ENVISAT, operated by the European Space Agency. TEMIS accumulated the seasonal average UVD data over a 6-year collection period, between August 1995 and September 2001. The seasonal values were calculated by averaging the daily UVD during the spring, summer, fall, and winter months to provide an average UVD for each location during each of the four seasons. Total UVD for each vacation was calculated by multiplying the seasonal UVD of the location by the number of days spent there. Summary UVD exposure variables were created by summing the individual trip UVD exposures across vacations.

[6] www.temis.nl/uvradiation/

Because many of the vacations reported by parents were not to locations where a significant amount of sun exposure would be expected, the reported vacations were classified as either ''waterside'' or ''nonwaterside.'' A waterside vacation was defined as any vacation to a destination with a body of water known to be associated with recreational activities that would lead the participant to get significant sun exposure (e.g., surfing, water skiing, and boating but excluding fishing). Our definition also required that the climate permit waterside activities; therefore, some locations were only considered ''waterside'' during warmer seasons. Within the United States, only Hawaii and vacation destinations <27.5°N qualified as ''waterside'' year-round. Other water destinations in the United States were deemed ''waterside'' only during the summer months of June, July, and August. When the participant traveled outside of the United States, the same water and climate guidelines were applied. When only a country name and no city was provided, the vacation was coded as nonwaterside, with the exception of Australia, which was coded as waterside during all seasons of the year due to the extreme sun exposure and concentration of the population in coastal areas.

Under these specifications, a location such as Duck, North Carolina (an oceanside resort town) was considered a waterside vacation during the summer months but not during spring, winter, or fall because it is >27.5°N. Padre Island, Texas and Miami, Florida were considered waterside vacations year-round because they are <27.5°N. Similarly, lakeside locations such as Lake McConaughy, Nebraska (a common vacation location for Coloradans) were considered waterside vacations only in the summer. San Francisco, CA was not considered a waterside vacation in any season of the year because it is not typically associated with water activities that lead to significant sun exposure, although it is by a body of water.

Using these definitions, simple counts of the number of waterside and nonwaterside vacations taken by each child were produced. In addition, the number of days spent on waterside vacations and the UVD (using the UVD data described above) received on waterside vacations were calculated. Based on speculation by Milne et al. (33), we expected a latency period between sun exposure and subsequent nevus development of at least 1 year. Thus, the 2005 vacation data were separated from vacation data through 2004 so that each indicator (number of waterside vacations, number of nonwaterside vacations, days on waterside vacations, and UVD on waterside vacations) was available for birth to age 6 and separately for ages 6 to 7.

Demographic Variables. Parent's educational level was reduced to ''less than college degree'' versus ''college degree or higher.'' Household income was collapsed to ''<$75,000,'' ''$75,000 to $99,000,'' and ''≥$100,000'' for descriptive purposes and used in its original 7-point ordinal scale for multivariate analysis. Hispanic ethnicity was determined by asking parents whether their child was of Hispanic or Latino background.

Phenotype Variables. Sun sensitivity was measured using a question that asked parents to indicate their child's skin reaction to the sun after 1 h unprotected at the beginning of summer using four categories: ''a painful sunburn the next day with no tan 1 week later'' (type 1), ''a painful sunburn the next day with a light tan 1 week later'' (type 2), ''slight burn the next day and a light tan 1 week later'' (type 3), and ''no burn the next day and a good tan 1 week later'' (type 4). Sun sensitivity was collapsed into type 4 versus all others for the regression analyses based on univariate analysis showing that type 4 children had the fewest nevi. Eye color was reduced to blue, green/hazel, or brown for descriptive analysis, and in regression analysis, blue, green, and hazel were combined and brown eyes served as the reference. Hair color was recoded as blonde-light brown, red, medium-dark brown, or black. Degree of facial freckling was consolidated to ''none'' versus ''any.'' Colorimeter measurements for base skin color were used in the original continuous format for regression analysis. For the descriptive analysis, skin color was dichotomized as ''lighter skin'' (L score ≥ 60) versus ''darker skin'' (L score < 60) based on consensus among the authors of what would be considered ''fair'' skin.

Sun Exposure, Sun Protection, and Sunburn Variables. Usual midday sun exposure was measured by questions assessing the number of days per week the child spends >15 min outside between 11:00 a.m. and 3:00 p.m. and the usual number of hours the child spends outside during these occasions. These variables were multiplied to create a single variable representing the total number of hours outside per week between 11:00 a.m. and 3:00 p.m. Usual midday exposure was dichotomized as 0 to 14 versus ≥15 h/wk for descriptive analysis but used as a continuous variable in multivariate analysis. Sunscreen, clothing, and hat use were assessed using questions that asked the frequency of using sunscreen, clothes covering most of the body, and hats while outside between 11:00 a.m. and 3:00 p.m. for >15 min (5, all of the time; 4, most of the time; 3, about half the time; 2, not very often; 1, never). These were dichotomized as half time or less versus most or all of the time for descriptive analyses and used in the full 5-point scale in multivariate analysis. Lifetime severe sunburns were assessed at enrollment with the question, ''Has [child's name] ever had a blistering sunburn?'' and on the follow-up interviews with the question, ''Has [child's name] had a blistering sunburn since this time last year?'' Additional detailed questions regarding the number of severe burns and the parts of the body involved were asked for each blistering sunburn reported. Because there were very few children who had a history of more than one severe sunburn, children were placed into two groups: those with any severe burn and those with no severe burns. Sunburns in the past year were assessed with the question: ''I'd like to find out if your child has had any sunburns in the last year, that is, since this time last year. By sunburned, I mean any reddening of the skin that lasts until the next day,'' with follow-up questions regarding the number of burns, the month and parts of the body involved in each burn, and the severity of each burn. Because severe sunburns were captured in the previously described variable, any severe burns in the last year were subtracted out, and experience of burns in the past year was then collapsed into two categories: one or more nonsevere burn versus no nonsevere burn in the past year.

