

Original Investigation

Association Between Eczema and Stature in 9 US Population-Based Studies

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IMPORTANCE Atopic dermatitis (eczema) is a chronic inflammatory disorder that is associated with other chronic diseases (eg, asthma), major quality-of-life impairment, sleep disturbance, and the use of potent topical and sometimes systemic corticosteroids, all of which might affect growth in childhood and adolescence. However, previous smaller-scale studies found conflicting results.

OBJECTIVE To determine whether eczema is associated with short stature.

DESIGN, SETTING, AND PARTICIPANTS We used data from 9 US population-based studies, including the National Survey of Children's Health (2003-2004 and 2007-2008), National Health Interview Survey (children's health, 2008-2012; adult health, 2010 and 2012), and National Health and Nutrition Examination Survey (2003-2004 and 2005-2006). Participants included 264 326 children and adolescents and 83 511 adults.

EXPOSURE History of eczema.

MAIN OUTCOMES AND MEASURES Percentiles of height for age and sex in children and height in adults. We constructed multivariate survey linear or logistic regression models for individual studies with Box-Cox transformed or dichotomized height, respectively. Pooled analyses used generalized linear mixed models.

RESULTS Overall, eczema was not associated with significant differences of height (continuous or <5th or <25th percentiles) in any of the studies or in the pooled analyses. We found a significant interaction by age, such that eczema was associated with shorter stature at 12 to 13 but not 14 to 15 or 16 to 17 years of age or in adulthood. Moderate to severe eczema was associated with shorter stature (continuous and <25th percentile). In particular, short stature (<5th percentile) was associated with eczema only when accompanied by an indicator of insufficient sleep (ie, 0 to 3 nights of sufficient sleep per week) (1.3% of children with eczema) but was not associated with asthma, hay fever, or use of prescription medication. The interaction between eczema and insufficient sleep remained significant at 10 to 11 years of age ($P = .003$) but not at other ages ($P > .08$ for all).

CONCLUSIONS AND RELEVANCE Eczema is not associated with short stature overall. However, a small subset of children and adolescents with severe eczema accompanied by prominent insufficient sleep may have potentially reversible vertical growth impairment.

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Atopic dermatitis (AD) or eczema is a chronic inflammatory skin disorder that affects approximately 10% of children¹ and adults² in the United States. Eczema is associated with intense itch, fatigue, sleep disturbance,² and a number of comorbid medical disorders, including asthma, hay fever, food allergy,³ recurrent ear infections, visual and dental health problems,³ cutaneous and extracutaneous infections,⁴ mental health comorbidity,⁵ injuries requiring medical attention,⁶ and epilepsy.⁷

Eczema has a number of sequelae that may have a negative effect on vertical growth during childhood and adolescence, such as sleep impairment, chronic inflammation, treatment with systemic corticosteroids, and multiple comorbid chronic medical conditions. Some studies⁸⁻¹⁰ previously demonstrated that children with eczema have significantly shorter stature than those without eczema. However, another study¹¹ found no association between eczema and stature. Some of these studies had smaller sample sizes that limited the ability to perform subset analyses and thereby identify the major disease factors that might drive short stature. Sleep disturbances secondary to eczema are of particular interest because growth hormone secretion is highly regulated by normal sleep architecture.¹²⁻¹⁴ Patients with eczema have high rates of fatigue and sleep disturbance, which are major predictors of overall quality of life.¹⁵ We hypothesized that childhood eczema, particularly with greater severity and more sleep impairment, is associated with shorter stature. The present study analyzed data from 9 different large-scale studies to determine whether eczema is associated with short stature.

Methods

Study Sources

After approval by Northwestern University's institutional review board, deidentified data were assessed from the following studies: the National Health Interview Survey (NHIS) (annually in 2008-2012 for children's health and 2010 and 2012 for adult health), the 2003-2004 and 2007-2008 National Survey of Children's Health (NSCH), and the 2003-2004 and 2005-2006 National Health and Nutrition Examination Survey (NHANES). Informed consent was obtained for each study as per protocol. The characteristics of these studies are summarized in eTable 1 in the Supplement. Using data from the US Census Bureau, sample weights were created for each study by their sponsors, which factored age, sex, race, ethnicity, household size, and educational attainment of the most educated household member using a multistage area probability sampling design. These sample weights are needed to provide nationally representative prevalence estimates for each state's population of noninstitutionalized adults. All frequency data are presented as raw values, whereas prevalence estimates reflect this complex weighting.

Statistical Analysis

All data processing and statistical analysis were performed using commercially available software (SAS, version 9.4; SAS

Institute, Inc). The frequency of missing values is presented in eTable 2 in the Supplement. We performed complete data analysis for all variables; that is, participants with missing data were excluded, except for the following 4 exceptions for which the missing values included more than 5% of respondents: household income in the 2003-2004 and 2007-2008 NSCH and height in the 2003-2004 and 2005-2006 NHANES. Therefore, we used the multiple imputation of missing household income levels for the 2003-2004 NSCH¹⁶ and the 2007-2008 NSCH¹⁷ that were generated by the National Center for Health Statistics. The National Center for Health Statistics previously evaluated the nonresponse rates for the NSCH and found minimal or no response bias for multiple questions.¹⁸ Analysis of the pattern of missing values for height in the NHANES revealed that missing values were more likely in children aged 2 to 9 years and in respondents from households with 1 person, but we found no major differences across sex, race/ethnicity, household income, or history of eczema, asthma, or hay fever. Therefore, sensitivity analyses that excluded children aged 2 to 9 years and respondents from households with 1 person were performed.

We performed outlier detection for height and excluded the outliers. All heights were standardized to inches, and pediatric heights were converted into percentiles of height for age and sex using the growth charts from the Centers for Disease Control and Prevention,¹⁹ termed *height percentiles* throughout this report. Height percentiles were transformed using the Box-Cox family of power transformations⁴⁰ to approach normality of distribution and constancy of error variance. For models of pediatric height percentiles and adult height, multivariate linear regression models were constructed for individual studies using commercially available software (SURVEY Procedures; SAS Institute, Inc) that accounted for the surveys' complex weighting factors. The dependent variables consisted of transformed height percentiles in children and adolescents and height in adults, and the independent variables included history of eczema and eczema severity. Coefficients from regression models should be interpreted with caution because the transformed height variables are not the same scale as the original raw variables. Furthermore, Box-Cox transformations are nonlinear; thus, reverse transformation of coefficients is not possible. Therefore, coefficients should be interpreted as measures of overall association by their direction (positive or negative) and significance. Because similar results were found in models of untransformed variables, only data for transformed variables are shown.

For models of short stature, pediatric height percentiles were dichotomized (<5th or <25th percentile). In addition, adult heights were divided empirically into less than the 5th or less than the 25th percentile by combining 1 or 5 vigintiles (20 groups). Again, multivariate logistic regression models were constructed for dichotomized percentiles in individual studies using software (SURVEY Procedures) that accounted for the surveys' complex weighting factors. In addition, generalized linear mixed models with identity (height percentiles) or logit (<5th or <25th percentile) link function were constructed for pooled analysis of all studies that included a random effect for the individual study (PROC

GLIMMIX; SAS Institute, Inc). The complex weighting factors for all studies could not be combined given the varied sampling and study designs and were therefore not included in the generalized linear mixed models. Multivariate models included a history of or current eczema, asthma, and hay fever; age; race/ethnicity; household income; highest level of education in the household; US birthplace; number of persons in the home; use of prescription medication; and maternal/paternal height when available. We estimated least squares means, adjusted odds ratios, and 95% CIs. Our a priori hypothesis was that sleep disturbance in eczema is associated with growth retardation. The 2003-2004 and 2007-2008 NSCH assessed the number of nights per week with sufficient sleep. However, the distribution of this variable was bimodal and highly skewed; therefore, it was dichotomized into 0 to 3 vs 4 to 7 nights of sufficient sleep, similar to a previous study.³ The dichotomized variable for nights of sufficient sleep and a statistical interaction term between sufficient sleep and a history of eczema were included as covariates. Interactions were also tested between eczema and a history of asthma and/or hay fever or use of prescription medication. Estimates of effect size for significant interactions between 2 variables were conducted for the levels of one variable at a fixed level of the other variable. Least squares means and adjusted odds ratios (95% CIs) were estimated for each combination of factors included in the interaction effects.

Results

Prevalence of Eczema and Other Atopic Disorders

We collected data on 264 326 children and adolescents and 83 511 adults, representing all age, sex, racial/ethnic, household educational attainment, and household income groups. The pooled US prevalence of eczema in childhood was 11.4% (95% CI, 11.3%-11.5%); in adults, it was 8.8% (95% CI, 8.6%-9.0%). Among the children with eczema, 23.0% (95% CI, 22.5%-23.5%) had a history of asthma and 31.9% (95% CI, 31.4%-32.4%) had hay fever and/or respiratory allergies; 13.1% (95% CI, 12.9%-13.4%) of adults with eczema had a history of asthma and 33.2% (95% CI, 31.4%-34.9%) had hay fever and/or respiratory allergies.

In generalized linear mixed models that controlled for random effects for different studies, prevalence of eczema was significantly associated with female sex, higher household income, more people in the household, a higher level of household educational attainment, and US birthplace in children and adults (eTable 3 in the Supplement). Eczema prevalence was significantly lower in Hispanic and Asian children and adults but significantly higher in those who self-identified as multi-racial or race other than Hispanic or Asian. In contrast, eczema prevalence was significantly higher in black children but lower in black adults.

Association Between Height Percentiles and Eczema

To model height percentiles across studies that had different levels of variance and skew, we performed Box-Cox transformations for pediatric height percentiles ($\lambda = 0.50$) and adult

height ($\lambda = -0.75$). Eczema was not associated with significant differences of transformed height percentiles in any of the 8 studies of children and adolescents (survey linear regression) (Figure 1). Furthermore, we found no significant association between eczema and height percentiles in the pooled analysis using generalized linear mixed models of all 8 data sets ($\beta = -0.002$ [95% CI, -0.008 to -0.004]; $P = .44$).

Given that vertical growth and eczema activity may vary at different ages, generalized linear mixed models including 2 studies of children and adolescents aged 0 to 17 years (2003-2004 NSCH and 2005-2006 NHANES), 1 study of adolescents aged 10 to 17 years (2007-2008 NSCH), and 5 studies of adolescents aged 12 to 17 years (NHIS for 2008-2012) were stratified by 2-year age intervals. Least squares mean height percentiles were significantly lower at ages 4 to 5 and 12 to 13 years, higher at ages 6 to 7 and 8 to 9 years, and not different at ages 10 to 11, 14 to 15, or 16 to 17 years (eFigure in the Supplement). Finally, eczema was not associated with significant differences in any of the 4 adult studies using transformed height distributions (Figure 1). Similar results were found in sensitivity analyses of the NHANES data that excluded children aged 2 to 9 years and participants from a household with 1 person.

Association Between Short Stature and Eczema

To determine whether a subset of patients with eczema were at higher risk for very short stature, we constructed survey logistic regression models for each of the 8 pediatric and 4 adult studies. We found no significantly different odds of being at less than the 5th or less than the 25th percentile in people with eczema in any of the 12 studies, suggesting that overall eczema is not associated with very short stature (Table 1).