Table 1. Characteristics of study participants and associations with nevi, number of waterside vacations, number of days on waterside vacations, and UVD on waterside vacations

Characteristic		No. nevi <2 mm at age 7	Any nevi ≥2 mm at age 7	Total no. waterside vacations (birth to age 6)	Total no. days on waterside vacations (birth to age 6)	Total UV exposure dose (kJ/m^2) on waterside vacations (birth to age 6)
	n (%)	GM (95% CI)	%	Mean (SD)	Mean (SD)	Mean (SD)
Gender						
Male	325 (47.7)	22.6 (17.8-20.6)*	70.2	1.43 (1.68)	11.14 (21.19)	47.61 (86.83)
Female	356 (52.3)	19.1 (20.9-24.2)	63.2	1.36 (1.46)	9.37 (18.09)	41.28 (82.54)
Ethnicity						
White non-Hispanic	611 (89.7)	22.0 (20.8-23.2)†	69.1†	1.43 (1.59)	10.62 (20.43)	46.00 (87.95)
White Hispanic	70 (10.3)	12.3 (10.5-14.4)	44.3	1.11 (1.38)	6.70 (9.85)	29.50 (44.04)
Household income‡						
<$75,000	279 (42.5)	21.0 (19.3-22.8)	66.7	1.14 (1.40)†	7.85 (19.08)§	34.80 (88.70)§
$75,000-99,999	187 (28.5)	19.8 (17.9-21.9)	65.8	1.49 (1.69)	11.48 (22.08)	49.04 (90.83)
≥$100,000	191 (29.1)	20.9 (19.0-23.1)	68.1	1.70 (1.63)	11.97 (14.35)	51.94 (60.86)
Parent education						
Some college or less	180 (26.4)	19.1 (17.3-21.2)	60.1	0.97 (1.36)†	8.34 (27.94)	36.26 (122.82)
College graduate	296 (43.5)	20.5 (18.9-22.2)	67.9	1.50 (1.63)	10.40 (16.36)	44.79 (67.75)
Beyond college	205 (30.1)	22.6 (20.6-24.9)	70.2	1.61 (1.59)	11.60 (14.41)	50.69 (62.27)
Sun sensitivity						
Painful burn/ no tan (type 1)	54 (7.9)	18.7 (15.5-22.4)*	72.2	1.39 (1.48)	8.33 (11.91)	36.41 (49.84)
Painful burn/ light tan (type 2)	173 (25.4)	21.9 (19.7-24.2)	69.9	1.38 (1.54)	9.14 (12.58)	38.67 (51.87)
Slight burn/ little tan (type 3)	325 (47.8)	22.0 (20.4-23.7)	67.1	1.35 (1.49)	10.55 (21.54)	46.23 (95.33)
No burn/ good tan (type 4)	128 (18.8)	17.4 (15.4-19.6)	58.6	1.52 (1.83)	11.66 (24.55)	50.54 (101.78)
Hair color						
Blonde-light brown	334 (49.0)	21.6 (20.1-23.3)†	72.2*	1.43 (1.57)	10.07 (15.64)	42.97 (63.93)
Red	18 (2.6)	11.9 (8.7-16.3)	61.1	1.06 (1.26)	7.33 (8.82)	31.17 (35.84)
Medium-dark brown	312 (45.8)	21.1 (19.6-22.8)	62.2	1.38 (1.61)	10.49 (23.82)	46.39 (105.00)
Black	17 (2.5)	10.8 (7.8-15.0)	41.2	1.35 (1.11)	11.06 (12.93)	46.12 (55.33)
Eye color						
Blue	220 (32.3)	22.1 (20.1-24.2)*	70.5*	1.27 (1.37)	8.34 (11.85)	35.83 (49.18)
Green/hazel	244 (35.8)	22.1 (20.2-24.1)	70.9	1.50 (1.64)	10.21 (13.81)	45.17 (61.62)
Brown	217 (31.9)	18.1 (16.5-19.8)	57.6	1.41 (1.68)	12.13 (29.14)	51.93 (125.17)
Facial freckling						
None	295 (43.3)	18.2 (16.8-19.7)†	59.3*	1.42 (1.63)	10.98 (24.33)	48.40 (107.65)
Any	386 (56.7)	22.8 (21.3-24.5)	72.0	1.37 (1.52)	9.64 (15.13)	41.18 (61.52)
Base skin color (L scale)						
Light (≥60)	253 (37.2)	22.8 (18.3-20.9)*	68.8	1.29 (1.44)	9.37 (20.38)	40.59 (92.75)
Other (<60)	428 (62.8)	19.5 (21.0-24.5)	65.2	1.45 (1.64)	10.72 (19.20)	46.49 (79.47)
Sunscreen frequency∥						
Half time or less	82 (12.3)	20.2 (17.4-23.4)	58.5	1.21 (1.45)	9.23 (30.28)	40.33 (142.13)
Mostly-always	582 (87.7)	20.8 (19.7-22.0)	67.4	1.43 (1.59)	10.41 (17.80)	45.12 (73.77)
Hat frequency¶						
Half time or less	535 (80.7)	21.3 (20.2-22.6)§	66.2	1.40 (1.54)	9.53 (16.76)§	41.48 (75.46)
Mostly-always	128 (19.3)	18.3 (16.2-20.6)	66.4	1.41 (1.70)	13.39 (29.09)	57.47 (117.11)
Clothes frequency¶						
Half time or less	567 (85.5)	21.0 (19.8-22.2)	66.3	1.40 (1.51)	10.04 (19.96)	43.89 (86.80)
Mostly-always	96 (14.5)	19.3 (16.8-22.2)	65.6	1.41 (1.93)	11.67 (18.55)	48.40 (75.14)
Time in midday sun (11-3) per week**						
Half time or less	610 (91.0)	20.7 (19.6-21.9)	66.6	1.37 (1.53)	10.00 (20.06)	43.39 (86.43)
Most-all the time	60 (9.0)	20.5 (17.2-24.5)	70.0	1.62 (1.98)	12.63 (16.62)	54.20 (71.27)
Lifetime history of severe sunburn (birth to age 7)						
None	633 (93.0)	20.3 (19.2-21.5)*	66.8	1.41 (1.58)	10.44 (20.14)	45.30 (86.83)
Any	48 (7.0)	26.6 (21.9-32.4)	62.5	1.21 (1.44)	7.21 (10.66)	31.14 (45.08)
Past year history of nonsevere sunburn (ages 6-7)						
None	309 (45.4)	19.3 (17.9-20.8)§	66.0	1.50 (1.62)	11.97 (25.56.)§	51.07 (109.51)
Any	372 (54.6)	22.0 (20.5-23.6)	66.9	1.31 (1.52)	8.76 (12.68)	38.70 (55.77)
Total	681 (100)	20.7 (19.7-21.8)	66.5	1.39 (1.57)	10.22 (19.64)	44.30 (84.61)