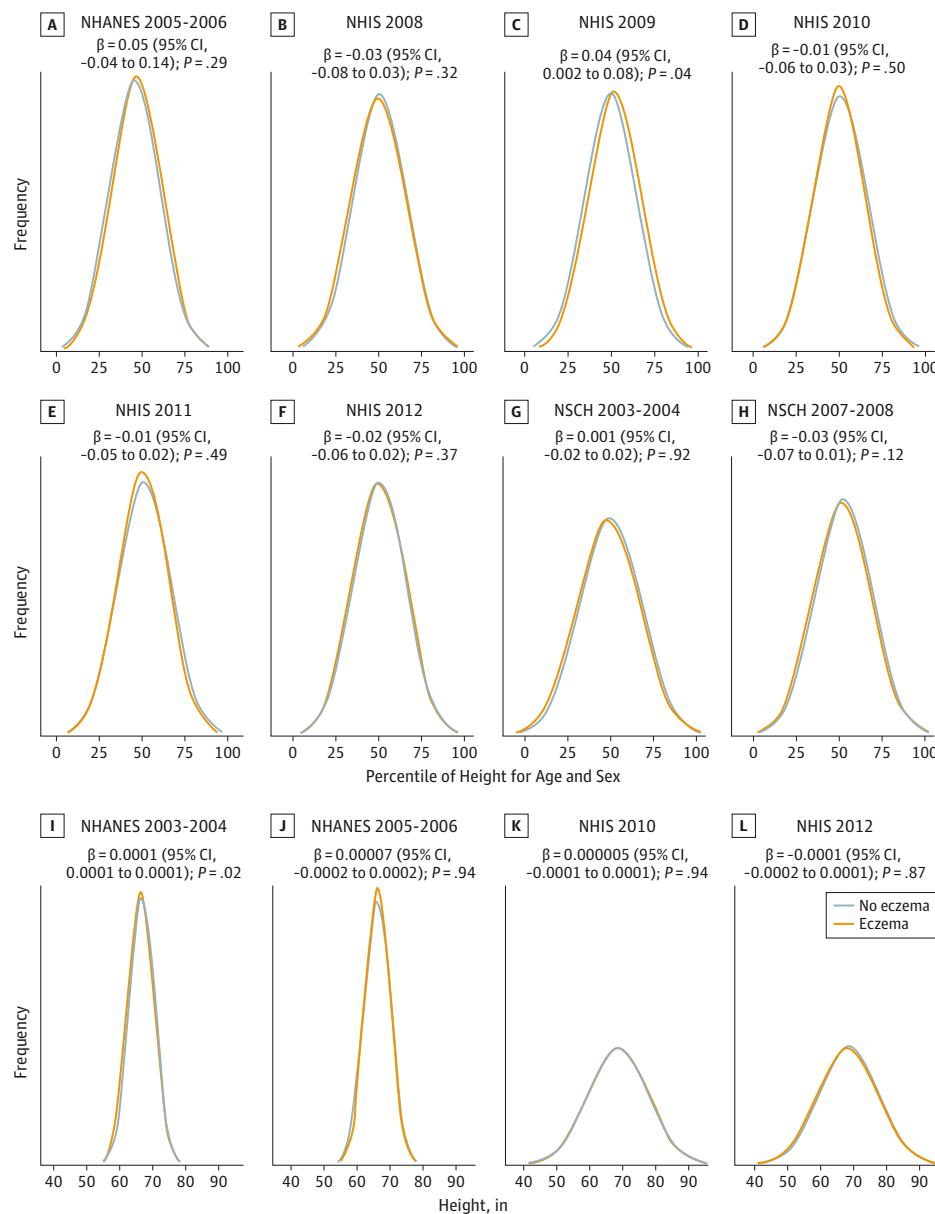
Association Between Moderate to Severe Eczema and Shorter Stature

The 2007-2008 NSCH assessed for self-reported eczema severity in those children and adolescents who were reported to have eczema. The associations²⁰ and comorbidities^{3,21} of moderate to severe eczema from this cohort were described previously. Moderate to severe eczema was associated with significantly lower transformed height percentiles compared with mild disease ($\beta = -0.07$ [95% CI, -0.12 to -0.02]; $P = .004$) (Figure 2). In contrast, mild eczema was not associated with lower height percentiles compared with no eczema ($\beta = -0.001$ [95% CI, -0.03 to 0.03]; $P = .95$). Moderate ($\beta = 2.06$ [95% CI, 1.28 - 3.33]; $P = .003$) and severe ($\beta = 2.29$ [95% CI, 1.17 - 4.48]; $P = .02$) eczema were associated with significantly higher odds of having less than 25th but not less than the 5th height percentiles (Table 2).

Association Among Eczema, Sleep Disturbance, and Shorter Stature

Several measures of sleep disturbance were reported in different studies. The 2003-2004 and 2007-2008 NSCH assessed for the number of nights with sufficient sleep, whereas the 2012 NHIS assessed for fatigue, daytime sleepiness, and insomnia in children. Overall, we found no significant interaction between eczema and insufficient sleep as predictors of height per-

Figure 1. Association Between History of Eczema and Height Percentiles



Survey linear regression models were constructed with Box-Cox-transformed percentiles of height for age and sex in children and adolescents and for height in adults as the dependent variables using a normal link function. The independent variable was history of eczema. Multivariate models included history of or current asthma, history of or current hay fever, age, race/ethnicity, household income, highest level of educational attainment in the household, US birthplace, number of persons in the home, and use of prescription medication. Least squares means (β values), 95% CIs, and P values are presented for each study. A, National Health and Nutrition Examination Survey (NHANES) 2005-2006 in children and adolescents. B, National Health Interview Survey (NHIS) 2008 in children and adolescents. C, NHIS 2009 in children and adolescents. D, NHIS 2010 in children and adolescents. E, NHIS 2011 in children and adolescents. F, NHIS 2012 in children and adolescents. G, National Survey of Children's Health (NSCH) 2003-2004 in children and adolescents. H, NSCH 2007-2008 in children and adolescents. I, NHANES 2003-2004 in adults. J, NHANES 2005-2006 in adults. K, NHIS 2010 in adults. L, NHIS 2012 in adults.

centiles ($P = .47$) (Figure 2B). However, we found a significant interaction between eczema and nights of sufficient sleep, such that adolescents with eczema and 0 to 3 nights of sufficient sleep per week had significantly higher odds of less than the fifth height percentiles (Table 3). Only 1.3% of children with eczema had 0 to 3 nights of sufficient sleep and short stature, suggesting that only a small fraction of children with eczema are at higher risk for short stature. Furthermore, this interaction remained significant only at ages 10 to 11 years ($P = .003$) and not at other ages ($P > .08$ for all), suggesting that the association may be reversible. We found no significant associations between nights of insufficient sleep and having less than 25th height percentiles. Also, we found no significant interactions of eczema with fatigue, daytime sleepiness, or insomnia

as predictors of overall height percentiles, less than the 5th height percentile, or less than the 25th height percentile ($P \geq .15$). Finally, we found no significant interactions between eczema and history of asthma and/or hay fever ($P = .44$) or between eczema and use of prescription medication ($P = .41$).