NOTE: Colorado children born in 1998 (n = 681).
* $P < 0.01$.
† $P < 0.0001$.
‡ 24 missing cases.
§ $P < 0.05$.
∥ 17 missing cases.
¶ 18 missing cases.
** 11 missing cases.

Table 2. Univariate associations between vacation indicators and nevi at age 7

Vacation indicator		No. nevi <2 mm at age 7				Any nevi ≤2 mm at age 7	
	n (%)	GM (95% CI)	ANOVA	r*	P	%	χ^2
Total no. waterside vacations (birth to age 6)							
0	247 (36.3)	19.4 (17.8-21.2)	$F(5,675) = 1.27$, $P = 0.28$	0.09	0.02	64.8	$\chi^2(5) = 4.22$, $P = 0.52$ †
1	189 (27.8)	20.6 (18.6-22.7)				67.7	$\chi^2(1) = 0.02$, $P = 0.89$ ‡
2	104 (15.3)	22.9 (20.0-26.2)				73.1	
3	71 (10.4)	20.4 (17.4-24.0)				59.2	
4	39 (5.7)	22.6 (18.2-28.1)				66.7	
≥5	31 (4.6)	24.0 (18.8-30.6)				67.7	
Total no. waterside vacations (ages 6-7)							
0	461 (67.7)	20.4 (19.1-21.7)	$F(3,677) = 1.18$, $P = 0.32$	0.01	0.81	66.4	$\chi^2(3) = 2.00$, $P = 0.57$ †
1	168 (24.7)	22.3 (20.1-24.8)				65.5	$\chi^2(1) = 0.41$, $P = 0.52$ ‡
2	39 (5.7)	18.2 (14.7-22.7)				66.7	
≥3	13 (1.9)	20.1 (13.7-29.3)				84.6	
Total no. nonwaterside vacations (birth to age 6)							
0	39 (5.7)	20.0 (16.1-24.9)	$F(5,675) = 0.62$, $P = 0.68$	0.07	0.09	64.1	$\chi^2(5) = 1.25$, $P = 0.94$ †
1	53 (7.8)	18.8 (15.5-22.6)				71.7	$\chi^2(1) = 0.02$, $P = 0.88$ ‡
2	93 (13.7)	20.0 (17.4-23.1)				63.4	
3	81 (11.9)	19.7 (16.9-22.9)				65.4	
4	93 (13.7)	20.7 (17.9-23.8)				67.7	
≥5	322 (47.3)	21.6 (20.1-23.3)				66.8	
Total no. nonwaterside vacations (ages 6-7)							
0	166 (24.4)	19.5 (17.6-21.7)	$F(3,677) = 0.84$, $P = 0.47$	0.04	0.26	59.6	$\chi^2(3) = 6.96$, $P = 0.07$ †
1	178 (26.1)	20.4 (18.4-22.6)				65.7	$\chi^2(1) = 6.65$, $P = 0.01$ ‡
2	146 (21.4)	21.0 (18.8-23.5)				67.1	
≥3	191 (28.0)	21.9 (19.8-24.2)				72.8	
Total no. days on waterside vacations (birth to age 6)							
0	247 (36.3)	19.4 (17.8-21.2)	$F(3,676) = 1.20$, $P = 0.31$	0.05	0.19	64.8	$\chi^2(3) = 0.87$, $P = 0.83$ †
1-7	176 (25.9)	21.0 (19.0-23.3)				65.9	$\chi^2(1) = 0.64$, $P = 0.43$ ‡
8-14	114 (16.8)	21.5 (19.0-24.5)				69.3	
≥15	143 (21.0)	22.0 (19.6-24.6)				67.8	
Total no. days on waterside vacations (ages 6-7)							
0	461 (67.7)	20.4 (19.1-21.7)	$F(3,677) = 1.08$, $P = 0.36$	-0.001	0.98	66.4	$\chi^2(3) = 1.35$, $P = 0.72$ †
1-7	136 (20.0)	20.6 (18.4-23.2)				64.0	$\chi^2(1) = 0.45$, $P = 0.51$ ‡
8-14	51 (7.5)	24.5 (20.2-29.7)				70.6	
≥15	33 (4.8)	20.2 (15.9-25.6)				72.7	
UVD on waterside vacations (birth to age 6)							
0	247 (36.3)	19.4 (17.8-21.2)	$F(3,676) = 1.75$, $P = 0.16$	0.05	0.24	64.8	$\chi^2(3) = 2.68$, $P = 0.44$ †
1-23.9	107 (15.7)	19.8 (17.4-22.7)				62.6	$\chi^2(1) = 0.90$, $P = 0.34$ ‡
24-39.9	101 (14.9)	22.5 (19.6-25.7)				72.3	
≥40	225 (33.1)	21.8 (20.0-23.9)				67.6	
UVD on waterside vacations (ages 6-7)							
0	461 (67.7)	20.4 (19.1-21.7)	$F(3,677) = 0.51$, $P = 0.68$	-0.01	0.89	66.4	$\chi^2(3) = 0.26$, $P = 0.97$ †
1-23.9	77 (11.3)	20.2 (17.3-23.7)				66.2	$\chi^2(1) = 0.07$, $P = 0.79$ ‡
24-39.9	75 (11.0)	21.8 (18.6-25.5)				65.3	
≥40	68 (10.0)	22.3 (18.9-26.3)				69.1	