Association Between Parental and Child Stature in Relation to Eczema

The NHIS from 2008 through 2012 assessed for height in other members of the child's household, including the mother and father (26 283 parents [22.5% of those cohorts]). As expected, pediatric height percentiles were significantly associated with maternal height (survey linear regression; $\beta = 0.04$ [95% CI, 0.03-0.04]; $P < .001$) and paternal height

Table 1. Association Between Eczema and Short Stature^a

Percentile of Height for Age by Study	No Eczema		Eczema			P Value
	Frequency, No. of Participants	Prevalence, % (95% CI)	Frequency, No. of Participants	Prevalence, % (95% CI)	AOR (95% CI)	
Children and Adolescents (n = 264 326)						
NSCH 2003-2004 ^b						
<5th	4031	11.2 (10.6-11.8)	390	10.9 (9.1-12.7)	0.91 (0.72-1.14)	.39
≥5th	39 316	88.8 (88.2-89.4)	3570	89.1 (87.3-90.9)	1 [Reference]	NA
<25th	10 203	26.2 (25.4-26.9)	1021	27.4 (24.9-29.8)	1.00 (0.86-1.16)	.99
≥25th	33 144	73.8 (73.1-74.6)	2939	72.6 (70.2-75.1)	1 [Reference]	NA
NSCH 2007-2008 ^b						
<5th	3869	11.6 (10.7-12.4)	499	12.2 (10.0-14.3)	1.34 (0.97-1.86)	.08
≥5th	36 414	88.4 (87.6-89.3)	4555	87.8 (85.7-90.0)	1 [Reference]	NA
<25th	9845	27.8 (26.6-28.9)	1191	27.3 (24.1-30.5)	1.11 (0.87-1.43)	.40
≥25th	30 438	72.2 (71.1-73.4)	3364	72.7 (69.5-75.9)	1 [Reference]	NA
NHIS 2008 ^c						
<5th	138	5.2 (4.2-6.3)	17	8.2 (3.9-12.5)	1.78 (0.86-3.70)	.12
≥5th	2437	94.8 (93.7-95.8)	231	91.8 (87.5-96.1)	1 [Reference]	NA
<25th	662	24.4 (22.3-26.4)	74	29.0 (22.0-36.0)	1.20 (0.79-1.82)	.40
≥25th	1913	75.6 (73.6-77.7)	174	71.0 (64.0-78.0)	1 [Reference]	NA
NHIS 2009 ^c						
<5th	192	5.7 (4.5-6.8)	15	4.5 (1.7-7.4)	0.98 (0.50-1.93)	.96
≥5th	3091	94.3 (93.2-95.5)	294	95.5 (92.6-98.3)	1 [Reference]	NA
<25th	881	25.0 (23.0-27.1)	69	18.4 (13.3-23.5)	0.74 (0.50-1.09)	.13
≥25th	2402	75.0 (72.9-77.0)	240	81.6 (76.5-86.7)	1 [Reference]	NA
NHIS 2010 ^c						
<5th	211	5.7 (4.7-6.6)	19	5.4 (2.5-8.3)	0.88 (0.47-1.63)	.67
≥5th	3241	94.3 (93.4-95.3)	345	94.6 (91.7-97.5)	1 [Reference]	NA
<25th	7087	25.3 (24.7-25.9)	700	23.5 (21.6-25.4)	1.06 (0.73-1.53)	.76
≥25th	18 781	74.7 (74.1-75.3)	2074	76.5 (74.6-78.4)	1 [Reference]	NA
NHIS 2011 ^b						
<5th	209	5.8 (4.8-6.7)	17	5.2 (2.1-8.3)	0.84 (0.41-1.73)	.64
≥5th	3342	94.2 (93.3-95.2)	414	94.8 (91.7-97.9)	1 [Reference]	NA
<25th	891	24.6 (22.8-26.3)	106	24.1 (19.0-29.2)	0.86 (0.62-1.20)	.37
≥25th	2660	75.4 (73.7-77.2)	325	75.9 (70.8-81.0)	1 [Reference]	NA
NHIS 2012 ^b						
<5th	231	6.1 (5.1-7.1)	24	7.0 (3.5-10.4)	1.23 (0.69-2.20)	.49
≥5th	3507	93.9 (92.9-94.9)	368	93.0 (89.6-96.5)	1 [Reference]	NA
<25th	943	24.5 (22.7-26.1)	107	28.0 (22.2-33.8)	1.28 (0.91-1.80)	.16
≥25th	2795	75.5 (73.8-77.3)	285	72.0 (66.2-77.8)	1 [Reference]	NA
NHANES 2005-2006						
<5th	101	8.4 (6.2-10.6)	16	12.6 (5.4-19.9)	1.39 (0.72-2.69)	.33
≥5th	946	91.6 (89.4-93.8)	149	87.4 (80.1-94.6)	1 [Reference]	NA
<25th	383	33.6 (29.7-37.5)	55	31.2 (22.0-40.4)	0.83 (0.51-1.35)	.45
≥25th	664	66.4 (62.5-70.3)	110	68.8 (59.6-78.0)	1 [Reference]	NA
Adults (n = 83 511) ^d						
NHIS 2010						
<5th	1178	4.2 (3.9-4.5)	128	4.1 (3.2-4.9)	0.97 (0.73-1.28)	.80
≥5th	23 320	95.8 (95.5-96.1)	2513	95.9 (95.1-96.8)	1 [Reference]	NA
<25th	7679	28.4 (27.8-29.1)	873	29.6 (27.5-31.6)	0.93 (0.81-1.06)	.28
≥25th	16 819	71.6 (70.9-72.2)	1768	70.4 (68.4-72.5)	1 [Reference]	NA
NHIS 2012						
<5th	1495	4.0 (3.8-4.3)	113	4.0 (3.0-4.9)	0.79 (0.59-1.05)	.11
≥5th	30 528	96.0 (95.7-96.2)	2477	96.0 (95.1-97.0)	1 [Reference]	NA

(continued)

Table 1. Association Between Eczema and Short Stature^a (continued)

Percentile of Height for Age by Study	No Eczema		Eczema			P Value
	Frequency, No. of Participants	Prevalence, % (95% CI)	Frequency, No. of Participants	Prevalence, % (95% CI)	AOR (95% CI)	
<25th	9879	28.3 (27.6-28.9)	866	32.7 (30.3-35.2)	0.99 (0.86-1.15)	.96
≥25th	22 144	71.7 (71.1-72.4)	1611	67.3 (64.8-69.7)	1 [Reference]	NA
NHANES 2003-2004						
<5th	225	3.1 (2.6-3.6)	61	3.7 (2.6-4.8)	1.11 (0.76-1.62)	.60
≥5th	6360	96.9 (96.4-97.4)	1153	96.3 (95.2-97.4)	1 [Reference]	NA
<25th	1682	23.5 (22.3-24.7)	299	22.1 (19.5-24.6)	0.86 (0.70-1.06)	.15
≥25th	4903	76.5 (75.3-77.7)	854	77.9 (75.4-80.5)	1 [Reference]	NA
NHANES 2005-2006						
<5th	285	4.4 (3.7-5.1)	17	4.0 (1.8-6.2)	0.93 (0.44-1.95)	.85
≥5th	4503	95.6 (94.9-96.3)	308	96.0 (93.8-98.2)	1 [Reference]	NA
<25th	1556	28.6 (27.0-30.2)	89	24.7 (19.2-30.3)	0.64 (0.44-0.95)	.03
≥25th	3232	71.4 (69.8-73.0)	236	75.3 (69.7-80.8)	1 [Reference]	NA

Abbreviations: AOR, adjusted odds ratio; NA, not applicable; NHANES, National Health and Nutrition Examination Survey; NHIS, National Health Interview Survey; NSCH, National Center for Health Statistics.