NOTE: Colorado children born in 1998 (n = 681).
* Pearson product moment correlation.
† Pearson χ^2.
‡ Mantel-Haenszel trend, linear by linear association.

Data Analysis. Nevi were separated into nevi <2 and ≥2 mm because of prior research suggesting that different factors may be associated with the presence of smaller versus larger nevi (22). Nevi ≥2 mm were infrequent compared with smaller nevi, with 33% of children having no nevi ≥2 mm (see Results). Because only 8% of children had any nevi ≥5 mm, these were included with nevi ≥2 mm. Counts were used to describe smaller nevi (<2 mm), whereas proportions (percentage of children with one or more) were used to describe larger nevi (≥2 mm). Nevus counts (<2 mm) were slightly positively skewed with a few children having very high counts, so geometric means (GM) were used to describe nevus counts in demographic and phenotypic subgroups of the study sample and a natural log transformation was used for inferential analyses (e.g., ANOVA and linear regression). ANOVA was used to statistically test for subgroup differences in mean log-transformed nevus counts (<2 mm), mean number of waterside vacations taken from birth to age 6, mean number of days on waterside vacations taken from birth to age 6, and mean total UV exposure at waterside locations from birth to age 6 (Table 1). For univariate relationships between vacation variables and small nevus counts (Table 2), we tested for both linear trends (using Pearson r) and nonlinear trends (using ANOVA). For nevi ≥2 mm, Mantel-Haenszel trend (linear by linear association) χ^2 was used to test for linear trends and Pearson χ^2 was used to test for nonlinear trends.

The associations between vacation indicators and log-transformed nevus counts (<2 mm) at age 7 were evaluated using multiple linear regression analyses. Multiple logistic regression was used to evaluate the associations between vacation indicators and the presence of ≥1 nevi ≥2 mm. Regression analyses controlled for routine sun exposure, sun protection, sun sensitivity, and phenotypic and demographic characteristics. Intervention group status for the randomized trial was tested in initial regression models, was not significantly related to vacation indicators or nevus prevalence at age 7, and was excluded from subsequent modeling. Diagnostic analyses showed moderate associations between hair color, eye color, skin color, sun sensitivity, and Hispanic ethnicity (all $P < 0.001$), and when all of these predictors were entered together into multivariate analyses, the regression coefficient for blonde hair color reversed from a positive value to a negative value suggesting multicollinearity. Thus, hair color was removed from multivariate analyses. Similarly, due to a moderate association between family income and educational level of the parent ($r = 0.25$; $P < 0.001$), only income was included in the multivariate analysis to represent socioeconomic status. Separate regression equations were estimated to test the relative predictive utility of the various indicators of sun exposure during vacations, including the (*a*) total number of waterside vacations, (*b*) total number of days on waterside vacations, (*c*) total UV exposure on waterside vacations, and (*d*) total number of nonwaterside vacations. In each of these regressions, the indicator of vacation sun exposure (e.g., number of waterside vacations) was split into two variables: exposure before age 6 (≥1 year before nevus counts) and exposure ages 6 to 7 (<1 year before nevus counts). Because vacations before age 6 were correlated with vacations ages 6 to 7, multivariate models were tested iteratively such that the vacation indicator for each period was evaluated independently of the other period in addition to testing the indicators for both periods jointly. This approach was used to ensure that the inclusion of one of the variables did not influence the regression coefficient of the other variable. We identified several cases with extreme values on two of the vacation variables (number of days on waterside vacations before age 6 and UVD on waterside vacations before age 6). Influence statistics showed that these cases had negligible effects on the regression coefficients; thus, these cases were retained in the analysis. For interpretation, the antilog was used to convert multiple linear regression coefficients and 95% CIs into the multiplicative factor by which nevus counts <2 mm are expected to change, on average, for every 1-unit increase in the predictor variable. The main analysis (prediction of small nevi) was repeated using nevus density as the dependent variable, with density calculated using the Mosteller formula, which takes into account the height (in) and weight (lb) of each child: body surface area (m^2) = SQRT (height × weight) / 3,131 (34).