^a We constructed binary survey logistic regression models with percentile of height for age as the binary dependent variable (<5th vs ≥5th or <25th vs ≥25th) and history of eczema as the binary independent variable. Multivariate models were constructed that included history of or current asthma, history of or current hay fever, age, sex, race/ethnicity, household income, highest level of educational attainment in the household, US birthplace, number of persons in the home, and use of prescription medication (when available). Adjusted ORs (95% CIs) were estimated.

^b Analyses were limited to adolescents aged 10 to 17 years, based on previous

NSCH studies that validated caregiver-reported height in those ages. Heights were converted to percentiles of height for age and sex using growth charts from the Centers for Disease Control and Prevention (CDC).¹⁹

^c Analyses were limited to adolescents aged 12 to 17 years, based on previous NHIS studies that validated caregiver-reported height in those ages. Heights were converted to percentiles of height for age and sex using growth charts from the CDC.¹⁹

^d Analyses included adults aged 18 to 85 years. Percentiles of height were calculated empirically based on the height distribution across all included data sets.

Table 2. Association Between Eczema Severity and Short Stature in Adolescents From the NSCH 2007-2008^a

Percentile of Height for Age	Eczema Severity									
	Mild		Moderate				Severe			
	Frequency, No. of Participants	Prevalence, % (95% CI)	Frequency, No. of Participants	Prevalence, % (95% CI) ^b	AOR (95% CI)	P Value	Frequency, No. of Participants	Prevalence, % (95% CI) ^b	AOR (95% CI)	P Value
<5th	314	10.6 (8.2-13.0)	141	11.6 (7.9-15.3)	1.01 (0.55-1.86)	.98	43	23.4 (12.0-34.8)	1.60 (0.71-3.58)	.26
≥5th	2685	89.4 (87.0-91.8)	1109	88.4 (84.7-92.1)	1 [Reference]	NA	256	76.6 (65.2-88.0)	1 [Reference]	NA
<25th	765	23.4 (19.9-27.0)	337	31.3 (24.5-38.0)	2.06 (1.28-3.33)	.003	87	40.4 (28.3-52.5)	2.29 (1.17-4.48)	.02
≥25th	2234	76.6 (73.0-80.1)	913	68.7 (62.0-75.5)	1 [Reference]	NA	212	59.6 (47.5-71.7)	1 [Reference]	NA

Abbreviations: AOR, adjusted odds ratio; NA, not applicable; NSCH, National Center for Health Statistics.

^a Binary survey logistic regression models were constructed with height (in inches) as the binary dependent variable (<5th vs ≥5th and <25th vs ≥25th percentiles) and history of eczema as the binary independent variable.

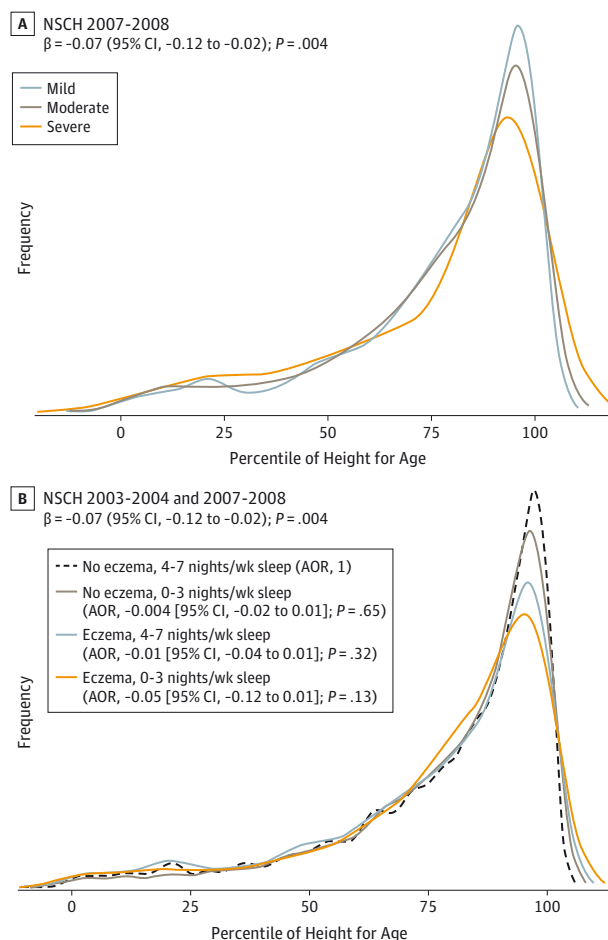
Multivariate models were constructed that included history of or current asthma, history of or current hay fever, age, sex, race/ethnicity, household income, highest level of educational attainment in the household, US birthplace, number of persons in the home, and use of prescription medication. Adjusted ORs (95% CIs) were estimated.

($\beta = 0.03$ [95% CI, 0.02-0.04]; $P < .001$). Parental height was not associated with one's child having eczema (survey logistic regression OR for the mother, 1.02 [95% CI, 0.98-1.06]; $P = .31$; survey logistic regression OR for the father, 1.03 [95% CI, 0.93-1.13]; $P = .63$). Furthermore, we found no interactions between a history of eczema and maternal or paternal height quartiles as predictors of the child's height ($P = .39$ and $P = .43$, respectively), and a history of eczema did not modify the effects of parental height on the child's height ($P \geq .09$ for all).