Results

Characteristics of Study Sample. Table 1 shows the characteristics of the sample included in this analysis and the relationships between these characteristics, nevi (<2 and ≥2 mm) and waterside vacation variables up to age 6 (number of vacations, days on vacations, and UVD on vacations). The sample was approximately equally split between males and females. Approximately 90% were non-Hispanic White. Forty-three percent of parents reported an annual household income <$75,000, whereas the rest were evenly split between $75,000 to $99,000 and ≥$100,000. Seventy percent of the responding parents were at least college educated. About one-third of children had sensitive skin types (I and II) according to parent report. About 52% of children had light hair color (blonde/light brown or red). Approximately one-third each had blue, green/hazel, and brown eyes. Slightly more than half of the children had visible facial freckling. Only 7% reported ever having a severe sunburn and slightly more than half of children had received a nonsevere sunburn between ages 6 and 7.

Nevus Prevalence. The GM total nevus count (all sizes) at age 7 was 22.3. Our sample had a preponderance of smaller nevi (<2 mm; GM = 20.7). Approximately one-third of the sample had no nevi ≥2 mm, 28% had only 1 nevus >2 mm, 15% had 2 nevi ≥2 mm, and the remaining 24% had ≥3 nevi ≥2 mm. As shown in Table 1, the number of nevi <2 mm differed as a function of child

Table 3. Results of multiple linear regression predicting natural log-transformed nevus counts <2 mm at age 7

Predictor	*B*	SE	*P*	Antilog(*b*)*	95% CI †
Total no. waterside vacations (birth to age 6)	0.046	0.018	0.01	1.05	1.01-1.09
Total no. waterside vacations (ages 6-7)	−0.026	0.036	0.47	0.97	0.91-1.04
Severe sunburn (birth to age 7; 1 = any, 0 = none)	0.163	0.106	0.12	1.17	0.96-1.45
Nonsevere sunburn (ages 6-7; 1 = any, 0 = none)	0.069	0.054	0.20	1.07	0.96-1.19
Average no. hours midday sun	0.004	0.005	0.40	1.00	0.99-1.02
Frequency of sunscreen use	0.004	0.036	0.92	1.00	0.94-1.08
Frequency of hat use	−0.044	0.028	0.12	0.96	0.91-1.01
Frequency of clothes use	−0.028	0.028	0.32	0.97	0.92-1.03
Sun sensitivity (1 = tans easily, 0 = other)	−0.099	0.072	0.17	0.91	0.79-1.04
Facial freckling (1 = any, 0 = none)	0.094	0.058	0.10	1.10	0.98-1.23
Child gender (1 = male, 0 = female)	0.172	0.057	0.003	1.19	1.06-1.33
Base skin color (L scale)	0.015	0.010	0.14	1.02	1.00-1.04
Eye color (1 = blue/green/hazel, 0 = brown)	0.028	0.063	0.66	1.03	0.91-1.16
Hispanic ethnicity (1 = Hispanic, 0 = non-Hispanic)	−0.431	0.101	<0.0001	0.65	0.53-0.79
Parent income	−0.019	0.022	0.40	0.98	0.98-1.03

NOTE: Colorado children born in 1998 ($n = 627$). Adjusted $R^2 = 0.09$; $F(15,611) = 5.07$, $P < 0.0001$.
* Multiplicative factor by which nevus counts <2 mm change for every 1-unit increase in predictor.
† 95% CI around antilog(*b*).

Table 4. Results of multiple logistic regression predicting ≥1 nevi ≥2 mm at age 7

Predictor	log (OR)	SE	P	OR (95% CI)
Total no. waterside vacations (birth to age 6)	0.029	0.062	0.64	1.03 (0.91-1.16)
Total no. waterside vacations (ages 6-7)	0.086	0.126	0.50	1.09 (0.85-1.40)
Severe sunburn (birth to age 7; 1 = any, 0 = none)	−0.191	0.347	0.58	0.83 (0.42-1.63)
Nonsevere sunburn (ages 6-7; 1 = any, 0 = none)	0.007	0.180	0.97	1.01 (0.71-1.43)
Average no. hours midday sun	0.006	0.017	0.72	1.01 (0.97-1.04)
Frequency of sunscreen use	0.010	0.117	0.93	1.01 (0.80-1.27)
Frequency of hat use	0.029	0.094	0.76	1.03 (0.86-1.24)
Frequency of clothes use	−0.022	0.092	0.81	0.98 (0.82-1.17)
Sun sensitivity (1 = tans easily, 0 = other)	−0.232	0.232	0.32	0.79 (0.50-1.25)
Facial freckling (1 = any, 0 = none)	0.540	0.189	0.004	1.72 (1.18-2.49)
Child gender (1 = male, 0 = female)	0.495	0.192	0.01	1.64 (1.13-2.39)
Base skin color (L scale)	−0.026	0.034	0.45	0.97 (0.91-1.04)
Eye color (1 = blue/green/hazel, 0 = brown)	0.247	0.206	0.23	1.28 (0.86-1.92)
Hispanic ethnicity (1 = Hispanic, 0 = non-Hispanic)	−0.799	0.316	0.01	0.45 (0.24-0.84)
Parent income	0.005	0.075	0.95	1.01 (0.87-1.16)

NOTE: Colorado children born in 1998 (n = 627). $\chi^2(15)$ = 34.56, P = 0.003.

gender, Hispanic ethnicity, skin sensitivity to the sun, hair color, eye color, facial freckling, base skin color, hat use, and sunburn history. The presence of nevi ≥2 mm differed by Hispanic ethnicity, hair color, eye color, and freckling.

Vacation Exposure. Regarding vacation exposure, higher household income was positively associated with all vacation variables and higher parental education was positively associated with total number of waterside vacations (Table 1). Higher hat use was associated with a greater number of days on waterside vacations, and children who had no nonsevere sunburns in the previous year had a higher number of days on waterside vacations.

Table 2 reports descriptive statistics for the indicators of vacation sun exposure as well as the GM number of nevi <2 mm and the proportion of children with any nevi ≥2 mm for each vacation category. From birth to age 6, nearly two-thirds of the children went on at least 1 waterside vacation, with a mean of 1.39 waterside vacations before age 6 and 0.44 waterside vacations between ages 6 and 7. The average length of a waterside vacation was 7 days and the average UVD on each waterside vacation was 30 kJ/m^2. The children spent a mean of 10 total days on waterside vacations and received a mean total UVD of 44 kJ/m^2 from birth to age 6, and for ages 6 to 7, the corresponding values were 3 total days and 13 kJ/m^2 UVD. The most common locations for waterside vacations were California (20%) and Colorado (18%). Florida was the location of 11% of waterside vacations and Hawaii was the location of 7% of waterside vacations. International waterside vacations were most commonly to Mexico (7%) and the Caribbean (5%).

For each vacation indicator, we examined the correlation between values for birth to age 6 and values for ages 6 to 7. Moderate correlations (r = 0.24-0.38) were found, with the highest correlation for number of waterside vacations before age 6 and number of waterside vacations ages 6 to 7 (r = 0.38; P < 0.0001).

Vacation Exposure and Nevus Prevalence. Tests for relationships between vacation variables and nevi are reported in Table 2. The only significant linear relationship between vacations and nevi <2 mm was for number of waterside vacations before age 6 (Pearson r = 0.09; P = 0.02). There were no nonlinear relationships. For larger nevi (≥2 mm), the only significant finding was a positive linear relationship with number of nonwaterside vacations ages 6 to 7.

Table 3 shows the results of multivariate linear regression analysis predicting nevus count at age 7 from the number of waterside vacations from birth to age 6, the number of waterside vacations between ages 6 and 7, and a set of exposure, demographic, and phenotype

Table 5. Comparison of vacation indicators in predicting natural log-transformed nevus counts <2 mm at age 7, adjusted for demographic, phenotypic, and sun exposure variables

Vacation indicator	b	SE	P	antilog(b)*	95% CI †
Total no. waterside vacations (birth to age 6)	0.046	0.018	0.01	1.05	1.01-1.09
Total no. waterside vacations (ages 6-7)	−0.026	0.036	0.47	0.97	0.91-1.04
Total no. days on waterside vacations (birth to age 6)	0.002	0.001	0.23	1.00	1.00-1.01
Total no. days on waterside vacations (ages 6-7)	−0.001	0.004	0.70	1.00	0.99-1.01
Total UV exposure on waterside vacations (birth to age 6)	0.000	0.000	0.27	1.00	1.00-1.001
Total UV exposure on waterside vacations (ages 6-7)	0.000	0.001	0.66	1.00	1.00-1.001
Total no. nonwaterside vacations (birth to age 6)	0.013	0.010	0.19	1.01	0.99-1.03
Total no. nonwaterside vacations (ages 6-7)	0.005	0.015	0.74	1.01	0.98-1.04

NOTE: Colorado children born in 1998 (n = 627). Covariates in models include severe sunburn; nonsevere sunburn; average number of hours in midday sun; frequency of use of sunscreen, hat, and clothes; sun sensitivity; facial freckling; gender; base skin color; eye color; Hispanic ethnicity; and income.
* Multiplicative factor by which nevus counts <2 mm change for every 1-unit increase in predictor.
† 95% CI around antilog(b).