Discussion

In the present study, we analyzed data from 9 US population-based studies and found that, in general, eczema in childhood or adulthood is not associated with short stature. In a single study that assessed for eczema severity, albeit self-reported, moderate to severe eczema was associated with significantly shorter stature compared with mild disease. In contrast, mild disease was not associated with shorter stature

Figure 2. Association of Moderate to Severe Eczema and Sleep Insufficiency With Lower Height Percentiles



Survey linear regression models were constructed with Box-Cox-transformed percentiles of height for age and sex in adolescents aged 10 to 17 years as the dependent variable using a normal link function. A, National Survey of Children's Health (NSCH) 2007-2008. The dependent variables were eczema severity (moderate to severe vs mild). Least squares mean (β value), 95% CI, and P value are presented. B, NSCH 2003-2004 and 2007-2008. The dependent variables included history of eczema, number of nights with sufficient sleep (0-3 vs 4-7), and an interaction term between them. Multivariate models included history of or current asthma, history of or current hay fever, age, race/ethnicity, household income, highest level of educational attainment in the household, US birthplace, number of persons in the home, and use of prescription medication. AOR indicates adjusted odds ratio.

compared with no eczema. Eczema accompanied by only 0 to 3 nights of sufficient sleep per week was associated with less than the fifth height percentile. This association occurred at ages 10 to 11 years and appeared to reverse at older ages. Finally, eczema did not modify the association between child and parental height. Together, these results suggest that, although eczema is not associated with short stature overall, a small subset of pediatric patients with moderate to severe disease may experience a negative effect on their growth. The association of short stature with eczema and sleep insufficiency at 10 to 11 but not 12 to 13, 14 to 15, or 16 to 17 years of age or in adulthood suggests that any growth impairment that

may occur in adolescence secondary to eczema is related to sleep impairment and probably reversible.

Previous studies found conflicting results about whether eczema is associated with short stature. A previous case-control study of 35 British adults with childhood onset and 35 without AD¹¹ found no significant differences of stature related to a history of AD. Furthermore, growth impairment was not related to body surface area affected, potency of topical corticosteroids used, or comorbid asthma.¹¹ In contrast, an earlier study of 89 British children⁸ found that 10% had standing heights of less than the third percentile, with growth impairment being associated particularly with widespread eczema, comorbid asthma, and use of potent topical corticosteroids. Another study⁹ found that children with lesional body surface area of less than 50% had normal heights, whereas those with lesional body surface area greater than 50% were significantly shorter. However, those studies were unable to generate estimates of risk for short stature in the pediatric and adult population with eczema owing to small sample size and selection bias of being a single referral center for the management of eczema. A recent study of 2372 Korean elementary schoolchildren¹⁰ found that AD, particularly when associated with sleep disturbance, was associated with shorter stature. Similarly, we found that eczema with only 0 to 3 nights of sufficient sleep per week was associated with shorter stature. Together, the results of the present study and the above-mentioned studies suggest that severe eczema accompanied by sleep impairment may contribute to reversible growth impairment in childhood. Distinguishing between the effects of itch per se and sleep disturbances in eczema is difficult. The associations observed for 0 to 3 nights of sufficient sleep per week may represent a distinct subset of patients with AD who have comorbid sleep disturbances (approximately 15% of children with AD) or may be a proxy measure of very severe AD. Either way, self-reported insufficient sleep appears to be a useful approach to identifying those children and adolescents at higher risk for growth impairment. Future studies are needed to determine the particular role of sleep impairment in AD and its effects on stature.

The mechanisms underlying the association between severe eczema and short stature are not fully understood. Our results suggest that the association is largely due to the harmful effects of poor sleep. Growth hormone secretion during sleep plays an important role in vertical growth, and disorders that are associated with impaired sleep, such as obstructive sleep apnea, are associated with short stature.²²⁻²⁵ However, children with eczema have a number of other known risk factors for growth impairment, including use of systemic corticosteroids²⁶ and perhaps topical corticosteroids,²⁷ depression and other psychological comorbidity,^{5,6} and restrictive diets that may result in malnutrition.²⁸ We were not able to control for these risk factors in the present study. In addition, chronic inflammation from eczema per se may contribute toward growth impairment. Previous studies²⁹⁻³¹ found growth impairment in multiple chronic inflammatory diseases, including Crohn disease and hepatitis B and C virus infection. We found no significant effects for history of asthma and/or hay fever or use of prescription medications. Future

Table 3. Association Among Eczema, Insufficient Sleep, and Short Stature in Adolescents From the NSCH 2003-2004 and 2007-2008^a

Eczema	Sufficient Sleep, Nights/wk	Percentiles of Height for Age and Sex					
		≥5th		<5th		AOR (95% CI)	P Value
		Frequency, No. of Participants	Prevalence, % (95% CI)	Frequency, No. of Participants	Prevalence, % (95% CI) ^b		
No	4-7	35 586	88.8 (87.9-89.6)	3714	11.3 (10.4-12.1)	1 [Reference]	NA
No	0-3	5268	90.1 (88.0-92.1)	421	9.9 (7.9-12.0)	0.84 (0.62-1.14)	.26
Yes	4-7	3806	88.2 (86.2-96.1)	480	11.8 (9.8-13.8)	1.26 (0.93-1.70)	.13
Yes	0-3	698	84.2 (76.7-91.6)	68	15.8 (8.4-23.3)	2.22 (1.09-4.53)	.03
		<25th		≥25th		AOR (95% CI)	P Value
		Frequency, No. of Participants	Prevalence, % (95% CI)	Frequency, No. of Participants	Prevalence, % (95% CI) ^b		
No	4-7	29 798	72.8 (71.7-74.0)	9502	27.2 (26.0-28.3)	1 [Reference]	NA
No	0-3	4410	74.4 (71.7-77.1)	1279	25.6 (22.9-28.3)	0.98 (0.79-1.22)	.86
Yes	4-7	3128	72.0 (68.8-75.2)	1158	28.0 (24.8-31.2)	1.10 (0.61-1.41)	.43
Yes	0-3	590	71.9 (64.3-79.5)	176	28.1 (20.5-35.7)	1.55 (0.97-2.48)	.07

Abbreviations: AOR, adjusted odds ratio; NA, not applicable; NSCH, National Center for Health Statistics.

^a Binary survey logistic regression models were constructed with height (in inches) as the binary dependent variable (<5th vs ≥5th and <25th vs ≥25th percentiles) and history of eczema, nights of sufficient sleep per week (0-3 vs 4-7), and an interaction term between them as the binary independent

variables. Multivariate models were constructed that included history of or current asthma, history of or current hay fever, age, sex, race/ethnicity, household income, highest level of educational attainment in the household, US birthplace, number of persons in the home, and use of prescription medication. Adjusted ORs (95% CIs) were estimated at each level of combination for eczema and nights of sleep.

studies are warranted to confirm the association between severe eczema and growth impairment using objective measures of disease severity and to determine the mechanisms thereof.

A recent study of adults from the 2012 NHIS found that sleep disturbance is a major driver of poor overall health status, lost workdays, and increased use of health care services in adults with eczema.¹⁵ Several other studies in children and adults³²⁻³⁶ found that sleep disturbance is one of the most important factors to have a negative effect on health-related quality of life. The present study demonstrates that sleep disturbance may have additional harmful consequences by retarding growth. Together, these studies emphasize the need for more rigorous screening for sleep disturbances in patients with pediatric eczema and for developing safer and more effective interventions aimed at reducing sleep disturbance in childhood eczema. The interaction between eczema and the number of nights of insufficient sleep but not fatigue, daytime sleepiness, or insomnia suggests that nights of sufficient sleep may be a simple and useful patient-reported outcome of chronic sleep disturbance in eczema. Future studies are needed to validate the use of this outcome in eczema.

This study has several strengths, including the 9 different US population-based studies with prospective data collection and a very large, random-sampled, diverse population that allowed for subset analyses and controlling for a large number of potential confounding factors. However,

this study has potential limitations. Eczema history was based on self-report in all studies and was not assessed clinically or verified with any diagnostic testing. However, self-report of eczema using different instruments has been validated and found to have good correlation with results of a clinical examination.^{37,38} Caregiver-reported height was previously validated in the NSCH for children and adolescents 10 years or older.³⁹ None of the studies categorized the type of prescription medications used. Thus, we were not able to control for the use of high-dose topical and/or oral corticosteroids or other specific treatments that may affect stature adversely. Future longitudinal studies with objective measures of eczema severity and height measurement and with assessment of the specific medications used are needed to identify which subset of patients with eczema, if any, is predisposed to short stature.

Conclusions

Childhood eczema is not associated with short stature overall, although severe disease with prominent sleep disturbance is associated with higher odds of short stature in early adolescence. Future studies are warranted to better characterize sleep disturbances and other risk factors and mechanisms of growth impairment in eczema and to determine whether such impairment is reversible.

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Supplementary Online Content

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eTable 1. Study Characteristics

eTable 2. Frequency of Missing Values for Variables Used in the Study

eTable 3. Associations of Eczema in Children and Adults

eFigure. Lack of Association Between History of Eczema and Height-Percentiles at Any Age During Childhood and Adolescence

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Study Characteristics

Study	Size	Age (yr)	Type	Languages	Height assessment
NSCH 2003 – 2004	102,353	0 – 17	Telephone	English Spanish Korean Mandarin Cantonese Vietnamese	Caregiver-report
NSCH 2007 – 2008	91,642	0 – 17	Telephone	English Spanish Korean Mandarin Cantonese Vietnamese	Caregiver-report
NHIS 2008	8,815	0 – 17	Household	English Spanish	Caregiver-report
NHIS 2009	11,156	0 – 17	Household	English Spanish	Caregiver-report
NHIS 2010	11,277	0 – 17	Household	English Spanish	Caregiver-report
NHIS 2010	27,157	18 – 85	Household	English Spanish	Caregiver-report
NHIS 2011	12,850	0 – 17	Household	English Spanish	Caregiver-report
NHIS 2012	13,275	0 – 17	Household	English Spanish	Caregiver-report
NHIS 2012	34,525	18 – 85	Household	English Spanish	Caregiver-report
NHANES 2003 – 2004	10,122	0 – 85	Household interview Health examination	English Spanish	Physical examination
NHANES 2005 – 2006	10,348	0 – 85	Household interview Health examination	English Spanish	Physical examination

NHANES, National Health and Nutrition Examination Survey; NHIS, National Health Interview Survey;

NSCH, National Center for Health Statistics.

eTable 2. Frequency of Missing Values for Variables Used in the Study

Study	Variable	Freq (%)
NSCH 2003 – 2004	Height	1316 (2.7)
	Eczema	176 (0.2)
	Asthma	218 (0.2)
	Hay fever	326 (0.3)
	Nights of sleep	623 (0.6)
	Age	0 (0.0)
	Race/ethnicity	1092 (1.0)
	Sex	80 (0.1)
	Household income	0 (0.0)*
	Highest level of education in the household	432 (0.4)
	US birthplace	959 (0.9)
	Number of persons in the home	13 (0.01)
	Prescription medication use	82 (0.1)
NSCH 2007 – 2008	Height	960 (2.1)
	Eczema	99 (0.1)
	Eczema severity	24 (0.03)
	Nights of sleep	634 (0.7)
	Asthma	117 (0.1)
	Hay fever	187 (0.2)
	Age	0 (0.0)
	Race/ethnicity	1546 (1.7)
	Sex	110 (0.1)
	Household income	0 (0.0)*
	Highest level of education	612 (0.7)
	US birthplace	961 (1.4)
	Number of persons	325 (0.4)
	Prescription medication use	52 (0.1)
NHIS 2008 – 2012	Height	1527 (1.9)
	Eczema	106 (0.1)
	Asthma	109 (0.1)
	Hay fever	196 (0.2)
	Fatigue	5 (0.01)
	Sleepiness	7 (0.01)
	Insomnia	8 (0.01)
	Age	0 (0.0)
	Race/ethnicity	178 (0.2)
	Sex	0 (0.0)
	Household income	4186 (3.6)
	Highest level of education in the household	4436 (3.8)
	US birthplace	46 (0.04)
	Number of persons	4186 (3.6)
	Prescription medication use	21 (0.01)
NHANES 2004 - 2005	Height	1941 (9.9)
	Eczema	10 (0.07)
	Asthma	32 (0.2)
	Hay fever	19 (0.2)
	Age	0 (0.0)
	Race/ethnicity	0 (0.0)

Sex	0	(0.0)
Household income	1048	(2.9)
Highest level of education in the household	162	(0.5)
US birthplace	7	(0.02)
Number of persons	0	(0.0)
Prescription medication use	0	(0.0)

Note: multiple imputation of missing values for household income were used. Missing values were encountered in 9.2% of subjects in the raw datasets.