Table 6. Comparison of vacation indicators in predicting ≥1 nevi ≥2 mm at age 7 adjusted for demographic, phenotypic, and sun exposure variables

Vacation indicator	log (OR)	SE	*P*	OR (95% CI)
Total no. waterside vacations (birth to age 6)	0.029	0.062	0.64	1.03 (0.91-1.16)
Total no. waterside vacations (ages 6-7)	0.086	0.126	0.50	1.09 (0.85-1.40)
Total no. days on waterside vacations (birth to age 6)	0.007	0.006	0.23	1.01 (1.00-1.02)
Total no. days on waterside vacations (ages 6-7)	−0.005	0.013	0.69	1.00 (0.97-1.02)
Total UV exposure on waterside vacations (birth to age 6)	0.001	0.001	0.27	1.00 (1.00-1.004)
Total UV exposure on waterside vacations (ages 6-7)	0.000	0.003	0.90	1.00 (0.99-1.005)
Total no. nonwaterside vacations (birth to age 6)	0.002	0.032	0.94	1.00 (0.94-1.07)
Total no. nonwaterside vacations (ages 6-7)	0.075	0.053	0.15	1.08 (0.97-1.20)

NOTE: Colorado children born in 1998 (n = 627). Covariates in models include severe sunburn; nonsevere sunburn; average number of hours in midday sun; frequency of use of sunscreen, hat, and clothes; sun sensitivity; facial freckling; gender; base skin color; eye color; Hispanic ethnicity; and income.

covariates. The anti-log transformations of the regression coefficients [antilog(b)] describe the multiplicative factors by which nevi <2 mm change per 1-unit increase in each predictor. Thus, each additional waterside vacation from birth to age 6 increased the nevus counts by a factor of 1.05, a 5% increase in nevi. Waterside vacations between ages 6 and 7 were unrelated to nevus counts at age 7, and this lack of relationship persisted when vacations before age 6 were removed from the model. Other statistically significant predictors of nevus counts include male gender (19% increase) and Hispanic ethnicity (35% decrease). The results of the regression analyses predicting density of nevi <2 mm were parallel for variables representing waterside vacations. However, two additional variables significantly predicted nevus density: history of any severe sunburn before age 7 (P < 0.04) and any facial freckling (P = 0.001; data not shown).

Table 4 reports the results of the multiple logistic regression predicting the presence of nevi ≥2 mm. Waterside vacations were not related to nevi ≥2 mm, neither before age 6 nor ages 6 to 7. Significant relationships were found for facial freckling [odds ratio (OR), 1.72], male gender (OR, 1.64), and Hispanic ethnicity (OR, 0.45).

Table 5 compares regression coefficients (b) and antilog transformations [antilog(b)] for four vacation variables separated into two age periods (birth to age 6 and ages 6-7). All covariates shown in Table 3 were included in these regression models. Of these vacation indicators, total number of waterside vacations up to age 6 was the only statistically significant predictor of nevus counts at age 7. Similar analyses were conducted for nevi ≥2 mm (Table 6). None of the vacation variables significantly predicted the presence of larger nevi (all P > 0.15).

Discussion

This study found that the number of waterside vacations from birth to age 6 is a significant predictor of the number of small nevi (<2 mm) among Colorado children at age 7. Recent vacations (within the past year) were found to have no effect on nevi <2 mm. Our findings indicate that this relationship is independent of acute sun exposure resulting in sunburns, routine (daily) exposure, and use of sun protection. Each vacation was associated with a 5% increase in nevi after controlling for other factors. The number of days on vacation and the related total calculated UVD across vacations had weaker and nonstatistically significant effects on nevus count. Whereas waterside vacations were found to significantly affect small nevus count, nonwaterside vacations did not. This is presumed to be because the amount of skin exposed and amount of time spent in the sun is greater for waterside locations. In contrast, we found no evidence that waterside vacations were related to the development of larger (≥2 mm) nevi. A significant univariate relationship between nonwaterside vacations ages 6 to 7 and larger nevi was not sustained in multivariate analysis. Autier et al. also found that UV-intense vacations increased the prevalence of small nevi but not large nevi, although they defined large nevi as those ≥5 mm (22). Several studies have found a relationship between sunburns and nevi (17, 18, 20-22), but in the present analysis this relationship became nonsignificant after controlling for the set of phenotypic, demographic, and sun exposure variables.

The finding that waterside vacations taken at least 1 year before the time of the skin exam significantly predicted nevus counts, whereas waterside vacations taken subsequently did not predict nevus counts has at least two possible explanations. First, it suggests a time lag of at least 1 year for the effects of sun exposure during waterside vacations to result in new nevi (33). Alternatively, the lack of a relationship between vacations taken from ages 6 to 7 and nevus development could be due to a physiologic change with age. That is, it is plausible that children's melanocytes become less susceptible to the intense sun exposure received on waterside vacations as they age and that after age 6 the effect of waterside vacations on nevus development becomes undetectable. Continuing to follow this cohort may help to distinguish between these two explanations and may help to identify developmental periods of greater or lesser susceptibility to intense sun exposure.

An interesting and potentially important finding is that the number of days spent on waterside vacations and the total UVD received on those vacations appeared to have no significant effect on nevus count, whereas the occurrence of the vacation had an effect. We offer the interpretation that a threshold of UV exposure is received relatively early during vacations of this nature; thus, vacations of, for example, 3 days are equivalent to vacations of 10 days in terms of their effect on nevus development. Studies using personal dosimeters on vacations might help to understand this potential threshold effect.