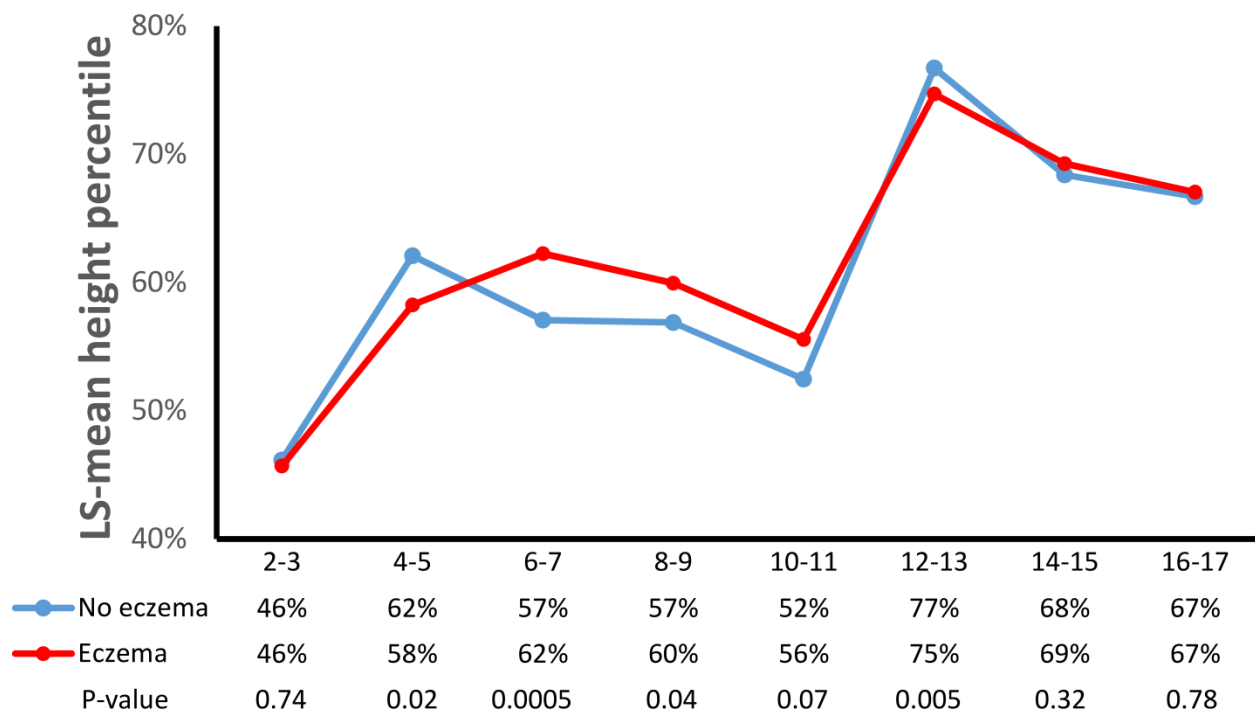
NHANES, National Health and Nutrition Examination Survey; NHIS, National Health Interview Survey; NSCH, National Center for Health Statistics.

eTable 3. Associations of Eczema in Children and Adults

Variable – no. (%)	Children (n=264,326)		Adults (n=83,511)	
	% Prev (95%CI)	Pooled OR (95% CI)	% Prev (95% CI)	Pooled OR (95% CI)
Sex				
Male	11.1 (11.0 – 11.3)	1.00 [ref]	7.5 (7.2 – 7.8)	1.00 [ref]
Female	11.7 (11.5 – 11.8)	1.006 (1.006 – 1.007)	9.9 (9.6 – 10.2)	1.533 (1.533 – 1.534)
Race				
Caucasian	10.4 (10.3 – 10.6)	1.00 [ref]	10.0 (9.7 – 10.3)	1.00 [ref]
Black/African-American	17.3 (16.9 – 17.8)	1.574 (1.573 – 1.574)	7.4 (7.0 – 7.9)	0.713 (0.712 – 0.713)
Hispanic	10.0 (9.7 – 10.3)	0.767 (0.766 – 0.767)	6.1 (5.7 – 6.5)	0.587 (0.587 – 0.588)
Asian	12.1 (11.2 – 13.1)	0.983 (0.982 – 0.985)	7.9 (7.0 – 8.7)	0.832 (0.830 – 0.833)
Multiracial / other	13.6 (13.1 – 14.2)	1.267 (1.266 – 1.269)	13.8 (12.2 – 15.4)	1.035 (1.034 – 1.035)
Household income (% FPL)				
0 – 99	11.7 (11.4 – 12.1)	0.923 (0.923 – 0.924)	8.5 (8.0 – 9.0)	0.737 (0.737 – 0.738)
100 – 299	11.3 (11.0 – 11.6)	0.886 (0.886 – 0.887)	8.3 (7.8 – 8.7)	0.696 (0.696 – 0.696)
300 – 399	11.3 (11.1 – 11.6)	0.948 (0.947 – 0.948)	8.8 (8.4 – 9.3)	0.919 (0.919 – 0.920)
≥ 400	11.8 (11.5 – 12.0)	1.00 [ref]	10.2 (9.8 – 10.6)	1.00 [ref]
No. of people in household				
1	3.2 (0.2 – 7.7)	0.264 (0.261 – 0.268)	9.3 (8.9 – 9.7)	1.570 (1.569 – 1.571)
2	13.2 (12.7 – 13.7)	1.215 (1.214 – 1.217)	9.7 (9.3 – 10.1)	1.511 (1.510 – 1.512)
3	11.9 (11.7 – 12.1)	1.152 (1.151 – 1.152)	8.3 (7.8 – 8.8)	1.289 (1.288 – 1.290)
≥4	11.0 (10.9 – 11.2)	1.00 [ref]	7.6 (7.2 – 8.0)	1.00 [ref]
Highest level of household education				
<High school	8.4 (7.9 – 8.8)	0.668 (0.668 – 0.669)	6.3 (5.7 – 6.8)	0.579 (0.579 – 0.580)
High school or GED	10.1 (9.8 – 10.3)	0.789 (0.789 – 0.790)	7.1 (6.7 – 7.5)	0.623 (0.623 – 0.624)
>High school	11.8 (11.6 – 12.0)	1.00 [ref]	9.9 (9.6 – 10.2)	1.00 [ref]
Birthplace in the US				
No	6.8 (6.3 – 7.3)	0.481 (0.480 – 0.482)	5.8 (5.4 – 6.1)	0.575 (0.575 – 0.576)
Yes	11.6 (11.5 – 11.7)	1.00 [ref]	9.6 (9.4 – 9.8)	1.00 [ref]

Generalized linear models were constructed with history of eczema as the binary dependent variable and socio-demographic factors as the binary/categorical independent variables. Models included a random effect for the study source. Pooled prevalence, OR and 95% CI were estimated. All associations were significant with a P-value <0.0001.

eFigure. Lack of Association Between History of Eczema and Height-Percentiles at Any Age During Childhood and Adolescence



Mixed models were constructed with Box-Cox transformed height-for-age and gender percentiles in children and adolescents as the dependent variable using a normal link function. Models included a random effect for the individual study. The independent variable was history of eczema. Multivariate models included ever or current history of asthma, ever or current history of hay fever, age, Race/ethnicity, household income, highest level of education in the household, US birthplace, number of persons in the home and prescription medication use. Least-squares means (95% CIs) are presented for each study.