Previous studies have estimated that about two-thirds of the variation in nevus counts is due to genetic factors and that the remaining variation is due to environmental exposure (12, 13). Vacation exposure is one of many environmental exposures that are likely to affect nevus development. We did not find evidence for an effect of number of hours spent outside in midday during the summer, which was somewhat unexpected. Several previous studies have found an effect for daily sun exposure (17, 24, 27), but some studies have not (25). Our measure of daily exposure was relatively crude, involving estimates by parents of the amount of time the child is usually outdoors between 11 a.m. and 3 p.m. in the summer. In univariate analysis, we found a statistically significant association between frequency of hat use and nevi, but this dipped below statistical significance in multivariate analysis. In a previous article, we reported that nevi are most dense on the face in our study population (20); thus, it reasonable that hat use (which protects only the face) could have an effect that is large enough to be seen in total body nevus counts. Previous studies have reported mixed results on the relationship between hat use and nevi (26, 28). We also found that Hispanic ethnicity and gender were significantly related to nevus counts. These variables could have both cultural and genetic components. With respect to Hispanic ethnicity, the negative relationship we found is most likely due to the generally darker skin (genetically determined) found in the Colorado Hispanic population, which is protective for both nevus development and melanoma (1, 32). With respect to gender, it is possible that boys' behavior leads them to greater sun exposure, which in turn results in nevus development, but it also possible that there is a genetically determined propensity to develop more nevi among males. Males have higher rates of melanoma than females in North America (1). Altogether, the variables included in our analysis of nevi <2 mm predicted only 9% of the total variance.

The participants in the present study spent their waterside vacations predominantly within North America, most commonly at locations in Colorado, California, and Florida. About 12% of waterside vacations were outside the United States, and those were usually to Mexico or another location in the Gulf of Mexico. The results of this study are similar to Northern European studies that evaluated the effects of vacations to the Mediterranean (17, 22, 24, 25, 28). Our study may also shed some light on the relationship between socioeconomic status and melanoma. A consistent finding of epidemiologic studies has been that higher socioeconomic status is associated with melanoma risk (35). Our results fit this pattern, as children whose parents had higher education and higher income were more likely to have taken waterside vacations; however, we did not find a relationship between socioeconomic variables and nevi at this young age.

A limitation of this study is that we did not collect specific behavioral information related to waterside vacations, including amount of time spent outside, type of clothing worn, or other sun protection measures used. We also did not ask specifically about sunburns received on these vacations, so we cannot determine whether the experience of sunburns, which studies indicate is related to nevus development and probably stimulates nevus development (17, 18, 20-25), is in the pathway between waterside vacations and nevus development. Our results show the effect of vacations on total nevus accumulation by age 7, and aside from indicating that there is a time lag of at least 1 year between vacation exposure and resultant nevus development, we were not able to speak to the issue of specific age intervals during which children might be more or less vulnerable to intense sun exposure. Such an analysis would require quantification of vacation exposure and nevus counts at yearly (or more frequent) intervals, which was not available for these 7-year-old children.

Our findings concerning vacation exposure, history of sunburns, and use of sun protection are based on parent report, which is subject to recall bias. Additionally, it is possible that sunburns may have been underreported and sun protection may have been overreported due to social desirability, that is, the desire to give answers that are perceived to reflect well on the respondent and this may have varied by study group. In analyses not reported in this article, we found that intervention group assignment was not related to vacations or nevi. However, the group that received the behavioral intervention may have been subject to more social desirability bias. We expect that this bias would pertain to use of sun protection behaviors (sunscreen, etc.) and reports of sunburns, but not to the report of vacations, as the intervention did not make recommendations about vacation locations. The overall effect of this bias, if present, would be to attenuate the relationships of sun protection and sunburns with nevus counts. Our attempt to control for sun protection behaviors and sunburns when assessing the effect of vacations on nevi may therefore not have fully accounted for the variance in nevi attributable to these factors. However, the addition of all the covariates in the model had minimal effect on the relationship between vacation exposure and nevi, suggesting that this relationship is largely independent of other factors.

In our interviews, we only recorded detailed information on the first seven vacations reported, including the location, length of time, and season of travel. However, 33% of participants reported taking more than seven vacations between child's birth and age 6, and 6% reported more than seven vacations in the year between ages 6 and 7. Also, although the UVD data take into account average weather and cloud cover over the course of the season, the data do not take into account the actual weather at the specific time of each vacation. There may also be some misclassification of waterside vacations, particularly if a family took a vacation in which they spent significant amounts of time around a swimming pool in a location not known for water activities. Each of these limitations would most likely attenuate relationships between vacations and nevi rather than overestimate the relationships.

This study has several notable strengths. It is one of the few large longitudinal cohort studies of nevus development in children; thus, it was possible for us to prospectively assess the effect of our main predictor variable (vacation exposure) on nevus count and to uncover evidence of a possible time lag between sun exposure and nevus development. It is the only study to date reporting the influence of vacations on nevus development in North America. Further, our study has shown high reliability of our skin examiners' nevus counts of children.

Our results suggest that, after controlling for sunburns, vacations impart more nevus risk than routine daily sun exposure received at home and that risk is conveyed on waterside vacations regardless of usual sun protection practices. Thus, parents should be aware of the effect that vacations may have on their children's risk for developing melanoma as adults and they should be cautious about selection of vacation locations. Because both parent education and income were associated with greater frequency of waterside vacations, children of higher socioeconomic status may be at greater risk in this respect.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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